UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended: **December 31, 2020**

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from to .

Commission File No.: 001-34705

Codexis, Inc.

(Exact name of registrant as specified in its charter)

Delaware	71-0872999
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
200 Penobscot Drive, Redwood City, California	94063
(Address of principal executive offices)	(Zip Code)

Registrant's telephone number, including area code: (650) 421-8100

Securities Registered Pursuant to Section 12(b) of the A:

Title of Each Class:	Trading Symbols(s):	Name of Each Exchange on which Registered:
Common Stock, par value $0.0001 per share	CDXS	The Nasdaq Global Select Market

Securities Registered Pursuant to Section 12(g) of the Act: None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act.	Yes	☒	No	☐
Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act.	Yes	☐	No	☒
Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days.	Yes	☒	No	☐
Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files).	Yes	☒	No	☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or emerging growth company. See the definitions of "large accelerated filer, "accelerated filer" and "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act:

Large accelerated filer	☒	Accelerated filer	☐	☐
Non-accelerated filer	☐	Smaller reporting company	☐	
		Emerging growth company	☐	☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C.7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☒	Yes	☒	No	☐
Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act).	Yes	☐	No	☒

The aggregate market value of voting and non-voting common stock held by non-affiliates of Codexis as of June 30, 2020 was approximately $655.8 million based upon the closing price reported for such date on the Nasdaq Global Select Market.

As of February 25, 2021, there were 64,400,716 shares of the registrant's Common Stock, par value $0.0001 per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's Definitive Proxy Statement to be filed with the Commission pursuant to Regulation 14A in connection with the registrant's 2021 Annual Meeting of Stockholders (the "Proxy Statement"), to be filed subsequent to the date hereof, are incorporated by reference into Part III of this Report. Such Definitive Proxy Statement will be filed with the Securities and Exchange Commission not later than 120 days after the conclusion of the registrant's fiscal year ended December 31, 2020. Except with respect to information specifically incorporated by reference in this Form 10-K, the Proxy Statement is not deemed to be filed as part of this Form 10-K.

Codexis, Inc.
Annual Report on Form 10-K
For The Year Ended December 31, 2020

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

The following discussion and analysis should be read in conjunction with our audited Consolidated Financial Statements and the related Notes that appear elsewhere in this Annual Report on Form 10-K. This Annual Report on Form 10-K contains "forward-looking statements" within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended ("the Exchange Act"), particularly in Part I, Item 1: "Business," Part I, Item 1A: "Risk Factors" and Part 2, Item 7: "Management's Discussion and Analysis of Financial Condition and Results of Operations." These statements are often identified by the use of words such as "may," "will," "expect," "believe," "anticipate," "intend," "could," "should," "estimate" or "continue," and similar expressions or variations. All statements other than statements of historical fact could be deemed forward-looking, including, but not limited to: any projections of financial information or performance; any statements about historical results that may suggest trends for our business; any statements of the plans, strategies, and objectives of management for future operations; any statements of expectation or belief regarding future events, technology developments, our products and product candidates, product sales, revenues, expenses, liquidity, cash flow, market growth rates or enforceability of our intellectual property rights and related litigation expenses; and any statements of assumptions underlying any of the foregoing. Such forward-looking statements are subject to risks, uncertainties and other factors that could cause actual results and the timing of certain events to differ materially from future results expressed or implied by such forward-looking statements. Accordingly, we caution you not to place undue reliance on these statements. For a discussion of some of the factors that could cause actual results to differ materially from our forward-looking statements, see the discussion on risk factors that appear in Part I, Item 1A: "Risk Factors" of this Annual Report on Form 10-K and other risks and uncertainties detailed in this and our other reports and filings with the Securities and Exchange Commission ("SEC"). The forward-looking statements in this Annual Report on Form 10-K represent our views as of the date of this Annual Report on Form 10-K. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so except to the extent required by applicable law. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this Annual Report on Form 10-K.

PART I

ITEM 1. BUSINESS

COMPANY OVERVIEW

We discover, develop and sell enzymes and other proteins that deliver value to our clients in a growing set of industries. We view proteins as a vast, largely untapped source of value-creating products, and we are using our proven technologies, which we have been continuously improving since our inception in 2002, to commercialize an increasing number of novel enzymes, both as proprietary Codexis products and in partnership with our customers.

We are a pioneer in harnessing computational technologies to drive biology advancements. Since 2002, we have made substantial investments in the development of our CodeEvolver® protein engineering technology platform, the primary source of our competitive advantage. Our technology platform is powered by proprietary, artificial intelligence-based, computational algorithms that rapidly mine the structural and performance attributes of our large and continuously growing library of protein variants. These computational outputs enable increasingly reliable predictions for next generation protein variants to be engineered, enabling time- and cost-efficient delivery of the targeted performance enhancements. In addition to its computational prowess, our CodeEvolver® protein engineering technology platform integrates additional modular competencies, including robotic high-throughput screening and genomic sequencing, organic chemistry and bioprocess development which are all coordinated to rapidly innovate novel, fit-for-purpose products.

The core historical application of the technology has been in developing commercially viable biocatalytic manufacturing processes for more sustainable production of complex chemicals. It begins by conceptually designing the most cost-effective and practical process for a targeted product. We then develop optimized biocatalysts to enable the designed process, using our CodeEvolver® platform. Engineered biocatalyst candidates, numbering many thousands for each project, are then rapidly screened and validated using high throughput methods under process-relevant operating conditions. This approach results in an optimized biocatalyst that enables cost-efficient processes that are relatively simple to run in conventional manufacturing equipment allowing for efficient technical transfer of our processes to our manufacturing partners. This also allows for efficient technical transfer of our processes to our manufacturing partners.

The successful embodiment of our CodeEvolver® protein engineering technology platform in commercial manufacturing processes requires well-integrated expertise in a number of technical disciplines. In addition to those competencies directly integrated in our CodeEvolver® protein engineering platform, such as molecular biology, enzymology, microbiology, cellular engineering, metabolic engineering, bioinformatics, biochemistry and high throughput analytical chemistry, our process development projects also involve integrated expertise in organic chemistry, chemical process development, chemical engineering, bioprocess development and fermentation engineering. Our integrated, multi-disciplinary approach to product and process development is a critical success factor for the Company.

We initially commercialized our CodeEvolver® protein engineering technology platform and products in the manufacture of small molecule pharmaceuticals, which remains a primary business focus. Our customers, which include many large, global pharmaceutical companies, use our technology, products and services in their process development and in manufacturing. Additionally, we have licensed our proprietary CodeEvolver® protein engineering technology platform to global pharmaceutical companies enabling them to use this technology, in house, to engineer enzymes for their own businesses. Most recently, in May 2019, we entered into a Platform Technology Transfer and License Agreement (the “Novartis CodeEvolver® Agreement”) with Novartis Pharma AG (“Novartis”). The Novartis CodeEvolver® Agreement (Codexis’ third such agreement with large pharma companies) allows Novartis to use our proprietary CodeEvolver® protein engineering platform technology in the field of human healthcare.

As evidence of our strategy to extend our technology beyond pharmaceutical manufacturing, we have also used the technology to develop biocatalysts and enzyme products for use in a broader set of industrial markets, including several large verticals, such as food, feed, consumer care and fine chemicals. In addition, we are using our technology to develop enzymes for various life science related applications, such as next generation sequencing (“NGS”) and polymerase chain reaction (“PCR/qPCR”) for in vitro molecular diagnostic and genomic research applications. In December 2019, we entered into a license agreement to provide Roche Sequencing Solutions, Inc. ("Roche") with our first enzyme for this target market: the Company’s EvoT4™ DNA ligase. In June 2020, we entered into a co-marketing and enzyme supply collaboration agreement with Alphazyme LLC for the production and co-marketing of enzymes for life science applications including, initially, high-fidelity DNA polymerase, T7 RNA polymerase and reverse transcriptase enzymes. In June 2020, we also entered into a Master Collaboration and Research Agreement with Molecular Assemblies, Inc. ("MAI") (the “MAI Agreement”) pursuant to which we are leveraging our CodeEvolver® platform technology to improve the DNA polymerase enzymes that are critical for enzymatic DNA

synthesis. Concurrently with the MAI Agreement, we entered into a Stock Purchase Agreement with MAI pursuant to which we purchased 1,587,050 shares of MAI's Series A preferred stock for $1.0 million and, in connection with the transaction, John Nicols, our President and Chief Operating Officer, also joined MAI's board of directors.

Approximately five years ago, we began using the CodeEvolver® protein engineering technology platform to develop early stage, novel biotherapeutic product candidates, both in partnership with customers and for our own proprietary Codexis drug candidates. Our first program was for the potential treatment of phenylketonuria ("PKU") in humans. PKU is an inherited metabolic disorder in which the enzyme that converts the essential amino acid phenylalanine into tyrosine is deficient. In October 2017, we entered into a Global Development, Option and License Agreement (the "Nestlé License Agreement") with Societé des Produits Nestlé S.A., formerly known as Nestec Ltd. ("Nestlé Health Science") to advance CDX-6114, our enzyme biotherapeutic product candidate for the potential treatment of PKU. In February 2019, Nestlé Health Science exercised its option to obtain an exclusive license to develop and commercialize CDX-6114. Also in October 2017, we entered into a strategic collaboration agreement with Nestle Health Science ("Nestlé SCA") in which we and Nestlé Health Science are collaborating to leverage the CodeEvolver® platform technology to develop other novel enzymes for Nestlé Health Science's established Consumer Care and Medical Nutrition business areas. In January 2020, we entered into a development agreement with Nestlé Health Science to advance a new lead candidate discovered under the Nestlé SCA, CDX-7108, into preclinical development and early clinical studies as a potential treatment for a gastro-intestinal disorder. In parallel, the Nestlé SCA was extended through December 2021 to support the discovery of therapeutic candidates for additional disorders. In March 2020, we entered into a Strategic Collaboration and License Agreement ("Takeda Agreement") with Shire Human Genetic Therapies, Inc., a wholly-owned subsidiary of Takeda Pharmaceutical Company Limited ("Takeda"), for the research and development of novel gene therapies for certain disease indications, including the treatment of lysosomal storage disorders and a blood factor deficiency.

BUSINESS SEGMENTS

We manage our business as two business segments: Performance Enzymes and Novel Biotherapeutics. See Note 15, "*Segment, Geographical and Other Revenue Information*" in the Notes to the Consolidated Financial Statements set forth in Item 8 of this Annual Report on Form 10-K.

Performance Enzymes

We initially commercialized our CodeEvolver® protein engineering technology platform and products in the manufacture of small molecule pharmaceuticals and, to date, this continues to be our largest market served. Our customers, which include many large global pharmaceutical companies, use our technology, products and services in their manufacturing processes and process development. We have also used the technology to develop customized enzymes for use in other industrial markets. These markets consist of several large industrial verticals, including food, feed, consumer care, and fine chemicals. We also use our technology in the life sciences markets to develop enzymes for customers using NGS and PCR/qPCR for in vitro molecular diagnostic and molecular biology research applications, as well DNA/RNA synthesis and health monitoring applications.

Novel Biotherapeutics

We are also targeting new opportunities in the pharmaceutical industry to discover, improve, and/or develop biotherapeutic drug candidates. We believe that our CodeEvolver® protein engineering platform technology can be used to discover novel biotherapeutic drug candidates that will target human diseases that are in need of improved therapeutic interventions. Similarly, we believe that we can deploy our platform technology to improve specific characteristics of a customer's pre-existing biotherapeutic drug candidate, such as its activity, stability or immunogenicity. Our first lead program was for the potential treatment of hyperphenylalaninemia ("HPA") (also referred to as PKU) in humans. PKU is an inherited metabolic disorder in which the enzyme that converts the essential amino acid phenylalanine into tyrosine is deficient. In October 2017, we announced a global development, option and license agreement with Nestlé Health Science to advance CDX-6114, our own novel orally administrable enzyme therapeutic candidate for the potential treatment of PKU. In July 2018, we announced that we had dosed the first subjects in a first-in-human Phase 1a dose-escalation trial with CDX-6114, which was conducted in Australia. The initiation of the trial triggered a $4.0 million milestone payment from Nestlé Health Science. The
$1.0 million milestone payment that was triggered by the achievement of a formulation relating to CDX-6114 was received in February 2019. In January 2019, we received notice from the U.S. Food and Drug Administration ("FDA") that it had completed its review of our investigational new drug application ("IND") for CDX-6114 and concluded that we may proceed with the proposed Phase 1b multiple ascending dose study in healthy volunteers in the United States. In February 2019, Nestlé Health Science exercised its option to obtain an exclusive, worldwide, royalty-bearing, sub-licensable license for the global development and commercialization of CDX-6114 for the management of PKU. As a result of the option exercise, we earned a

milestone and recognized $3.0 million in revenues in the first quarter of 2019. Upon exercising its option, Nestlé Health Science assumed all responsibilities for future clinical development and commercialization of CDX-6114.

In October 2017, we separately entered into the Nestlé SCA with Nestlé Health Science pursuant to which we and Nestlé Health Science are collaborating to leverage the CodeEvolver® platform technology to develop other novel enzymes for Nestlé Health Science's established Consumer Care and Medical Nutrition business areas. In January 2020, we and Nestlé Health Science entered into a development agreement pursuant to which we and Nestlé Health Science are collaborating to advance into pre-clinical and early clinical studies a lead candidate targeting a gastro-intestinal disorder, CDX-7108, discovered through the Nestlé SCA. The Nestlé SCA was extended through December 2021. During 2020, we, together with Nestlé Health Science, continued to advance CDX-7108 towards initiation of a Phase 1 clinical trial which we anticipate will begin in 2021. Additionally, the parties initiated two new programs under the Nestlé SCA targeting a gastro-intestinal disorder.

In March 2020, we entered into the Takeda Agreement with Takeda pursuant to which we are collaborating to research and develop protein sequences for use in gene therapy products for certain disease indications in accordance with the respective program plans for Fabry Disease, Pompe Disease, and an undisclosed blood factor deficiency. In March 2020, we received a one-time, non-refundable cash payment of $8.5 million. Of these programs, the Fabry disease program is the most advanced, with multiple sequences, including CDX-6311, having been provided to Takeda.

BUSINESS UPDATE REGARDING COVID-19

We are subject to risks and uncertainties as a result of the current COVID-19 pandemic. The COVID-19 pandemic has presented a substantial public health and economic challenge around the world and is affecting our employees, communities and business operations, as well as the U.S. economy and other economies worldwide. The full extent to which the COVID-19 pandemic will directly or indirectly impact our business, results of operations and financial condition will depend on future developments that are highly uncertain and may not be accurately predicted, including the duration and severity of the pandemic and the extent and severity of the impact on our customers, new information that may emerge concerning COVID-19, the actions taken to contain it or treat its impact and the economic impact on local, regional, national and international markets.

To date, we and our collaboration partners have been able to continue to supply our enzymes to our customers worldwide. However, we are dependent on our manufacturing and logistics partners and consequently, disruptions in operations of our partners and customers may affect our ability to supply enzymes to our customers. Furthermore, our ability to provide future research and development ("R&D") services will continue to be impacted as a result of governmental orders and any disruptions in operations of our customers with whom we collaborate. We believe that these disruptions had a negative impact on our revenue for the year ended December 31, 2020, although we are unable to fully determine and quantify the extent to which this pandemic has affected the amount and timing of our total revenues. The extent to which the pandemic may impact our business operations and operating results will continue to remain highly dependent on future developments, which are uncertain and cannot be predicted with confidence.

In the U.S., the impact of COVID-19, including governmental orders ("Orders") governing the operation of businesses during the pandemic, caused the temporary closure of our Redwood City, California facilities and has disrupted our R&D operations. R&D operations for several projects were temporarily suspended from mid-March 2020 through the end of April 2020 in accordance with these Orders. In May 2020, we re-initiated limited R&D operations and have ramped up operations such that we are currently utilizing the majority of our normal R&D capacity while following county, state and federal COVID-19 guidance for the protection of our employees. Additionally, we resumed small scale manufacturing at our Redwood City pilot plant in May 2020.

Our future results of operations and liquidity could be adversely impacted by delays in payments of outstanding receivable amounts beyond normal payment terms, supply chain disruptions and uncertain demand, and the impact of any initiatives or programs that we may undertake to address financial and operations challenges faced by our customers. The extent to which the COVID-19 pandemic may materially impact our financial condition, liquidity, or results of operations in the future is uncertain.

For additional information on the various risks posed by the COVID-19 pandemic, see "Risk Factors" set forth in Item 1A of this Annual Report on Form 10-K.

RECENT INVESTING AND FINANCING ACTIVITIES

In June 2020, we entered into a Stock Purchase Agreement with MAI pursuant to which we purchased 1,587,050 shares of MAI's Series A preferred stock for $1.0 million. In connection with the transaction, John Nicols, our President and Chief Operating Officer, also joined MAI's board of directors. Concurrently with our initial equity investment, we entered into the MAI Agreement pursuant to which we are performing services utilizing our CodeEvolver® protein engineering platform technology to improve DNA polymerase enzymes in exchange for compensation in the form of additional shares of MAI's Series A preferred stock. We received 714,171 shares of MAI's Series A preferred stock from research and development activities in the year ended December 31, 2020, and recognized $0.9 million in research and development revenue from these activities with MAI in the year ended December 31, 2020. At December 31, 2020, we had $0.5 million of financial assets due from MAI for services rendered.

In November 2020, we announced the SynBio Innovation Accelerator ("Accelerator") collaboration with Casdin Capital, LLC ("Casdin"). The goal of the Accelerator is to fund the early-stage companies with disruptive technology platforms or unique product development capabilities in the field of synthetic and industrial biotechnology. The first investment by Codexis associated with the Accelerator collaboration was made in Arzeda Corp., a privately-held computational protein design company that focuses on computational approaches to designing novel enzyme functionality. We invested $1.0 million in Arzeda and received a convertible subordinated note issued by Arzeda Corp. The note is an available-for-sale non-marketable interest-bearing debt security which will mature within one year.

In December 2020, we completed an underwritten public offering of 4,928,572 shares of our common stock, including the exercise in full by the underwriters of their option to purchase an additional 642,857 of our shares, at a public offering price of $17.50 per share. After deducting the underwriting discounts, commissions, and estimated offering expenses, net proceeds were approximately $80.8 million.

OUR STRATEGY

Our strategy is to grow our revenues, profits, and stockholder value by leveraging our CodeEvolver® protein engineering technology platform in the following ways:

- *Licensing our CodeEvolver® protein engineering technology platform.* We intend to continue to pursue opportunities to license our CodeEvolver® protein engineering technology platform to third parties so they can create cost-saving biocatalyst solutions utilizing their own in-house protein engineering capability.
- *Growing our pharmaceutical biocatalysts business.* We intend to continue to pursue opportunities in the pharmaceutical market to use our protein catalysis products and services to reduce the costs for manufacturing small molecule drugs. We intend to increase the number of pharmaceutical customers and processes that utilize and benefit from our novel, cost-saving biocatalyst solutions.
- *Creating and advancing novel biotherapeutic drug candidates.* We intend to continue to pursue opportunities to apply our protein engineering capabilities to the creation and development of novel biotherapeutic drug candidates, both in partnership with customers and as proprietary Codexis drug candidates. We have also invested in research and development in an effort to generate additional early stage novel biotherapeutic candidates.
- *Extending our biocatalysts and industrial enzymes business into new markets.* We intend to continue to pursue opportunities to use biocatalyst products and services to reduce the costs and improve sustainability for manufacturing in markets such as food and food ingredients. We intend to increase the number of customers and industrial verticals that utilize and benefit from our novel performance enzyme solutions.
- *Developing high-performance enzymes for use in diagnostic applications* We intend to offer high-performance enzymes to customers using NGS and PCR/qPCR for *in vitro* molecular diagnostic applications.

In this Annual Report, the "Company," "we," "us" and "our" refer to Codexis, Inc. and its subsidiaries on a consolidated basis.

OUR MARKET OPPORTUNITIES

Pharmaceutical Market

We believe the pharmaceutical industry represents a significant market opportunity for us and is our primary business focus. Pharmaceutical companies are in constant search for new drugs to offer to their customers, and are under significant competitive pressure both to reduce costs and to increase the speed to market for their products. To meet these pressures, pharmaceutical companies are discovering and developing novel protein-based drug products, as well as seeking manufacturing processes for their new and existing drugs that reduce overall costs, simplify production and increase efficiency and product yield, while not affecting drug safety and efficacy. Cost reduction is even more important to developers (known as innovators) of patent-protected pharmaceutical products when the patents for those products expire and such innovators are forced to compete with manufacturers of generic drugs.

The pharmaceutical product lifecycle begins with the discovery of new chemical entities and continues through preclinical and clinical development, regulatory review and approval, commercial scale-up, product launch, and, ultimately, patent expiration and the transition from branded to generic products. As innovators develop, produce and then market products, manufacturing priorities and processes evolve. Historically, innovators have focused on production cost reduction in the later stages of clinical development and have been reluctant to make process changes after a product has been launched. However, as pressures to reduce costs have increased, innovators have pursued cost reduction measures much earlier in the pharmaceutical product lifecycle and are increasingly looking for opportunities to improve their operating margins, including making manufacturing process changes for marketed products after the products have been launched if these changes can result in significant cost reductions. As a result, innovators are investing in new technologies, including our CodeEvolver® protein engineering technology platform, to improve their manufacturing productivity and efficiency or outsourcing the manufacture of their intermediates and APIs.

Our Solutions for the Pharmaceutical Market

Small Molecule Manufacturing Cost Reduction

Our pharmaceutical customers, which include many large global pharmaceutical companies, use our technology, products and services in their manufacturing processes and process development. Our CodeEvolver® protein engineering technology platform enables us to deliver solutions to our customers in this market by developing and delivering optimized biocatalysts that perform chemical transformations at a lower cost and improve the efficiency and productivity of manufacturing processes. We provide value throughout the pharmaceutical product lifecycle. Our products and services allow us to provide benefits to our pharmaceutical customers in a number of cost saving ways, including any - and sometimes all - of the following:

- reducing the use of raw materials and reagents;
- eliminating multiple steps in the manufacturing process;
- improving purity, productivity and yield;
- using water as a primary solvent;
- eliminating hazardous inputs;
- enabling the use of simple equipment and reducing the need for capital expenditure;
- reducing energy requirements;
- reducing the generation of chemical byproducts or waste; and
- reducing the need for late-stage purifications.

Early in a pharmaceutical product’s lifecycle, pharmaceutical manufacturers can use our biocatalyst products and services to reduce manufacturing costs. If an innovator incorporates our products or processes into an approved product, we expect the innovator to continue to use our products or processes at least over the patent life of the marketed drug.

Pharmaceutical manufacturers can also use our products and services to reduce manufacturing costs after a product is launched. At this stage, changes in the manufacturing process originally approved by the drug regulator may require additional regulatory review. Typically, pharmaceutical companies will only seek regulatory approval for a manufacturing change if substantial cost savings are realizable. We believe that the cost savings associated with our products may lead our customers to change their manufacturing processes for approved products and, if necessary, seek regulatory approval of the new processes which

incorporate our biocatalyst products. Moreover, we believe these cost savings are potentially attractive to generics manufacturers, who compete primarily on price.

In addition, manufacturing processes that utilize our biocatalysts can frequently enable processes that are more sustainable and environmentally friendly compared to alternative, traditional manufacturing approaches. This has led us to earn three U.S. EPA Presidential Green Chemistry Challenge awards for improved pharmaceutical manufacturing processes since we were founded. All three of these awards were associated with blockbuster drug products.

Biotherapeutic Discovery and Development Partnerships

We are also targeting new opportunities in the pharmaceutical industry to discover or improve biotherapeutic drug candidates for our customers. We believe that our CodeEvolver® protein engineering platform technology can be used to discover novel biotherapeutic drug candidates that will target human diseases that are in need of improved therapeutic interventions. Similarly, we believe that we can deploy our platform technology to improve specific characteristics of a customer's pre-existing biotherapeutic drug candidate, such as its activity, stability or immunogenicity.

We approach biopharmaceutical companies to collaborate and utilize our platform technology for the discovery of specific novel biotherapeutic candidates. We currently have one such biotherapeutic discovery partnership in progress under the Nestlé SCA with Nestlé Health Science. We continue to pursue other customers who could benefit by applying our CodeEvolver® protein engineering platform technology to improve the discovery and/or development of other biotherapeutics in partnership with us.

Biotherapeutic Product Discovery and Development

We are also using our platform technology to self-fund the development of our own early stage, novel enzyme therapeutic product candidates. The lead product candidate is CDX-6114, an enzyme which we have engineered to be orally administered and is being developed as a potential treatment of PKU in humans. PKU is an inborn metabolic disorder in which the enzyme that converts the essential amino acid phenylalanine into tyrosine is deficient. As a result, phenylalanine accumulates to toxic levels in the brain, causing serious neurological problems including intellectual disability, seizures and cognitive and behavioral problems. To avoid toxic levels of phenylalanine in their blood, individuals with PKU must follow a strict, life-long diet that is low in phenylalanine and supplement their diet with a synthetic phenylalanine-free formula to provide them with sufficient nutrients. Maintaining a strict, life-long diet can be challenging for individuals with PKU. There are an estimated 50,000 people with PKU in the developed world.

In addition to the PKU program, we have focused our self-funded biotherapeutic investments with aim to discover therapeutic solutions for four additional rare disease conditions. Two of those programs are targeting potential enzyme replacement treatments for patients with inborn errors of amino acid metabolism diseases. The other two programs are targeting potential treatments for patients with lysosomal storage diseases. We expect to continue to make additional investments with the aim of generating additional product candidates targeting these, and potentially other therapeutic areas.

Nestlé Health Science

In October 2017, we entered into the Nestlé License Agreement with Nestlé Health Science pursuant to which we granted to Nestlé Health Science, under certain of our patent rights and know-how: (i) an option to obtain an exclusive, worldwide, royalty-bearing, sublicensable license to develop and commercialize certain products (each, a "Product") based on CDX-6114 and our other therapeutic enzyme product candidates covered by specified patent applications for the treatment of HPA, and (ii) an exclusive right of first negotiation (the "Right of First Negotiation") for a period of five years to obtain an exclusive worldwide license to develop and commercialize up to two enzymes discovered by us for use in the field of the prevention, diagnosis, treatment and management of inborn errors of amino acid metabolism. We are not under any obligation to undertake any research and development activities relating to inborn errors of amino acid metabolism. HPA (also referred to as PKU) is a medical condition characterized by elevated concentrations of the amino acid phenylalanine in the blood. PKU can result in severe HPA.

In February 2019, Nestlé Health Science exercised its option to receive an exclusive license to further develop and commercialize CDX-6114 and our other therapeutic enzyme product candidates covered by specified patent applications for the treatment of PKU (each, a "Compound"). Under the terms of the Nestlé License Agreement, upon option exercise, Nestlé Health Science received a license to the Compound, other than any enzyme that has other clinically significant, specified activity against another molecule, unless that enzyme's specified activity against phenylalanine is ten times greater than its activity against such other molecule (in which case it is not excluded). Furthermore, we generally will retain the right to use any enzyme as a biocatalyst, provided that preclinical development of such enzyme has not commenced. The first Compound to be developed under the Nestlé License Agreement was our enzyme CDX-6114.

The Nestlé License Agreement also sets forth the parties' respective obligations for development, commercialization, regulatory and manufacturing and supply activities for CDX-6114 and Product containing CDX-6114. Prior to Nestlé Health Science exercising its option to receive an exclusive license to CDX-6114, we were generally responsible for development activities, including conducting a Phase 1a clinical study. Upon exercising its option, Nestlé Health Science assumed all responsibilities for future clinical development and commercialization of CDX-6114, with the exception of the completion of an extension study, CDX-6114-004, which was substantially completed in the fourth quarter of 2019. Our development activities were governed by a development plan and overseen by a joint steering committee. The parties established a patent committee to discuss strategies and coordinate activities for the patents related to CDX-6114 and product containing CDX-6114, and we will jointly own all inventions and information that result from each party's activities performed under the Nestlé License Agreement. The Nestlé License Agreement also contains customary representations and warranties by the parties, intellectual property protection provisions, certain indemnification rights in favor of each party and customary confidentiality provisions and limitations of liability.

Nestlé Health Science paid us an upfront cash payment of $14.0 million in 2017. In July 2018, we announced that we had dosed the first subjects in a first-in-human Phase 1a dose-escalation trial with CDX-6114 which was conducted in Australia. In November 2018, we announced top-line results from the Phase 1a study in healthy volunteers with CDX-6114. The $4.0 million milestone payment that was triggered by the initiation of the trial was received in September 2018 and the $1.0 million milestone payment that was triggered by the achievement of a formulation relating to CDX-6114 was received in February 2019. In January 2019, we received notice from the U.S. Food and Drug Administration (the "FDA") that it had completed its review of our IND for CDX-6114 and concluded that we may proceed with the proposed Phase 1b multiple ascending dose study in healthy volunteers in the United States. In February 2019, Nestlé Health Science exercised its option to obtain an exclusive license for the global development and commercialization of CDX-6114 for the management of PKU. The exercise of the option triggered a $3.0 million milestone payment.

Other potential payments from Nestlé Health Science to us under the Nestlé License Agreement include (i) development and approval milestones of up to $85.0 million, (ii) sales-based milestones of up to $250.0 million in the aggregate, which aggregate amount is achievable if net sales exceed $1.0 billion in a single year, and (iii) tiered royalties, at percentages ranging from the middle single digits to low double-digits, of net sales of products containing an enzyme covered by the agreement as its sole active ingredient.

In October 2017, we entered into the Nestlé SCA pursuant to which we and Nestlé Health Science are collaborating to leverage the CodeEvolver® protein engineering technology platform to develop novel enzymes for Nestlé Health Science's established Consumer Care and Medical Nutrition business areas. The Nestlé SCA has been extended through December 2021.

In January 2020, we entered into a development agreement with Nestlé Health Science pursuant to which we and Nestlé Health Science are collaborating to advance a lead candidate targeting a gastro-intestinal disorder discovered through the Nestlé SCA into pre-clinical and early clinical studies.

Shire Human Genetic Therapies/Takeda Pharmaceutical

In March 2020, we entered into the Takeda Agreement with Takeda under which we will research and develop protein sequences for use in gene therapy products for certain diseases (each, a "Field") in accordance with each applicable program plan (each, a "Program Plan"). We received an upfront nonrefundable cash payment of $8.5 million and we initiated activities under three Program Plans for Fabry Disease, Pompe Disease, and an undisclosed blood factor deficiency, respectively (the "Initial Programs"). We are primarily responsible for the research and development of protein sequences under the Program Plans (the "Protein Sequences") and we are eligible to earn up to $15.4 million of research and development fees and pre-clinical milestone payments for the Initial Programs. Takeda has the right, but not the obligation, to develop, manufacture and commercialize gene therapy products that include nucleic acid sequences that encode the Protein Sequences ("Products") at their expense. Takeda has the right to a certain number of additional disease indications ("Reserved Target Indications") for a limited time period during which Takeda may initiate a Program Plan for one or more Reserved Target Indications ("Additional/Option Program," with Initial Programs, the "Programs"), provided, (a) if Takeda elects to initiate an Additional/Option Program while the parties are collaborating on three other Programs at the time of such election, or (b) if Takeda elects to initiate an Additional/Option Program using the last remaining Reserved Target Indication, then Takeda must pay us an option exercise fee to initiate such Additional/Option Program. We will own all rights to the Protein Sequences and corresponding nucleic acid sequences and related intellectual property rights and Takeda will own all rights to Products and related intellectual property rights.

We granted to Takeda an exclusive, worldwide, royalty-bearing, sublicensable license to use the Protein Sequences and their corresponding nucleic acid sequences to develop, manufacture and commercialize the applicable Products in the applicable Field. We also granted to Takeda a limited non-exclusive, worldwide, sublicensable license (a) to research the Protein Sequences within or outside the applicable Fields and (b) to research the Products outside of the applicable Fields, which such

rights exclude Takeda's right to perform any Investigational New Drug-enabling activities. The licenses to research the Protein Sequences expire after a pre-determined period of time.

The term of the Takeda Agreement begins on the effective date of the Takeda Agreement and continues on a Product-by-Product and country-by-country basis, until the expiration of Takeda's obligation to pay royalties to the Company with respect to that Product in that country. The Takeda Agreement expires in its entirety upon the expiration of Takeda's obligation to pay royalties to the Company with respect to the Products in all countries worldwide. Subject to the terms of the Takeda Agreement, and after the first anniversary of the Effective Date with respect to the Initial Programs or after the first anniversary of confirmation of the applicable Program Plan by the parties with respect to the Additional/Option Programs, Takeda may terminate a Program upon specified prior written notice to the Company. Subject to the terms of the Takeda Agreement, Takeda may terminate the Takeda Agreement, at will, on a Product-by-Product basis upon specified prior written notice to the Company and the Takeda Agreement in its entirety upon specified prior written notice to the Company. Subject to the terms of the Takeda Agreement, Takeda may terminate the Takeda Agreement on a Product-by-Product basis for safety reasons upon specified prior written notice to the Company. Either party may terminate the Takeda Agreement for an uncured material breach by the other party, or the other party's insolvency or bankruptcy. We are eligible to receive certain development and commercialization milestone payments up to $100.0 million per target gene, the modulation of which would lead to the treatment of the disease indications by the applicable Product. We are also eligible to receive tiered royalties based on net sales of Products at percentages ranging from the middle-single digits to low single-digits.

Licensing Our CodeEvolver® Protein Engineering Technology Platform

Licensing our CodeEvolver® protein engineering technology platform to pharmaceutical companies enables them to rapidly develop custom-designed enzymes that are highly optimized for efficient manufacturing processes. To date, we have entered into platform technology licensing agreements with each of GlaxoSmithKline Intellectual Property Development Limited, a subsidiary of GlaxoSmithKline plc ("GSK"), Merck, Sharp & Dohme ("Merck") and Novartis Pharma AG ("Novartis"), and we intend to continue to enter into license arrangements with third parties that will allow them to use our CodeEvolver® protein engineering technology platform to discover and develop novel proteins for their internal use.

GlaxoSmithKline

We entered into our first CodeEvolver® protein engineering Platform Technology Transfer, Collaboration and License Agreement ("GSK CodeEvolver® Agreement") in July 2014 with GlaxoSmithKline Intellectual Property Development Limited, a subsidiary of GSK, pursuant to which we granted GSK a non-exclusive, worldwide license to use our CodeEvolver® protein engineering technology platform in the field of human healthcare for its internal development purposes.

Under the GSK CodeEvolver® Agreement, we transferred our CodeEvolver® protein engineering technology platform to GSK over a twenty-one-month period that began in July 2014. As a part of this technology transfer, we provided to GSK our proprietary enzymes, proprietary protein engineering protocols and methods, and proprietary software algorithms. In addition, teams of our and GSK scientists participated in technology training sessions and collaborative research projects at our laboratories in Redwood City, California and at GSK's laboratories in Upper Merion, Pennsylvania. The technology transfer was completed in April 2016 and our CodeEvolver® protein engineering technology platform has been installed at GSK's Upper Merion, Pennsylvania site. We have the potential to receive additional contingent payments that range from $5.75 million to $38.5 million per project based on GSK's successful application of the licensed technology.

We are also eligible to receive royalties based on net sales, if any, of a limited set of products developed by GSK using our CodeEvolver® protein engineering technology platform.

The licenses to GSK were granted under certain patents, patent applications and know-how that we owned or controlled as of the effective date of the GSK CodeEvolver® Agreement and that cover our CodeEvolver® protein engineering technology platform and certain enzymes useful in the Field. Any improvements to our CodeEvolver® protein engineering technology platform during the technology transfer period were included in the license grants from us to GSK.

Under the GSK CodeEvolver® Agreement, GSK owns (the "GSK-Owned Technology") (a) any enzyme technology that was developed during a project under the GSK CodeEvolver® Agreement that used our CodeEvolver® protein engineering technology platform during the technology transfer period and (b) the methods of use of any Project Enzyme in compound synthesis that were developed during the technology transfer period. GSK granted to us a worldwide, non-exclusive, fully paid-up, royalty-free license, with the right to grant sublicenses, to use outside of the GSK Exclusive Field, the GSK-Owned Technology that was developed during the technology transfer period.

The term of the GSK CodeEvolver® Agreement continues, unless earlier terminated, until the expiration of all payment obligations under the GSK CodeEvolver® Agreement. GSK can terminate the GSK CodeEvolver® Agreement by providing 90 days written notice to us.

In 2019, we received a $2.0 million milestone payment on the advancement of an enzyme developed by GSK using our CodeEvolver® protein engineering platform technology.

Merck

In August 2015, we entered into a CodeEvolver® Platform Technology Transfer and License Agreement (the "Merck CodeEvolver® Agreement") with Merck. The Merck CodeEvolver® Agreement allows Merck to use our proprietary CodeEvolver® protein engineering platform technology in the field of human and animal healthcare.

Under the terms of the Merck CodeEvolver® Agreement, we granted to Merck a non-exclusive worldwide license to use the CodeEvolver® protein engineering technology platform to research, develop and manufacture novel enzymes for use by Merck in its internal research programs ("Merck Non-Exclusive Field"). The license to Merck is exclusive for the research, development and manufacture of novel enzymes for use by Merck in the chemical synthesis of therapeutic products owned or controlled by Merck ("Merck Exclusive Field"). Merck has the right to grant sublicenses to affiliates of Merck and, in certain limited circumstances, to third parties. We also granted to Merck a license to make or have made products manufactured using the CodeEvolver® protein engineering technology platform with a right to grant sublicenses solely to affiliates of Merck, contract manufacturing organizations and contract research organizations. The manufacturing license is exclusive in the Merck Exclusive Field and non-exclusive in the Merck Non-Exclusive Field. The licenses are subject to certain limitations based on pre-existing contractual obligations that apply to the technology and intellectual property that are the subject of the license grants. The licenses do not permit the use of the CodeEvolver® protein engineering technology platform to discover any therapeutic enzyme, diagnostic product or vaccine. In addition, Merck is prohibited from using the CodeEvolver® protein engineering technology platform to develop or produce enzymes or any other compounds for or on behalf of any third parties except in a very limited manner when Merck divests a therapeutic product that is manufactured using an enzyme developed using the CodeEvolver® protein engineering technology platform.

Under the terms of the Merck CodeEvolver® Agreement, Merck paid us upfront technology transfer and license fees and milestone payments over the technology transfer period of 15 months from August 2015. We also have the potential to receive product-related payments of up to $15.0 million for each API that is manufactured by Merck using one or more enzymes that have been developed or are in development using the CodeEvolver® protein engineering technology platform during the 10-year period that begins on the conclusion of the 15-month technology transfer period. These product-related payments, if any, will be paid by Merck to us for each quarter that Merck manufactures API using a CodeEvolver®-developed enzyme. The payments will be based on the total volume of API produced using the CodeEvolver®-developed enzyme. We have the right to conduct an annual audit to confirm that all payments that are owed to us have been paid in full and on time.

The licenses to Merck are granted under patents, patent applications and know-how that we owned or controlled as of the effective date of the Merck CodeEvolver® Agreement and that cover the CodeEvolver® protein engineering technology platform. Any improvements to the CodeEvolver® protein engineering technology platform during the technology transfer period are also included in the license grants from Codexis to Merck. Following the technology transfer period, Merck can exercise annual options that, upon payment of certain option fees, would extend Merck's license to include certain improvements to the CodeEvolver® protein engineering technology platform that arise during the three-year period that begins at the end of the technology transfer period.

Under the Merck CodeEvolver® Agreement, we own any improvements to our protein engineering methods, processes and algorithms that arose and any enzyme technology or process technology that are developed during an evolution program or additional services. Merck owns (the "Merck-Owned Technology") (a) any enzyme technology that is developed solely by Merck under the Merck CodeEvolver® Agreement using the CodeEvolver® protein engineering technology platform (a "Project Enzyme") and (b) the methods of use of any Project Enzyme or any enzyme developed jointly by Merck and us using the CodeEvolver® protein engineering technology platform. Merck granted to us a worldwide, non-exclusive, fully paid-up, royalty-free license, with the right to grant sublicenses, to use the Merck-Owned Technology outside of the Merck Exclusive Field.

For each API that Merck manufactures using an enzyme developed with the CodeEvolver® protein engineering technology platform, we will have a right of first refusal to supply Merck with the enzyme used to manufacture the API if Merck outsources the supply of the enzyme. Our right of first refusal applies during the period that begins on the completion of a Phase 3 clinical trial for the product containing the API and ends five years following regulatory approval for such product.

The Merck CodeEvolver® Agreement has a term that continues, unless earlier terminated, until the expiration of all payment obligations under the agreement. Merck may terminate the Merck CodeEvolver® Agreement by providing 90 days written notice to us. We can terminate the Merck CodeEvolver® Agreement by providing 30 days written notice to Merck if we determine, pursuant to our contractual audit rights under the Merck CodeEvolver® Agreement, that Merck has repeatedly failed to make required payments to us and/or materially underpaid us an amount due under the Merck CodeEvolver® Agreement. In the event the Merck CodeEvolver® Agreement is terminated earlier by Merck, or by us due to an uncured material breach by Merck, or if Merck sells or transfers to a third party any Merck business or facility that includes any of our proprietary materials, information or technology, we have the right to conduct an audit of Merck's facilities to confirm that all of our proprietary materials, information and technology have been destroyed. The Merck CodeEvolver® Agreement contains indemnification provisions under which Merck and we have agreed to indemnify each other against certain third party claims.

In September 2016, we completed the full transfer of the engineering platform technology. In October 2018, we entered into an amendment to the Merck CodeEvolver® Agreement whereby we amended certain licensing provisions and one exhibit. In January 2019, we entered into an amendment to the Merck CodeEvolver® Agreement whereby we installed certain CodeEvolver® protein engineering technology upgrades into Merck's platform license installation. We will maintain those upgrades for a multi-year term expiring in January 2022.

Novartis

In May 2019, we entered into a Platform Technology Transfer and License Agreement (the "Novartis CodeEvolver® Agreement") with Novartis.

The Novartis CodeEvolver® Agreement allows Novartis to use our proprietary CodeEvolver® protein engineering platform technology (the "CodeEvolver® Platform Technology") in the field of human healthcare. The CodeEvolver® Platform Technology enables rapid development of custom-designed enzymes that are highly optimized for efficient manufacturing processes. The CodeEvolver® Platform Technology, which is comprised of proprietary methods for the design and generation of diverse genetic libraries, automated screening techniques, algorithms for the interpretation of screening data and predictive modelling, is covered by more than 250 issued patents and patent applications worldwide.

Under the Novartis CodeEvolver® Agreement, Codexis will transfer its CodeEvolver® Platform Technology to Novartis over approximately 20 months starting with the date on which Codexis commences the technology transfer (the "Technology Transfer Period"). As a part of this technology transfer, Codexis will provide to Novartis Codexis' proprietary enzymes, proprietary protein engineering protocols and methods, and proprietary software algorithms. In addition, teams of Codexis and Novartis scientists will participate in technology training sessions and collaborative research projects at Codexis' laboratories in Redwood City, California and at a designated Novartis laboratory in Basel, Switzerland. Upon completion of technology transfer, Novartis will have CodeEvolver® Platform Technology installed at its designated laboratory.

Under the terms of the Novartis CodeEvolver® Agreement, Codexis granted to Novartis a worldwide license to use Codexis' CodeEvolver® Platform Technology to research, develop and manufacture novel enzymes for use by or on behalf of Novartis as biocatalysts in the chemical synthesis of small molecule and bioconjugate active pharmaceutical ingredients ("API"). The license to Novartis is exclusive for the research, development and manufacture of novel enzymes for use by Novartis as biocatalysts in the chemical synthesis of API owned or controlled by Novartis ("Novartis Exclusive Field") and non-exclusive for the research, development and manufacture of novel enzymes for use by Novartis in the chemical synthesis of API not owned or controlled by Novartis or any third party ("Novartis Non-Exclusive Field"). Novartis has the right to grant sublicenses to affiliates of Novartis and, in certain limited circumstances, to third parties. Codexis has also granted to Novartis a license to make or have made enzymes engineered using the CodeEvolver® Platform Technology for use in the manufacture of therapeutic products or API with a right to grant sublicenses solely to affiliates of Novartis, contract manufacturing organizations and contract research organizations. The manufacturing license is exclusive in the Novartis Exclusive Field and non-exclusive in the Novartis Non-Exclusive Field. The licenses are subject to certain limitations based on pre-existing contractual obligations that apply to the technology and intellectual property that are the subject of the license grants. The licenses do not permit the use of the CodeEvolver® Platform Technology to discover any biologic, therapeutic enzyme, diagnostic product or vaccine. In addition, Novartis is prohibited from using the CodeEvolver® Platform Technology to develop or produce enzymes or any other compounds for or on behalf of any third parties except in a very limited manner when Novartis divests an API that is manufactured using an enzyme developed using the CodeEvolver® Platform Technology.

Novartis will pay Codexis up to $14.0 million over approximately the period through March 2021, of which $5.0 million was received shortly after the effective date of the Novartis CodeEvolver® Agreement. In the second quarter of 2020, we completed the second technology milestone transfer under the agreement and became eligible to receive a milestone payment of $4.0 million, which we subsequently received in July 2020. We have also billed $3.4 million for partial completion of the third technology milestone and we expect to receive payment in the first quarter of 2021. In addition to this payment, we are eligible

for an additional payment of $1.6 million for completion of the third technology milestone transfer, which would bring total cash payment for this milestone to $5 million as specified in the Novartis CodeEvolver® Agreement. In consideration for the continued disclosure and license of improvements to our technology and materials during a multi-year period that begins on the conclusion of the Technology Transfer Period ("Improvements Term"), Novartis will pay us annual payments which amount to an additional $8.0 million. Codexis also has the potential to receive quantity-dependent, usage payments for each API that is manufactured by Novartis using one or more enzymes that have been developed or are in development using the CodeEvolver® Platform Technology during the period that begins on the conclusion of the Technology Transfer Period and ends on the expiration date of the last to expire licensed patent. These product-related usage payments, if any, will be paid by Novartis to Codexis for each quarter that Novartis manufactures API using a CodeEvolver® -developed enzyme. The usage payments will be based on the total volume of API produced using the CodeEvolver® -developed enzyme. These usage payments can begin in clinical stage and will extend throughout the commercial life of each API. Codexis has the right to conduct an annual audit to confirm that all payments that are owed to Codexis have been paid in full and on time.

The licenses to Novartis are granted under patents, patent applications and know-how that Codexis owns or controls as of the effective date and that cover the CodeEvolver® Platform Technology. Any improvements to the CodeEvolver® Platform Technology during the Technology Transfer Period will also be included in the license grants from Codexis to Novartis.

Under the Novartis CodeEvolver® Agreement, Codexis will own any improvements to Codexis' protein engineering methods, processes and algorithms that arise and any enzyme technology or process technology that is developed during the Technology Transfer Period or during the Improvements Term. Novartis will own (a) any enzyme technology that is developed solely by Novartis or jointly by Novartis and Codexis under an enzyme evolution project using the CodeEvolver® Platform Technology (a "Project Enzyme") and (b) the methods of use of any Project Enzyme or any enzyme developed solely by Novartis or jointly by Novartis and Codexis under an enzyme evolution project using the CodeEvolver® Platform Technology ("Process Technology"). Novartis granted to Codexis a worldwide, exclusive, fully paid-up, royalty-free license, with the right to grant sublicenses, to use Project Enzymes outside of the Novartis Exclusive Field. Novartis also granted to Codexis a worldwide, non-exclusive, fully paid-up, royalty-free license, with the right to grant sublicenses, to use the Process Technology outside of the Novartis Exclusive Field.

For each Novartis-controlled API that Novartis manufactures using an enzyme developed using the CodeEvolver® Platform Technology, Codexis will have a right of first refusal to supply Novartis with the enzyme used to manufacture the API, once Novartis's requirement for such enzyme exceeds a certain quantity, if Novartis self-produces or outsources the supply of the enzyme. Codexis' right of first refusal applies during the period that begins on the completion of a Phase 1 clinical trial for the first therapeutic product containing the API and ends on the earlier of five years following regulatory approval for such product and termination of the Novartis CodeEvolver® Agreement.

The Novartis CodeEvolver® Agreement has a term that begins on its effective date and continues unless and until terminated under the Novartis CodeEvolver® Agreement. At any time following the first technology transfer stage, Novartis may terminate the Novartis CodeEvolver® Agreement by providing 90 days written notice to Codexis. If Novartis exercises this termination right prior to making the first technology transfer milestone payment, Novartis will make a one-time termination payment of $9.0 million to Codexis. If Novartis exercises this termination right after making the first technology transfer milestone payment but prior to making the second technology transfer milestone payment, Novartis will make a one-time termination payment of $5.0 million to Codexis. In addition, either party may terminate the Novartis CodeEvolver® Agreement for the other party's uncured material breach or insolvency or bankruptcy. In the event the Novartis CodeEvolver® Agreement is terminated by Novartis, or by Codexis due to an uncured material breach by Novartis or insolvency or bankruptcy of Novartis, or if Novartis sells or transfers to a third party any Novartis business or facility that includes any Codexis proprietary materials, information or technology, Codexis has the right to conduct an audit of Novartis's facilities to confirm that all proprietary Codexis materials, information and technology have been destroyed. The Novartis CodeEvolver® Agreement also contains indemnification provisions under which Novartis and Codexis indemnify each other against certain third party claims.

Fine Chemicals and Industrial Enzyme Markets

Beyond the pharmaceutical industry, our CodeEvolver® protein engineering platform technology has enabled cost-savings for our partners in the fine chemicals markets, and the food industry in particular. In November 2016, we entered into an exclusive agreement with Tate & Lyle, a market-leading food ingredients company, to supply a proprietary enzyme for use in Tate & Lyle's food ingredient production. In March 2017, we entered into a multi-year research and development agreement with Tate & Lyle for the development of a second ingredient for the food ingredient industry. We engineered a suite of enzymes that enable Tate & Lyle's novel bioconversion route for the manufacture of their newly-launched zero-calorie TASTEVA® M Stevia sweetener.

We are seeking to expand our enzyme offerings in the fine chemical and industrial enzyme markets within and beyond the food

industry, including, for example, to the animal feed, agricultural chemicals, consumer care, flavors and fragrances markets.

Molecular Biology and *In Vitro* Diagnostic Enzymes

We believe that our protein engineering capability can also be deployed to commercialize novel enzymes as improvements to enzymes consumed by customers in many industrial sectors. As our first effort in this strategy, we have developed enzymes for customers using NGS and PCR/qPCR for in vitro molecular diagnostic applications. In December 2019, we entered into a license agreement to provide Roche with our EvoT4™ DNA ligase high-performance molecular diagnostic enzyme. This enzyme was developed using our proprietary CodeEvolver® protein engineering platform and is expected to be incorporated into Roche's NGS library preparation kits and other sequencing products. We are also currently working on a second enzyme independently of Roche, a DNA polymerase, which is being prepared for beta testing.

Biocatalyst Products and Services

Our biocatalyst products and services can deliver value to our customers in multiple potential ways:

- manufacture their products at lower cost;
- manufacture their products with lower fixed capital investment;
- reduce the cost of development of complex chemical synthesis processes;
- enable their products to achieve higher product purity;
- allow the removal of entire steps from chemical production; and
- provide flexibility to apply at any point across their product's lifecycle.

Our products include biocatalysts, chemical intermediates and Codex® biocatalyst panels and kits. We sell our products worldwide primarily through our direct sales and business development force in the United States and Europe.

In addition to products, we also offer research and development services to our customers. These research and development service agreements often contain service fee payments and intellectual property provisions under which we screen and/or engineer biocatalysts for customers in connection with their process development efforts. In these collaborations, we typically receive consideration in the form of one or more of the following: upfront payments, milestone payments, payments for screening and engineering services, licensing fees and royalties.

Biocatalysts

We often sell biocatalysts, by the gram or kilogram, that have already been engineered, scaled up, and installed in a customer's commercial process. For example, we sell biocatalysts to Merck for their manufacture of sitagliptin, the active ingredient in Januvia®. We also sell biocatalysts which are in developmental stages. These are enzymes that are sold by the batch or by the gram or kilogram that are in the process of being engineered or scaled up by Codexis, or are in the process of being trialed or approved for use in the customer's process. We may sell batches of specific biocatalysts that are in the midst of protein engineering efforts, in order to test their performance at a larger scale or to accelerate a customer's process development. We may also sell batches of specific biocatalysts for use in a customer's developmental products (for example, for use in the manufacture of a customer's Phase 2 drug candidate). Finally, we may sell batches of specific biocatalysts as a customer performs trials for approval in their commercial manufacturing operations.

Chemical Intermediates

In some cases, we sell intermediate chemicals products that are produced in a process that uses our biocatalysts. These chemical intermediates are then used by our customer for further chemical processing.

Codex® Biocatalyst Panels and Kits

We sell kits and panels of our biocatalysts. These kits and panels assemble a relevant subset of our engineered enzymes to enable customers to perform chemistry screening on their own. These kits and panels are organized by specific types of chemical reactions that are widely applicable in the pharmaceutical and fine chemical markets.

Biocatalyst Screening Services

If a customer prefers, rather than purchasing our Codex® Biocatalyst Panels or Kits to use for its own screening, it may send us its starting materials and desired chemical reaction, and we will test against our existing libraries of enzymes on a research and development service fee basis. If we detect desired activity in a specific enzyme, we can supply the customer with this enzyme or perform engineering services to improve the performance of the enzyme.

Protein Engineering Services

We work with our customers throughout their product development lifecycle to optimize enzymes that have been engineered specifically to perform a desired process according to a highly selective set of specifications. We typically charge customers for research and development services by project or project-month. These are typically larger research and development service fees than screening services.

The protein engineering process starts by identifying genes that code for enzymes known to have the general type of catalytic reactivity for a desired chemical reaction. Typically, we identify gene sequences from our extensive in-house collection or from published databases and then synthesize candidate genes having those sequences. Using a variety of biotechnology tools, we diversify these genes by introducing mutations, giving rise to changes in the enzymes for which they encode. The methods for diversifying these genes, and types of diversity being tested, often vary over the course of a protein engineering program. For finding initial diversity, methods typically include random mutagenesis and site-directed (included computational structure-guided) mutagenesis. We also test mutational variations from related enzymes found in different organisms.

Once we have identified potentially beneficial mutations, we create libraries of thousands of variants with combinations of these mutations. With our proprietary genetic manipulation tools, we generate libraries of genes that have programmed and random combinations of mutations for testing. The pool of genes is used to transform host cells, which entails introducing the various genes into host cells. These cells are then grown into colonies. Cells from individual colonies are cultured in high throughput to produce the enzyme encoded by the genetic variant in those cells. The enzymes expressed by these cells are then screened in high throughput using test conditions relevant to the desired application. The screening results allow us to identify and catalog individual genes that produce improved enzymes with beneficial mutations as well as enzymes having detrimental ones. Using specifically developed test conditions and analytical methods, we can identify variant enzymes that exhibit various improved performance characteristics, such as stability, activity and selectivity, under conditions relevant to the desired chemical process.

In the next step in our optimization process, we use our proprietary bioinformatics software to analyze protein sequence-activity relationships. Our software and algorithms relate the screening results to the mutations and rank the individual and interacting protein sequence mutations with regard to their degree of benefit or detriment, relative to the process parameter(s) tested. Using this information, we can create a select pool of mutational diversity in the next iteration to further the accumulation of beneficial diversity and cancel out detrimental diversity in the individual genes in the resulting library. The gene that codes for the best performing enzyme in one iteration is used as the starting gene for the next iteration of recombination and screening. As the enzymes improve over these iterations, the screening conditions are made increasingly more stringent. In this way, the biocatalyst is rapidly optimized until all in-process performance requirements have been achieved and the economic objectives for the desired process have been met.

INTELLECTUAL PROPERTY

Our success depends in large part on our ability to protect our proprietary products and technology under patent, copyright, trademark and trade secret laws. We also rely heavily on confidential disclosure agreements for further protection of our proprietary products and technologies. Protection of our technologies is important for us to offer our customers and partners proprietary services and products that are not available from our competitors, and to exclude our competitors from practicing technology that we have developed or exclusively licensed from other parties. For example, our ability to supply innovator pharmaceutical manufacturers depends on our ability to supply proprietary enzymes or methods for making pharmaceutical intermediates or APIs that are not available from our competitors. Likewise, in the generic pharmaceutical area, proprietary protection, through patent, trade secret or other protection of our enzymes and methods of producing a pharmaceutical product is important for us and our customers to maintain a lower cost production advantage over competitors.

As of December 31, 2020, we owned or controlled approximately 1,635 issued patents and pending patent applications in the United States and in various foreign jurisdictions, many of which are directed to our enabling technologies and specific methods and products that support our business in the pharmaceutical markets. In addition, our portfolio includes patents and pending patent applications that support our businesses in the biotherapeutics, molecular diagnostics, food and other markets. Our patents and pending patent applications, if issued, have terms that expire between 2021 and approximately 2041. Our United States patents and pending patent applications directed to the CodeEvolver® proprietary enabling technology platform developed internally by us have terms that expire between 2029 and approximately 2034. It is possible that some US patents may be entitled to patent term extensions and/or patent term adjustments, which would extend the protection beyond these expiration dates. It is also possible that some patents in other jurisdictions will be entitled to additional patent term. Our current intellectual property rights also include patents, trademarks, copyrights, software and certain assumed contracts that we acquired from Maxygen, Inc. (“Maxygen”) in October 2010, which are associated with directed evolution technology, known as

the MolecularBreeding™ technology platform developed by Maxygen. The intellectual property rights and assets that we acquired from Maxygen continue to be subject to existing exclusive and non-exclusive license rights granted by Maxygen to third parties. We continue to file new patent applications, for which terms generally extend 20 years from the non-provisional filing date in the United States.

As of December 31, 2020, we owned approximately 110 trademark registrations in the United States and foreign jurisdictions, as well as many common law trademarks. These include, but are not limited to: Codexis®, Codex®, CodeEvolver®, Mosaic®, Sage®, Microcyp®, MCYP®, ProSAR®, Unlock the Power of Proteins®, the Codexis Protein Engineering Experts® logo, Strategist™, Continuity®™, Ameli™, Forager®™, Analogene®™, Harvester®™, Atoms®™, Riptide®™, APS™ and a Codexis design mark (i.e., the stylized Codexis logo).

COMPETITION

We face differing forms of competition in the small molecule pharmaceuticals, biotherapeutics and fine chemicals markets, as set forth below.

Small Molecule Pharmaceuticals

We market our biocatalyst products and services to manufacturers of small molecule pharmaceutical intermediates and APIs. Our primary competitors in that market are companies marketing either conventional, non-enzymatic catalysts or alternative biocatalyst products and services. We also sometimes face competition from existing in-house technologies (both biocatalysts and conventional catalysts) within our client and potential client companies. The principal methods of competition and competitive differentiation in this market are price, product quality and performance, including manufacturing yield, safety and environmental benefits and speed of delivery of product. Pharmaceutical manufacturers that use biocatalytic processes can face increased competition from manufacturers that use more conventional processes and/or manufacturers that are based in regions (such as India and China) with lower regulatory, safety and environmental costs.

The market for the manufacture and supply of APIs and intermediates is large, with many established companies. These companies include many of our large innovator and generic pharmaceutical customers, such as Merck, GSK, Novartis, Pfizer Inc. ("Pfizer"), Bristol-Myers Squibb Company ("Bristol-Myers"), KYORIN Pharmaceutical Co., Ltd. ("Kyorin"), Urovant Sciences GmbH ("Urovant"), and Teva Pharmaceutical Industries Limited ("Teva"), which have significant internal research and development efforts directed at developing processes to manufacture APIs and intermediates. The processes used by these companies include classical conventional organic chemistry reactions, chemo-catalytic reactions, biocatalytic reactions or combinations thereof. Our biocatalyst based manufacturing processes must compete with these internally developed routes.

Companies developing and marketing conventional catalysts include Solvias AG, BASF, Johnson-Matthey and Takasago International Corporation.

The market for supplying enzymes for use in pharmaceutical manufacturing is quite fragmented. There is competition from large industrial enzyme companies, such as Novozymes and Dupont, as well as subsidiaries of larger contract research/contract manufacturing organizations (“CRO/CMO”), such as Royal DSM N.V. (“DSM”), Cambrex Corporation, Lonza, WuXi STA and Almac Group Ltd. Some fermentation pathway design companies, like Ginkgo Bioworks and Zymergen, whose traditional focus has been to design microorganisms that express small molecule chemicals, could extend into designing organisms that express enzymes. There is also competition in the enzyme customization and optimization area from several smaller companies, such as BRAIN AG, Arzeda, c-LEcta GmbH and Evocatal GmbH.

We believe that our principal advantage is our ability to rapidly deliver customized biocatalysts for existing and new intermediates and APIs in the pharmaceutical manufacturing market. This capability has allowed us to create a breadth of biocatalysts with improved performance characteristics including, for example, better activity, stability, and activity on a range of substrates, compared to traditional chemistry-based manufacturing processes and naturally occurring (and thus not optimized) biocatalysts. We believe that our CodeEvolver® protein engineering platform technology provides substantially superior results, in shorter time frames, than companies offering competing biocatalyst development services.

Biotherapeutics

There are other companies that participate in the biotherapeutics market generally and the PKU market specifically. Many of these companies are large, successful and well-capitalized. BioMarin Pharmaceutical Inc. (“BioMarin”) and Daiichi Sankyo Company market Kuvan® in the United States, Europe and Japan for the treatment of a certain type of PKU. In addition, BioMarin had gained FDA approval in May 2018 and began the commercial sales of Palynziq®, an injectable enzyme substitution therapy to address different options for care in the treatment of PKU. Subsequently in May 2019, BioMarin obtained marketing authorization for Palynziq® from the European Commission. Several companies, including Synlogic,

Homology Medicines and Rubius have reported clinical efforts to develop biotherapeutic candidates for PKU. Beyond targeting PKU, Takeda, Genzyme / Sanofi S.A., BioMarin, and other companies market or are actively developing enzyme therapeutics. There are numerous companies that are developing other forms of therapeutics, such as small molecules, gene therapy, as well as therapies based on gene editing, which could compete with biotherapeutics.

Fine Chemicals

We entered the fine chemicals market in 2013 by applying our protein engineering technology in the manufacture of food ingredients. We face similar forms of competition in this market as in the small molecule pharmaceutical markets, with the exception that the risk of losing opportunities to larger competitors in fine chemicals is greater given the larger scale of opportunities available in the fine chemicals market compared to the pharmaceutical market. Our significant competitors in the fine chemicals markets include companies that have been in these marketplaces for many years, such as DuPont Industrial Biosciences (DuPont Genencor), DSM, Novozymes and A.B. Enzymes. These companies have greater resources in these markets than we do and have long-term supply arrangements already in place with customers. Our ability to compete in these markets may be limited by our relatively late entrance. We also face competition in both the fine chemicals and small molecule pharmaceutical markets from emerging companies, like Zymergen and Gingko Bioworks, who offer engineered microbe metabolic pathway approaches to these markets.

Core Technology

We are a leader in the field of protein engineering to create novel biocatalysts. Both our pharmaceuticals and fine chemicals businesses rely on our core technology. We are aware that other companies, organizations and persons have developed technologies that appear to have some similarities to our patented proprietary technologies. For example, we are aware that other companies, including DSM, Bayer and BASF, have alternative methods for obtaining and generating genetic diversity or use mutagenesis techniques to produce genetic diversity. In addition, academic institutions such as the California Institute of Technology, the Max Planck Institute and the Austrian Centre of Industrial Biotechnology are also working in this field. This field is highly competitive with companies and academic and research institutions actively seeking to develop technologies that could be competitive with our technologies.

Technological developments by others may result in our products and technologies, as well as products manufactured by our customers using our biocatalysts, becoming obsolete. We monitor publications and patents that relate to directed molecular evolution to be aware of developments in the field and evaluate appropriate courses of action in relation to these developments.

Many of our competitors have substantially greater manufacturing, financial, research and development, personnel and marketing resources than we do. As a result, our competitors may be able to develop competing and/or superior technologies and processes, and compete more aggressively and sustain that competition over a longer period of time than we could. Our technologies and products may be rendered obsolete or uneconomical by technological advances or entirely different approaches developed by one or more of our competitors.

OPERATIONS

Our corporate headquarters are located in Redwood City, California and provide general administrative support to our business and are the center of our research, development and business operations. We have limited internal manufacturing capacity at our headquarters in Redwood City. We expect to rely on third-party manufacturers for commercial production of our biocatalysts for the foreseeable future. Our in-house manufacturing is dedicated to producing both Codex® biocatalyst panels and kits and enzymes for use by our customers in pilot scale production. We also supply initial commercial quantities of biocatalysts for use by our collaborators to produce pharmaceutical intermediates and manufacture biocatalysts that we sell. In the first quarter of 2021, we entered into an arrangement with a lessor to lease a facility in San Carlos, California to serve as additional office and research and development laboratory space which we expect to occupy in November 2021. Please see Note 15, "*Segment, Geographical and Other Revenue Information*" in the Notes to our Consolidated Financial Statements set forth in Item 8 of this Annual Report on Form 10-K for a description of our revenues and long-lived assets both within and outside of the United States. Please see Note 15, "*Segment, Geographical and Other Revenue Information*" for a description of our revenues and long-lived assets both within and outside of the United States, and with respect to the San Carlos facility, please see Note 17, "*Subsequent Events*" in the Notes to our Consolidated Financial Statements set forth in Item 8 of this Annual Report on Form 10-K.

Our research and development operations include efforts directed towards engineering biocatalysts, bioprocess development, cellular engineering, biocatalyst screening, metabolites, strain improvement, fermentation development and process engineering. We conduct enzyme evolution, enzyme production development, microbial bioprocess development, cellular engineering, microbial evolution and process engineering evaluations and design primarily at our headquarters in Redwood

City, California. For more information on our research and development expenditures, see Item 8 of this Annual Report on Form 10-K. Manufacturing of our enzymes is conducted primarily in three locations, at our in-house facility in Redwood City, California and at third-party contract manufacturing organizations, Lactosan GmbH & Co. KG ("Lactosan") in Kapfenberg, Austria and DPhar S.p.A. ("DPhar") in Anagni, Italy. Generally, we perform smaller scale manufacturing in-house and outsource the larger scale manufacturing and a large percentage of our production of novel enzymes to contract manufacturing organizations.

GOVERNMENT REGULATION

In the United States, the FDA extensively regulates, among other things, the research, development, testing, manufacture, quality control, import, export, safety, effectiveness, labeling, packaging, storage, distribution, record keeping, approval, advertising, promotion, marketing, post-approval monitoring, and post-approval reporting of drug and biologic products under the Federal Food, Drug and Cosmetic Act, its implementing regulations and other laws, including, in the case of biologics, the Public Health Service Act. Our biotherapeutic product candidates are subject to regulation by the FDA as biologics. Biologics require the submission of a biologics license application ("BLA") and licensure, which constitutes approval, by the FDA before being marketed in the United States. We, along with third-party contractors and our collaborators, will be required to navigate the various preclinical, clinical and commercial approval requirements of the governing regulatory agencies of the countries in which we wish to conduct studies or seek approval or licensure of our product candidates. The process of obtaining regulatory approvals and the subsequent compliance with applicable federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources.

The process required by the FDA before a biologic product may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests and animal studies performed in accordance with the FDA's good laboratory practice ("GLP") regulations;
- submission to the FDA of an IND, which must become effective before clinical trials in the United States may begin;
- approval by an institutional review board ("IRB"), or ethics committee at each clinical site before the trial is commenced;
- performance of adequate and well-controlled human clinical trials to establish the safety, purity, and potency of the product candidate for each proposed indication, conducted in accordance with the FDA's good clinical practice ("GCP") regulations;
- preparation and submission to the FDA of a BLA after completion of all pivotal clinical trials:
- satisfactory completion of an FDA Advisory Committee review, if applicable;
- a determination by the FDA within 60 days of its receipt of a BLA to file the application for review;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with current good manufacturing practice ("cGMP") regulations and to assure that the facilities, methods and controls are adequate to preserve the biological product's continued safety, purity and potency, and of selected clinical investigation sites to assess compliance with Good Clinical Practices, or GCPs; and
- FDA review and approval of the BLA prior to any commercial marketing, sale or distribution of the product.

Preclinical and Clinical Trials

Once a product candidate is identified for development, it enters the preclinical testing stage. Preclinical studies include laboratory evaluations of drug chemistry, formulation and stability, as well as studies to evaluate toxicity in animals, which must be conducted in accordance with GLP requirements. The results of preclinical studies, together with manufacturing information and analytical data, are submitted to the FDA as part of an IND. An IND is a request for authorization from the FDA to administer an investigational new drug to humans. The central focus of an IND submission is on the general investigational plan and the protocol(s) for clinical studies. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises concerns or questions about the conduct of the clinical trial, including concerns that human research subjects will be exposed to unreasonable health risks, and imposes a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin.

A separate submission to an existing IND must also be made for each successive clinical trial conducted during product development, and the FDA must grant permission, either explicitly or implicitly by not objecting, before each clinical trial can begin. Progress reports detailing the results of the clinical trials, among other information, must be submitted at least annually to the FDA and written IND safety reports must be submitted to the FDA and the investigators for serious and unexpected suspected adverse events, findings from other studies or animal or in vitro testing that suggest a significant risk for human subjects and any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure.

Clinical trials involve the administration of the product candidate to human subjects under the supervision of qualified investigators in accordance with GCPs, which include the requirement that all research subjects provide their informed consent for their participation in any clinical study. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial and the parameters and criteria to be used in monitoring safety and evaluating effectiveness. Each protocol must be submitted to the FDA as part of the IND. An independent IRB for each investigator site proposing to participate in a clinical trial must also review and approve the clinical trial and its informed consent form before it can begin at that site, and the IRB must monitor the clinical trial until it is completed. The FDA, the IRB, or the sponsor may suspend or discontinue a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk or that the trial is unlikely to meet its stated objectives. Some studies also include oversight by an independent group of qualified experts organized by the clinical study sponsor, known as a data safety monitoring board, which provides authorization for whether or not a study may move forward at designated check points based on access to certain data from the study and may halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy. There are also requirements governing the reporting of ongoing clinical studies and clinical study results to public registries.

For purposes of BLA approval, clinical trials are typically conducted in three sequential phases, which may overlap or be combined.

- *Phase 1*-Phase 1 clinical trials involve initial introduction of the investigational product into healthy human subjects or patients with the target disease or condition. These studies are typically designed to test the safety, dosage tolerance, absorption, metabolism and distribution of the investigational product in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence of effectiveness.
- *Phase 2*-Phase 2 clinical trials typically involve administration of the investigational product to a limited patient population with a specified disease or condition to evaluate the preliminary efficacy, optimal dosage and dosing schedule and to identify possible adverse side effects and safety risks.
- *Phase 3*-Phase 3 clinical trials typically involve administration of the investigational product to an expanded patient population to further evaluate dosage, to provide statistically significant evidence of clinical efficacy and to further test for safety, generally at multiple geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the investigational product and to provide an adequate basis for product approval and physician labeling.

In some cases, the FDA may condition approval of a BLA on the sponsor's agreement to conduct additional clinical trials to further assess the biologic's safety and effectiveness after BLA approval. Such post-approval clinical trials are typically referred to as Phase 4 clinical trials. Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the biologic and finalize a process for manufacturing the biologic in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and manufacturers must develop, among other things, methods for testing the identity, strength, quality and purity of the final biological product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

Although most clinical research performed in the United States in support of a BLA must be authorized in advance by the FDA, under the IND regulations and procedures described above, there are certain circumstances under which clinical trials can be conducted without submission of an IND. For example, a sponsor who wishes to conduct a clinical trial outside the United States may, but need not, obtain FDA authorization to conduct the clinical trial under an IND.

BLA Submission and FDA Review

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, the results of preclinical studies and clinical trials, together with other detailed information, including extensive manufacturing information and information on the composition of the biologic, are submitted to the FDA in the form of a BLA requesting approval to market the biologic for one or more specified indications. The BLA must include all relevant data available from preclinical and

clinical studies, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product's chemistry, manufacturing, controls, and proposed labeling, among other things. Data can come from company-sponsored clinical studies intended to test the safety and effectiveness of a use of the product, or from a number of alternative sources, including studies initiated by investigators. The submission of a BLA requires payment of a substantial user fee unless a waiver is granted. Each BLA submitted to the FDA is reviewed for administrative completeness and reviewability within 60 days of the FDA's receipt of the application. If the BLA is found to be complete, the FDA will file the BLA, triggering a full substantive review of the application. The FDA may refuse to file any BLA that it deems incomplete or not properly reviewable at the time of submission.

Once a BLA has been accepted for filing under the Prescription Drug User Fee Act, the FDA has a goal of reviewing BLAs within ten months of the 60-day filing date for BLAs designated for standard review or six months for priority review, but the overall timeframe is often extended by FDA requests for additional information or clarification. The FDA reviews a BLA to determine, among other things, whether the biological product is safe, pure and potent and whether the facility or facilities in which it is manufactured meet standards designed to assure the product's continued safety, purity and potency. The FDA may refer the application to an advisory committee for review, evaluation and recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations.

Before approving a BLA, the FDA will inspect the facility or the facilities at which the biologic product is manufactured, and will not license the product unless cGMP compliance is satisfactory. The FDA may also inspect the sites at which the clinical trials were conducted to assess their compliance with GCP requirements, and will not license the biologic unless compliance with such requirements is satisfactory. If the FDA determines that the application, manufacturing process or manufacturing facilities are not acceptable, it will outline the deficiencies in the submission and often will request additional testing or information. Notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

After the FDA evaluates a BLA and conducts inspections of manufacturing facilities where the investigational product and/or its drug substance will be produced, the FDA may issue an approval letter or a Complete Response Letter ("CRL"). An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A CRL will describe all of the deficiencies that the FDA has identified in the BLA, except that where the FDA determines that the data supporting the application are inadequate to support approval, the FDA may issue the CRL without first conducting required inspections, testing submitted product lots, and/or reviewing proposed labeling. In issuing the CRL, the FDA may recommend actions that the applicant might take to place the BLA in condition for approval, including requests for additional information or clarification. The FDA may delay or refuse approval of a BLA if applicable regulatory criteria are not satisfied, require additional testing or information and/or require post-marketing testing and surveillance to monitor safety or efficacy of a product.

If regulatory approval of a product is granted, such approval will be granted for particular indications and may entail limitations on the indicated uses for which such product may be marketed. For example, the FDA may approve the BLA with a Risk Evaluation and Mitigation Strategy ("REMS"), to ensure the benefits of the product outweigh its risks. A REMS is a safety strategy implemented to manage a known or potential serious risk associated with a product and to enable patients to have continued access to such medicines by managing their safe use, and could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. The FDA also may condition approval on, among other things, changes to proposed labeling or the development of adequate controls and specifications. Once approved, the FDA may withdraw the product approval if compliance with pre- and post-marketing requirements is not maintained or if problems occur after the product reaches the marketplace. The FDA may require one or more Phase 4 post-market studies and surveillance to further assess and monitor the product's safety and effectiveness after commercialization, and may limit further marketing of the product based on the results of these post-marketing studies.

Expedited Development and Review Programs

The FDA maintains several programs intended to facilitate and expedite development and review of new drugs and biologics to address unmet medical needs in the treatment of serious or life-threatening diseases or conditions.

For example a product candidate is eligible for Fast Track designation if it is intended to treat a serious or life-threatening disease or condition and demonstrates the potential to address unmet medical needs for such disease or condition. Fast Track designation applies to the combination of the product candidate and the specific indication for which it is being studied. Fast Track designation provides increased opportunities for sponsor meetings with the FDA during preclinical and clinical development, in addition to the potential for rolling review once a marketing application is filed, meaning that the FDA may review portions of the marketing application before the sponsor submits the complete application, if the sponsor provides a schedule for the submission of the sections of the BLA, the FDA agrees to accept sections of the BLA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the BLA.,

In addition, a product candidate may be eligible for Breakthrough Therapy designation if it is intended to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product candidate may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Breakthrough Therapy designation provides all the features of Fast Track designation in addition to intensive guidance on an efficient development program beginning as early as Phase 1, and FDA organizational commitment to expedited development, including involvement of senior managers and experienced review staff in a cross-disciplinary review, where appropriate.

Any product candidate submitted to the FDA for approval, including a product candidate with Fast Track or Breakthrough Therapy designation, may also be eligible for additional FDA programs intended to expedite the review process, including Priority Review designation and Accelerated Approval. A BLA is eligible for Priority Review if the product candidate is designed to treat a serious or life-threatening disease or condition, and if approved, would provide a significant improvement in safety or effectiveness in the treatment, diagnosis or prevention of a serious disease or condition.

Additionally, product candidates studied for their safety and effectiveness in treating serious or life-threatening diseases or conditions may receive Accelerated Approval if they can be shown to have an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or an effect on a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality which is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of accelerated approval, the FDA will generally require the sponsor to perform adequate and well-controlled post-marketing clinical studies to verify and describe the anticipated effect on irreversible morbidity or mortality or other clinical benefit. Products receiving accelerated approval may be subject to expedited withdrawal procedures if the sponsor fails to conduct the required post-marketing studies or if such studies fail to verify the predicted clinical benefit. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product.

Fast Track designation, Breakthrough Therapy designation, Priority Review designation and Accelerated Approval do not change the standards for approval but may expedite the development or review process. Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

Orphan drug designation and exclusivity

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biologic intended to treat a rare disease or condition, defined as a disease or condition with a patient population of fewer than 200,000 individuals in the United States, or a patient population greater than 200,000 individuals in the United States and when there is no reasonable expectation that the cost of developing and making available the drug or biologic in the United States will be recovered from sales in the United States for that drug or biologic. Orphan drug designation must be requested before submitting a BLA. After the FDA grants orphan drug designation, the generic identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA.

If a product candidate that has orphan drug designation subsequently receives the first FDA approval for a particular active ingredient for the disease for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications, including a full BLA, to market the same biologic for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity or if the FDA finds that the holder of the orphan drug exclusivity has not shown that it can assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the disease or condition for which the drug was designated. Orphan drug exclusivity does not prevent the FDA from approving a different drug or biologic for the same disease or condition, or the same drug or biologic for a different disease or condition. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the BLA application user fee.

A designated orphan drug many not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. In addition, orphan drug exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or, as noted above, if a second applicant demonstrates that its product is clinically superior to the approved product with orphan exclusivity or the manufacturer of the approved product is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition.

Post-Approval Requirements

Licensed biologics that are manufactured and distributed in the United States are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product distribution,

advertising and promotion and reporting of adverse experiences with the product. There is also a continuing, annual prescription drug program user fee.

Any biologics manufactured or distributed pursuant to FDA approvals remain subject to ongoing regulation by the FDA. Manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with ongoing regulatory requirements, including cGMP, which impose extensive procedural and documentation requirements. Failure to comply with statutory and regulatory requirements can subject a manufacturer to possible legal or regulatory action, such as warning letters, suspension of manufacturing, product seizures, injunctions, civil penalties or criminal prosecution.

Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information, requirements for post-market studies or clinical trials to assess new safety risks, imposition of distribution or other restrictions under a REMS. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters, untitled letters, or holds on post-approval clinical trials;
- refusal of the FDA to approve applications or supplements to approved applications, or suspension or revocation of product approvals;
- product seizure or detention, or refusal to permit the import or export of products;
- mandated modification of promotional materials and labeling and the issuance of corrective information;
- the issuance of safety alerts, Dear Healthcare Provider letters, press releases and other communications containing warnings or other safety information about the product; or
- injunctions or the imposition of civil or criminal penalties.

The FDA closely regulates the post-approval marketing and promotion of biologics, including standards and regulations for direct-to-consumer advertising, off-label promotion, industry-sponsored scientific and educational activities, and promotional activities involving the internet and social media. A company can make only those claims relating to safety and efficacy that are approved by the FDA. Physicians may prescribe legally available biologics for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances.

The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, impose stringent restrictions on manufacturers' communications regarding off-label use. Failure to comply with these requirements can result in adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties.

Biosimilars and Regulatory Exclusivity

As part of the Patient Protection and Affordable Care Act enacted in 2010, as amended by the Health Care and Education Reconciliation Act of 2010, the Biologics Price Competition and Innovation Act ("BPCIA") established an abbreviated pathway for the approval of biosimilar and interchangeable biological products. The abbreviated regulatory pathway provides legal authority for the FDA to review and approve biosimilar biologics based on their similarity to an existing brand product, referred to as a reference product, including the possible designation of a biosimilar as interchangeable with a brand product.

Biosimilarity, which requires that there be no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency, can be shown through analytical studies, animal studies, and a clinical study or studies. Interchangeability requires that a product is biosimilar to the reference product and the product must demonstrate that it can be expected to produce the same clinical results as the reference product in any given patient and, for products that are administered multiple times to an individual, the biologic and the reference biologic may be alternated or switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic.

Under the BPCIA, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. Moreover, the extent to which a biosimilar, once approved, will be substituted for a reference product in a way that is similar to traditional generic substitution for non-biological drug products is not yet clear and will depend on a number of marketplace and regulatory factors that are still developing. In addition, the period of exclusivity provided by the BPCIA only operates against third parties seeking approval via the abbreviated pathway, but would not prevent third parties from pursuing approval via the traditional BLA approval pathway.

In addition, a biological product can also obtain pediatric market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric study in accordance with an FDA-issued "Written Request" for such a study. The BPCIA is complex and continues to be interpreted and implemented by the FDA.

Other Healthcare Laws

Pharmaceutical companies are subject to additional healthcare regulation and enforcement by the federal government and by authorities in the states and foreign jurisdictions in which they conduct their business and may constrain the financial arrangements and relationships through which we and our partners research, sell, market and distribute any products for which we obtain marketing approval. Such laws include, without limitation, state and federal anti-kickback, fraud and abuse, false claims, data privacy and security and transparency laws regarding drug pricing and payments and other transfer of value to physicians and other healthcare providers. If their operations are found to be in violation of any of such laws or any other governmental regulations that apply, they may be subject to penalties, including, without limitation, administrative, civil and criminal penalties, damages, fines, disgorgement, the curtailment or restructuring of operations, integrity oversight and reporting obligations, exclusion from participation in federal and state healthcare programs and individual imprisonment.

Coverage and Reimbursement

Sales of any product depend, in part, on the extent to which such product will be covered by third-party payors, such as federal, state, and foreign government healthcare programs, commercial insurance and managed healthcare organizations, and the level of reimbursement for such product by third-party payors. Decisions regarding the extent of coverage and amount of reimbursement to be provided are made on a plan-by-plan basis. These third-party payors are increasingly reducing reimbursements for medical products, drugs and services. In addition, the U.S. government, state legislatures and foreign governments have continued implementing cost-containment programs, including price controls, restrictions on coverage and reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit sales of any product. Decreases in third-party reimbursement for any product or a decision by a third-party payor not to cover a product could reduce physician usage and patient demand for the product and also have a material adverse effect on sales.

Healthcare Reform

In March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, each as amended (collectively known as the "ACA"), was enacted, which substantially changed the way healthcare is financed by both governmental and private insurers, and significantly affected the pharmaceutical industry. The ACA contained a number of provisions, including those governing enrollment in federal healthcare programs, reimbursement adjustments and changes to fraud and abuse laws. For example, the ACA:

- increased the minimum level of Medicaid rebates payable by manufacturers of brand name drugs from 15.1% to 23.1% of the average manufacturer price;
- required collection of rebates for drugs paid by Medicaid managed care organizations;
- required manufacturers to participate in a coverage gap discount program, under which they must agree to offer 70 percent point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D; and
- imposed a non-deductible annual fee on pharmaceutical manufacturers or importers who sell "branded prescription drugs" to specified federal government programs.

Since its enactment, there have been judicial and Congressional challenges to certain aspects of the ACA.

The U.S. Supreme Court is currently reviewing the constitutionality of the ACA in its entirety, and it is unclear how the Supreme Court will rule.

Other legislative changes have been proposed and adopted since the Affordable Care Act was enacted, including aggregate reductions of Medicare payments to providers of 2% per fiscal year, which was temporarily suspended from May 1, 2020 through March 31, 2021, and reduced payments to several types of Medicare providers. Moreover, there has recently been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries, proposed and enacted legislation and executive orders issued by the President designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and

manufacturer patient programs, and reform government program reimbursement methodologies for drug products. Individual states in the United States have also become increasingly active in implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

CUSTOMERS

We rely on a limited number of key customers for the majority of our revenues. Customers that provided 10% or more of our total revenues in any of the past three fiscal years consist of the following:

	Percentage of Total Revenues For the Years Ended December 31.		
Customers:	2020	2019	2018
Merck	26 %	28 %	29 %
Nestlé Health Science	11 %	15 %	22 %
Novartis	*	23 %	*
Tate & Lyle	*	*	13 %
Takeda	19 %	*	*

* Percentage was less than 10%

HUMAN CAPITAL RESOURCES

As of December 31, 2020, we had 181 full-time employees and part-time employees worldwide. Of these employees, 105 were engaged in research and development, 24 were engaged in operations and quality control and 52 were engaged in selling, general and administrative activities. None of our employees is represented by a labor union. Supported by our annual employee survey, we believe our relationship with our employees to be generally good. Our scientists, bioinformatics experts and other professionals work collaboratively as interdisciplinary teams to unlock and advance technological innovation.

Compensation, benefits and development

Our goal is to attract, motivate and retain talent with a focus on encouraging performance, promoting accountability and adhering to our company values. We offer competitive compensation and benefit programs including a company-matched 401(k) Plan, stock options for eligible employees, health savings and flexible spending accounts, paid time off, education and training programs, and employee assistance programs. We believe it is important to help build community and enabling our employees actively participate in community service projects and in company-sponsored philanthropic activities.

Diversity, inclusion and belonging

We are committed to our continued efforts to increase diversity and foster an inclusive work environment that supports the global workforce and the communities we serve. We recruit the best people for the job regardless of gender, ethnicity or other protected traits and it is our policy to fully comply with all laws applicable to discrimination in the workplace. Our diversity, equity and inclusion principles are also reflected in our employee training and policies. We continue to enhance our diversity, equity and inclusion policies which are guided by our executive leadership team.

Health and safety

We are committed to maintain a safe and healthy workplace for our employees. Our policies and practices are intended to protect our employees and surrounding communities in which we operate.

In 2020, in response to the COVID-19 pandemic, we implemented safety protocols and new procedures to protect our employees. These protocols include complying with social distancing and other health and safety standards as required by state and local government agencies, taking into consideration guidelines of the Centers for Disease Control and Prevention and other public health authorities. In addition, we modified the way we conduct many aspects of our business including the practice of social distancing, wearing face coverings mandated by state and local regulations, and maintaining a quarantine for employees determined to be in close contact with a COVID-19 case. For example, we implemented day-time shift hours in our

R&D and small scale manufacturing at our Redwood City pilot plant to minimize the number of employees in close proximity to each other and we have significantly expanded the use of virtual interaction whenever possible in our business. For a detailed discussion of the impact of the COVID-19 pandemic on our human capital resources, see “Risk Factors" Item 1A of this Form 10-K.

We also launched the Employee-Requested Work from Home Policy in late 2020. This policy establishes the process and criteria to enable Redwood City employees to request permission to work from home on a regular basis.

CORPORATE & AVAILABLE INFORMATION

We were incorporated in Delaware in January 2002 as a wholly-owned subsidiary of Maxygen, Inc. We commenced independent operations in March 2002, after licensing core enabling technology from Maxygen, Inc. Our principal corporate offices are located at 200 Penobscot Drive, Redwood City, California 94063 and our telephone number is (650) 421-8100. Our internet address is www.codexis.com. The information on, or that can be accessed through, our website is not incorporated by reference into this Annual Report on Form 10-K or any other filings we make with the U.S. Securities and Exchange Commission (the “SEC”).

We make available on or through our website certain reports and amendments to those reports that we file with, or furnish to, the SEC in accordance with the Exchange Act. These include our Annual Reports on Form 10-K, our Quarterly Reports on Form 10-Q and our Current Reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act. We make this information available on or through our website free of charge as soon as reasonably practicable after we electronically file the information with, or furnish it to, the SEC. Copies of this information may be obtained at the SEC website at www.sec.gov. The contents of these websites are not incorporated into this filing. Further, the references to website URLs are intended to be inactive textual references only.

ITEM 1A. RISK FACTORS

You should carefully consider the risks described below together with the other information set forth in this Annual Report on Form 10-K, which could materially affect our business, financial condition or future results. The risks described below are not the only risks facing our company. Risks and uncertainties not currently known to us or that we currently deem to be immaterial also may materially adversely affect our business, financial condition and/or operating results.

RISK FACTORS SUMMARY

The following is a summary of the principal factors that cause an investment in the company to be speculative or risky:

- The ongoing COVID-19 pandemic has adversely affected and may continue in the future to, directly or indirectly, adversely affect our business, results of operations and financial condition.
- During our operating history, the markets in which we have participated have changed significantly, which may make it difficult to evaluate our current business and predict our future performance.
- Our quarterly or annual operating results may fluctuate in the future. As a result, we may fail to meet or exceed the expectations of research analysts or investors, which could cause our stock price to decline.
- We have a history of net losses and we may not achieve or maintain profitability.
- We are dependent on our collaborators, and our failure to successfully manage these relationships could prevent us from developing and commercializing many of our products and achieving or sustaining profitability, and could lead to disagreements with our current or former collaborators.
- We are dependent on a limited number of customers.
- Our product supply agreements with customers have finite duration, may not be extended or renewed and generally do not require the customer to purchase any particular quantity or quantities of our products.
- With respect to customers purchasing our products for the manufacture of active pharmaceutical products (API) for which they have exclusivity due to patent protection, the termination or expiration of such patent protection and any resulting generic competition may materially and adversely affect our revenues, financial condition or results of operations.
- We are dependent on a limited number of products in our biocatalysts business.
- We are dependent on a limited number of contract manufacturers for large scale production of substantially all of our enzymes.
- If we are unable to develop and commercialize new products for the pharmaceutical, fine chemicals, biotherapeutics, diagnostics and life science tools markets, our business and prospects will be harmed.
- Our biotherapeutic programs are early stage, highly regulated and expensive. Our ability to obtain additional development partners for the programs, to advance our product candidates to clinical trials and to ultimately receive regulatory approvals is highly uncertain.
- If either Nestlé Health Science or Takeda terminate their development programs under their respective license agreements with us, any potential revenue from those license agreements will be significantly reduced or non-existent, and our results of operations and financial condition will be materially and adversely affected.
- Our business could be adversely affected if our customers' products are not received well in the market, if their products, or the processes used by our customers to manufacture their final products, fail to be approved, or if our customers discontinue their development activities for any reason.
- We or our customers may not be able to obtain regulatory approval for the use of our products in food and food ingredients, if required, and, even if approvals are obtained, complying on an ongoing basis with the numerous regulatory requirements applicable to these products will be time-consuming and costly.
- Our efforts to deploy our technology in the life science tools markets may fail.
- The regulatory approval processes of the FDA and comparable foreign authorities are lengthy, time consuming and inherently unpredictable, and if we are ultimately unable to obtain regulatory approval for our product candidates, our business will be substantially harmed.
- Clinical trials are difficult to design and implement, expensive, time-consuming and involve an uncertain outcome, and the inability to successfully conduct clinical trials and obtain regulatory approval for our product candidates would substantially harm our business.

- Results of preclinical studies and early clinical trials of product candidates may not be predictive of results of later studies or trials. Our product candidates may not have favorable results in later clinical trials, if any, or receive regulatory approval.
- If any of our product candidates do not work as intended or cause undesirable side effects, it could hinder or prevent receipt of regulatory approval or realization of commercial potential for them or our other product candidates and could substantially harm our business.
- Even if we obtain regulatory approval for any products that we develop alone or with collaborators, such products will remain subject to ongoing regulatory requirements, which may result in significant additional expense.
- Our efforts to prosecute and protect our intellectual property may not be successful.
- Our ability to compete may decline if we do not adequately protect our proprietary technologies or if we lose some of our intellectual property rights.
- Third parties may claim that we are infringing their intellectual property rights or other proprietary rights, which may subject us to costly and time-consuming litigation and prevent us from developing or commercializing our products.
- We may be involved in lawsuits to protect or enforce our intellectual property rights, which could be expensive, time-consuming and unsuccessful.
- We may not be able to enforce our intellectual property rights throughout the world.
- If our biocatalysts, or the genes that code for our biocatalysts, are stolen, misappropriated or reverse engineered, others could use these biocatalysts or genes to produce competing products.
- Confidentiality agreements with employees and others may not adequately prevent disclosures of trade secrets and other proprietary information.
- We may need additional capital in the future in order to expand our business.
- If we are unable to maintain effective internal control over financial reporting in the future, the accuracy and timeliness of our financial reporting may be adversely affected.
- We are dependent on information technology systems, infrastructure and data, and any failure of these systems could harm our business. Security breaches, loss of data, and other disruptions could compromise sensitive information related to our business or prevent us from accessing critical information and expose us to liability, which could adversely affect our business, results of operations and financial condition.
- Competitors and potential competitors who have greater resources and experience than we do may develop products and technologies that make ours obsolete or may use their greater resources to gain market share at our expense.
- Business interruptions resulting from disasters or other disturbances could delay us in the process of developing our products and could disrupt our sales. Our business continuity and disaster recovery plans may not adequately protect us from a serious disaster or other disturbance.
- Epidemic diseases, or the perception of their effects, could have a material adverse effect on our business, financial condition, results of operations or cash flows.
- Sales of a substantial number of shares of our common stock in the public market could cause our stock price to fall.

Risks Relating to Our Business and Strategy

The ongoing COVID-19 pandemic has adversely affected and may continue in the future to, directly or indirectly, adversely affect our business, results of operations and financial condition.

In the United States, the COVID-19 pandemic has and may continue in the future to, directly or indirectly, adversely affect our business, results of operations and financial condition, including as a result of compliance with governmental orders governing the operation of businesses during the pandemic, the temporary closure of our Redwood City, California facilities and disruption of our research and development operations. We believe that these disruptions have had a negative impact on revenue for the twelve months ended December 31, 2020, although we are unable to fully determine and quantify the extent to which this pandemic has affected the amount and timing of our total revenues. In the future, our business could be materially adversely affected, directly or indirectly, by the widespread outbreak of contagious disease, including the ongoing COVID-19 pandemic. National, state and local governments in affected regions have implemented and may continue to implement safety

precautions, including quarantines, border closures, increased border controls, travel restrictions, governmental orders and shutdowns, business closures, cancellations of public gatherings and other measures. Organizations and individuals are taking additional steps to avoid or reduce infection, including limiting travel and staying home from work. These measures are disrupting normal business operations both in and outside of affected areas and have had significant negative impacts on businesses and financial markets worldwide.

The potential impact and duration of COVID-19 or another pandemic or public health crisis has had and could continue to have, significant repercussions across regional, national and global economies and financial markets, and could trigger a period of regional, national and global economic slowdown or regional, national or global recessions. The outbreak of COVID-19 in many countries continues to adversely impact regional, national and global economic activity and has contributed to significant volatility and negative pressure in financial markets. As a result, we may experience difficulty accessing debt and equity capital on attractive terms, or at all, due to the severe disruption and instability in the global financial markets. In addition, our customers may terminate or amend their agreements for the purchase of our products or services due to bankruptcy, lack of liquidity, lack of funding, operational failures, or other reasons.

We continue to monitor our operations and applicable government recommendations, and we have made modifications to our normal operations because of the COVID-19 pandemic, including requiring most office-based employees to work remotely. Notwithstanding these measures, the COVID-19 pandemic could affect the health and availability of our workforce as well as those of the third parties we rely on taking similar measures. If members of our management and other key personnel in critical functions across our organization are unable to perform their duties or have limited availability due to COVID-19, we may not be able to execute on our business strategy and/or our operations may be negatively impacted. We may also experience limitations in employee resources, including because of sickness of employees or their families or the desire of employees to avoid contact with individuals or large groups of people. In addition, we have experienced and will continue to experience disruptions to our business operations resulting from quarantines, self-isolations and other restrictions on the ability of our employees to perform their jobs.

The COVID-19 pandemic has disrupted, and may continue to disrupt, our business operations. The extent and severity of the impact on our business and clinical trials will be determined largely by the extent of disruptions in the supply chains for our products and product candidates; disruptions in access by patients to therapies for which our products are components of the supply chain; delays in the performance of R&D service work, and delays in current and future clinical trials that we or our collaboration partners may conduct. In addition, the impact of the COVID-19 pandemic on the operations of the FDA and other health authorities may delay potential approvals of product candidates for which our products are components of the supply chain.

While it is not possible at this time to estimate the entirety of the impact that the COVID-19 pandemic will have on our business, operations, employees, customers, suppliers or our collaboration partners, continued spread of COVID-19, measures taken by governments, actions taken to protect employees and the broad impact of the pandemic on all business activities may materially and adversely affect our business, results of operations and financial condition.

During our operating history, the markets in which we have participated have changed significantly, which may make it difficult to evaluate our current business and predict our future performance.

Our company has been in existence since January 2002. From 2002 until 2005, our operations focused on organizing and staffing our company and developing our technology platform. In 2005, we recognized our first revenues from product sales. From 2006 to August 2012, a major portion of our business revolved around our research and development collaboration with Shell with respect to advanced biofuels. The Shell collaboration was terminated in August 2012 and did not contribute to our revenues after the termination. As a result of the termination of the Shell collaboration, we undertook a significant restructuring of our operations and refocused our business on the biocatalysis market. In November 2013, we announced that we had begun to wind down our CodeXyme® cellulase enzymes program, and that we had stopped further development of our CodeXol® detergent alcohols program in the third quarter of 2013. Our Novel Biotherapeutics business is relatively new to Codexis. As a result of these changes in our business and any changes to our business focus that we may make as we move forward, our operating history in past periods may not provide a basis to evaluate our current business or be indicative of our future performance. We have encountered and will continue to encounter risks and difficulties frequently experienced by young companies in rapidly changing industries. If we do not address these risks successfully, our business will be harmed.

Our quarterly or annual operating results may fluctuate in the future. As a result, we may fail to meet or exceed the expectations of research analysts or investors, which could cause our stock price to decline.

Our financial condition and operating results have varied significantly in the past and may continue to fluctuate from quarter to quarter and year to year in the future due to a variety of factors, many of which are beyond our control. Factors relating to our

business that may contribute to these fluctuations include the following factors, as well as other factors described elsewhere in this report:

- our ability to achieve or maintain profitability;
- our relationships with, and dependence on, collaborators in our principal markets;
- our dependence on a limited number of customers;
- our product supply agreements with customers have finite duration, may not be extended or renewed and generally do not require the customer to purchase any particular quantity or quantities of our products.
- with respect to customers purchasing our products for the manufacture of active pharmaceutical products (API) for which they have exclusivity due to patent protection, the termination or expiration of such patent protection and any resulting generic competition may materially and adversely affect our revenues, financial condition or results of operations;
- our dependence on a limited number of products in our biocatalysis business;
- our reliance on a limited number of contract manufacturers for large scale production of substantially all of our enzyme products;
- our ability to develop and successfully commercialize new products for the biocatalysis market(s);
- our ability to obtain additional development partners for our biotherapeutic programs;
- potential of Nestlé Health Science or Takeda terminating any development program under their license agreements with us;
- our ability to deploy our technology platform in the fine chemicals market;
- the success of our customers' pharmaceutical products in the market and the ability of such customers to obtain regulatory approvals for products and processes;
- our or our customers' ability to obtain regulatory approval for the sale and manufacturing of food products using our enzymes;
- our ability to deploy our technology platform in life science tools markets;
- our ability to successfully achieve domestic and foreign regulatory approval for product candidates;
- our ability to successfully design and execute clinical testing at a reasonable cost and on an acceptable time-frame;
- our dependence on product candidates which could unexpectedly fail at any stage of preclinical or clinical development;
- our dependence on product candidates which may lack the ability to work as intended or cause undesirable side effects;
- our dependency on third parties to conduct clinical trials, research, and preclinical studies;
- our ability to successfully prosecute and protect our intellectual property;
- our ability to compete if we do not adequately protect our proprietary technologies or if we lose some of our intellectual property rights;
- our ability to avoid infringing the intellectual property rights of third parties;
- our involvement in lawsuits to protect or enforce our patents or other intellectual property rights;
- our ability to enforce our intellectual property rights throughout the world;
- our dependence on, and the need to attract and retain, key management and other personnel;
- our ability to prevent the theft or misappropriation of our biocatalysts, the genes that code for our biocatalysts, know-how or technologies;
- our ability to protect our trade secrets and other proprietary information from disclosure by employees and others;
- our ability to obtain substantial additional capital that may be necessary to expand our business;
- our ability to comply with the terms of our credit facility;
- our ability to timely pay debt service obligations;
- our customers' ability to pay amounts owed to us in a timely manner;

- our ability to avoid charges to earnings as a result of any impairment of goodwill, intangible assets or other long-lived assets;
- changes in financial accounting standards or practices may cause adverse, unexpected financial reporting fluctuations and affect our reported results of operations;
- our ability to maintain effective internal control over financial reporting;
- our dependency on information technology systems, infrastructure and data;
- our ability to control and to improve product gross margins;
- our ability to protect against risks associated with the international aspects of our business;
- the cost of compliance with European Union chemical regulations;
- potential advantages that our competitors and potential competitors may have in securing funding or developing products;
- our ability to accurately report our financial results in a timely manner;
- results of regulatory tax examinations;
- business interruptions due to natural disasters, disease outbreaks or other events beyond our control;
- public concerns about the ethical, legal and social ramifications of genetically engineered products and processes;
- our ability to integrate our current business with any businesses that we may acquire in the future;
- our ability to properly handle and dispose of hazardous materials in our business;
- potential product liability claims;
- changes to tax law and related regulations could materially affect our tax obligations and effective tax rate; and
- our ability to use our net operating loss carryforwards to offset future taxable income.

Due to the various factors mentioned above, and others, the results of any prior quarterly or annual periods should not be relied upon as indications of our future operating performance.

We have a history of net losses and we may not achieve or maintain profitability.

We have incurred net losses since our inception, including losses of $24.0 million in 2020, $11.9 million in 2019 and $10.9 million in 2018. As of December 31, 2020 and 2019, we had an accumulated deficit of $366.4 million and $342.4 million, respectively. If we are unable to expand our biocatalysis business, through new or expanded collaborations, development of new products or services, or increased sales of existing products and services, our net losses may increase and we may never achieve profitability. In addition, some of our collaboration agreements, including our collaboration with Nestlé Health Science and Takeda, provide for milestone payments and/or future royalty payments, which we will only receive if we and our collaborators develop and commercialize products. We also may fund development of additional proprietary biocatalysis and/or biotherapeutic products. There can be no assurance that any of these products will become commercially viable or that we will ever achieve profitability on a quarterly or annual basis. If we fail to achieve profitability, or if the time required to achieve profitability is longer than we anticipate, we may not be able to continue our business. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis.

We are dependent on our collaborators, and our failure to successfully manage these relationships could prevent us from developing and commercializing many of our products and achieving or sustaining profitability, and could lead to disagreements with our current or former collaborators.

Our ability to maintain and manage collaborations in our markets is fundamental to the success of our business. We currently have license agreements, research and development agreements, supply agreements and/or distribution agreements with various collaborators. For example, we have ongoing collaborations with GSK, Merck, Novartis, Nestlé Health Science and Takeda that are important to our business and financial results. We may have limited or no control over the amount or timing of resources that any collaborator is able or willing to devote to our partnered products or collaborative efforts. Any of our collaborators may fail to perform its obligations. These collaborators may breach or terminate their agreements with us or otherwise fail to conduct their collaborative activities successfully and in a timely manner. Further, our collaborators may not develop products arising out of our collaborative arrangements or devote sufficient resources to the development, manufacture, marketing or sale of these products. Moreover, disagreements with a collaborator could develop, and any conflict with a collaborator could lead to litigation and could reduce our ability to enter into future collaboration agreements and negatively impact our relationships

with one or more existing collaborators. If any of these events occur, especially if they occur in our collaborations with GSK, Merck, Novartis, Nestlé Health Science or Takeda, or if we fail to maintain our agreements with our collaborators, we may not be able to commercialize our existing and potential products or grow our business or generate sufficient revenues to support our operations, we may not receive contemplated milestone payments and royalties under the collaboration, and we may be involved in litigation. Our collaboration opportunities could be harmed and our financial condition and results of operations could be negatively affected if:

- we do not achieve our research and development objectives under our collaboration agreements in a timely manner or at all;
- we develop products and processes or enter into additional collaborations that conflict with the business objectives of our other collaborators;
- we, our collaborators and/or our contract manufacturers do not receive the required regulatory and other approvals necessary for the commercialization of the applicable product;
- we disagree with our collaborators as to rights to intellectual property that are developed during the collaboration, or their research programs or commercialization activities;
- we are unable to manage multiple simultaneous collaborations;
- our collaborators or licensees are unable or unwilling to implement or use the technology or products that we provide or license to them;
- our collaborators become competitors of ours or enter into agreements with our competitors;
- our collaborators become unable or less willing to expend their resources on research and development or commercialization efforts due to general market conditions, their financial condition or other circumstances beyond our control; or
- our collaborators experience business difficulties, which could eliminate or impair their ability to effectively perform under our agreements.

Even after collaboration relationships expire or terminate, some elements of the collaboration may survive. For instance, certain rights, licenses and obligations of each party with respect to intellectual property and program materials may survive the expiration or termination of the collaboration. Disagreements or conflicts between and among the parties could develop even though the collaboration has ended. These disagreements or conflicts could result in expensive arbitration or litigation, which may not be resolved in our favor.

Finally, our business could be negatively affected if any of our collaborators or suppliers undergoes a change of control or were to otherwise assign the rights or obligations under any of our agreements.

We are dependent on a limited number of customers.

Our current revenues are derived from a limited number of key customers. For the years ended December 31, 2020 and 2019, customers that each individually contributed 10% or more of our total revenue accounted for 56% and 66% of our total revenues in 2020 and 2019, respectively. We expect a limited number of customers to continue to account for a significant portion of our revenues for the foreseeable future. This customer concentration increases the risk of quarterly fluctuations in our revenues and operating results. The loss or reduction of business from one or a combination of our significant customers could, materially adversely affect our revenues, financial condition and results of operations.

Our product supply agreements with customers have finite duration, may not be extended or renewed and generally do not require the customer to purchase any particular quantity or quantities of our products.

Our product supply agreements with customers generally have a finite duration, may not be extended or renewed and generally do not require the customer to purchase any particular quantity or quantities of our products. While our products are not considered commodities and may not be easily substituted for by our customers, particularly when our products are used in the manufacture of active pharmaceutical ingredients, our customers may nevertheless terminate or fail to renew their product supply agreements with us or significantly curtail their purchases thereunder under certain circumstances. Any such termination or reduction could materially adversely affect our revenues, financial condition and results of operations. For the year ended December 31, 2020, we derived a majority of our product revenue from these product supply agreements.

With respect to customers purchasing our products for the manufacture of active pharmaceutical products (API) for which they have exclusivity due to patent protection, the termination or expiration of such patent protection and any resulting generic competition may materially and adversely affect our revenues, financial condition or results of operations.

With respect to customers purchasing our products for the manufacture of API for which exclusivity due to patent protection has or is about to expire, we can expect that the quantity of our products sold to such customers for such products may decline as generic competition for the API increases. While we anticipate that we may, in some cases, also be able to sell products to these generic competitors for the manufacture of these APIs, the overall effect on our revenues, financial condition and results of operations could be materially adverse.

We are dependent on a limited number of products in our biocatalysts business.

Our current product sales are derived from a limited number of biocatalyst products. We expect a limited number of biocatalyst products to continue to account for a significant portion of our product sales for the foreseeable future. This product concentration increases the risk of quarterly fluctuations in our revenues and operating results. The loss or reduction of business of one or a combination of our significant products could materially adversely affect our revenues, financial condition and results of operations.

We are dependent on a limited number of contract manufacturers for large scale production of substantially all of our enzymes.

Manufacturing of our enzymes is conducted primarily in three locations: our in-house facility in Redwood City, California, and at two third-party contract manufacturing organizations, Lactosan GmbH & Co. KG ("Lactosan"), in Kapfenberg, Austria, and DPhar S.p.A. ("DPhar"), in Anagni, Italy. Generally, we perform smaller scale manufacturing in-house and outsource the larger scale manufacturing to these contract manufacturers. We have limited internal capacity to manufacture enzymes. As a result, we are dependent upon the performance and capacity of third-party manufacturers for the larger scale manufacturing of the enzymes used in our pharmaceutical and fine chemicals business.

Accordingly, we face risks of difficulties with, and interruptions in, performance by third party manufacturers, the occurrence of which could adversely impact the availability, launch and/or sales of our enzymes in the future. Manufacturing delays at a contract manufacturer could negatively affect our business, reputation, results of operations and financial condition. The failure of any contract manufacturer to supply us enzymes on a timely basis, or to manufacture our enzymes in compliance with our specifications or applicable quality requirements or in volumes sufficient to meet demand, would adversely affect our ability to sell pharmaceutical and fine and complex chemicals products, could harm our relationships with our collaborators or customers and could negatively affect our revenues and operating results. We may be forced to secure alternative sources of supply, which may be unavailable on commercially acceptable terms, and could cause delays in our ability to deliver products to our customers, increase our costs and decrease our profit margins.

We currently have supply agreements in place with Lactosan and DPhar. In the absence of a supply agreement, a contract manufacturer will be under no obligation to manufacture our enzymes and could elect to discontinue their manufacture at any time. If we require additional manufacturing capacity and are unable to obtain it in sufficient quantity, we may not be able to increase our product sales, or we may be required to make substantial capital investments to build that capacity or to contract with other manufacturers on terms that may be less favorable than the terms we currently have with our suppliers. If we choose to build our own additional manufacturing facility, it could take two years or longer before our facility is able to produce commercial volumes of our enzymes. Any resources we expend on acquiring or building internal manufacturing capabilities could be at the expense of other potentially more profitable opportunities. In addition, if we contract with other manufacturers, we may experience delays of several months in qualifying them, which could harm our relationships with our collaborators or customers and could negatively affect our revenues or operating results.

If we are unable to develop and commercialize new products for the pharmaceutical, fine chemicals, biotherapeutics, diagnostics and other life science tools markets, our business and prospects will be harmed.

We plan to launch new products for the pharmaceutical, fine chemicals, biotherapeutics, diagnostics and other life science tools markets. These efforts are subject to numerous risks, including the following:

- customers in these markets may be reluctant to adopt new manufacturing processes that use our enzymes;
- we may be unable to successfully develop the enzymes or manufacturing processes for our products in a timely and cost-effective manner, if at all;

- we may face difficulties in transferring the developed technologies to our customers and the contract manufacturers that we may use for commercial scale production of intermediates and enzymes in these markets;
- the contract manufacturers that we may use may be unable to scale their manufacturing operations to meet the demand for these products and we may be unable to secure additional manufacturing capacity;
- customers may not be willing to purchase these products for these markets from us on favorable terms, if at all;
- we may face product liability litigation, unexpected safety or efficacy concerns and product recalls or withdrawals;
- changes in laws or regulations relating to the pharmaceutical industry or the industries into which we sell our fine chemicals products, including the food industry, could cause us to incur increased costs of compliance or otherwise harm our business;
- our customers' products may experience adverse events or face competition from new products, which would reduce demand for our products;
- we may face pressure from existing or new competitive products; and
- we may face pricing pressures from existing or new competitors, some of which may benefit from government subsidies or other incentives.

Our biotherapeutic programs are early stage, highly regulated and expensive. Our ability to obtain additional development partners for the programs, to advance our product candidates to clinical trials and to ultimately receive regulatory approvals is highly uncertain.

We are developing and have developed novel biotherapeutic candidates, including CDX-6114, the novel oral enzyme product candidate for the treatment of PKU that we licensed to Nestlé Health Science. We are also developing protein sequences for use in gene therapy products for Fabry Disease, Pompe Disease, and an undisclosed blood factor for Takeda. The successful development of biotherapeutic candidates involves many risks and uncertainties, requires long timelines and may lead to uncertain results. In addition, drug development is highly regulated and requires areas of expertise and capital resources we do not currently possess. In order to market a biologic product in the United States, we must undergo the following process required by the FDA:

- completion of extensive preclinical laboratory tests and preclinical animal studies, all performed in accordance with GLP requirements;
- submission to the FDA of an IND, which must become effective before human clinical studies may begin in the United States;
- approval by an independent IRB representing each clinical site before the clinical study may be initiated at the site;
- performance of adequate and well-controlled human clinical studies (generally divided into three phases) in accordance with GCP requirements to establish the safety and efficacy of the product candidate for each proposed indication;
- preparation of and submission to the FDA of a BLA after completion of all clinical studies;
- potential review of the product candidate by an FDA advisory committee;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facilities where the product candidate is produced to assess compliance with cGMP requirements; and
- FDA review and approval of a BLA prior to any commercial marketing or sale of the product in the United States.

If we fail to comply with applicable FDA or other regulatory requirements at any time during the drug development process, clinical testing, the approval process or after approval, we may become subject to administrative or judicial penalties, including the FDA's refusal to approve a pending application, withdrawal of an approval, warning letters, product recalls, and additional enforcement actions.

Our efforts to advance our biotherapeutic candidates that we develop are subject to numerous risks, including the following:

- The regulatory approval processes of the FDA and comparable foreign authorities are lengthy, time consuming and the results are inherently unpredictable. If we are ultimately unable to obtain regulatory approval for biotherapeutic product candidates, our business will be harmed. To obtain regulatory approval to market any product candidate, preclinical studies and costly and lengthy clinical trials are required, and the results of the studies and trials are highly uncertain. A failure of one or more pre-clinical or clinical trials can occur at any stage,

and many companies that have believed their drug candidates performed satisfactorily in pre-clinical and clinical testing have nonetheless failed to obtain marketing approval of their product candidates.

- We may find it difficult to enroll patients in our clinical trials for product candidates. Any enrollment difficulties could delay clinical trials and any potential product approval.
- We may experience difficulty or delay in obtaining the FDA's acceptance of an IND for product candidates we may seek to enter into clinical development, which would delay initiation of Phase 1 clinical testing. Delays in the commencement or completion of clinical testing could significantly affect our product development costs or the product development costs of our present and any future collaborators. We do not know whether planned clinical trials will begin on time or be completed on schedule, if at all. The commencement and completion of clinical trials can be delayed for a number of reasons. For example, a clinical trial may be suspended or terminated by us, by the IRB of the institution in which such trial is being conducted, or by the FDA due to a number of factors, including unforeseen safety issues, changes in governmental regulations or lack of adequate funding to continue the clinical trial.
- We have limited experience in drug development or regulatory matters related to drug development. As a result, we rely or will rely on third parties to conduct our pre-clinical and clinical studies, assist us with drug manufacturing and formulation and perform other tasks for us. If these third parties do not successfully carry out their responsibilities or comply with regulatory requirements, we may receive lower quality products or services, suffer reputational harm and not be able to obtain regulatory approval for product candidates.
- Our efforts to use CodeEvolver® protein engineering technology platform to generate new lead biotherapeutic candidates, whether under our collaborations with Nestlé Health Science, Takeda or otherwise, may not be successful in creating candidates of value.
- We will be exposed to potential product liability risks through the testing of experimental therapeutics in humans, which may expose us to substantial uninsured liabilities.
- Third parties may develop intellectual property that could limit our ability to develop, market and commercialize product candidates.
- Changes in methods of treatment of disease, such as gene therapy, could cause us to stop development of our product candidates or reduce or eliminate potential demand for CDX-6114, if approved, or any other product candidates that we may develop in the future.

If either Nestlé Health Science or Takeda terminate their development programs under their respective license agreements with us, any potential revenue from those license agreements will be significantly reduced or non-existent, and our results of operations and financial condition will be materially and adversely affected.

We have invested significant time and financial resources in the development of CDX-6114 and other product candidates for the treatment of HPA now included in the Nestlé License Agreement as well as in the development of candidates for the treatment of Fabry disease and Pompe disease which are now included in the Takeda Agreement.

Under the Nestlé License Agreement, we are eligible to receive from Nestlé Health Science development and approval milestones of up to $85.0 million, sales-based milestones of up to $250.0 million, and tiered royalties, at percentages ranging from the middle single digits to low double-digits, of net sales of products containing a licensed Compound as its sole active ingredient. Under the Takeda Agreement, we are eligible to earn up to $15.4 million of research and development fees and pre-clinical milestone payments from Takeda for the Initial Programs. We are eligible to receive certain development and commercialization milestone payments up to $100.0 million per target gene, the modulation of which would lead to the treatment of the disease indications by the applicable Product. We are also eligible to receive tiered royalties based on net sales of Products at percentages ranging from the middle-single digits to low single-digits. While we have received milestone payments under the Nestlé License Agreement to date there is no guarantee that we will receive further milestone payments under the Nestlé Agreement or Takeda Agreement in the future.

Under the Nestle Agreement and the Takeda Agreement, either Nestlé Health Science and Takeda, as applicable, may each terminate the entire agreement or specified programs thereunder at will under certain circumstances as described in more detail under "Item 1. Business--Our Market Opportunities--Pharmaceutical Market--Our Solutions for the Pharmaceutical Market--Biotherapeutic Product Discovery and Development" in this Annual Report on Form 10-K.

If Nestlé Health Science terminates its rights and obligations with respect to the Nestlé License Agreement and/or Takeda terminates its rights and obligations with respect to the Takeda Agreement, then depending on the timing of such event:

- the development of our product candidates subject to the respective agreements may be terminated or significantly delayed;
- our cash expenditures could increase significantly if it is necessary for us to hire additional employees and allocate scarce resources to the development and commercialization of product candidates;
- we would bear all of the risks and costs related to the further development and commercialization of product candidates that were previously the subject of the respective agreements, including the reimbursement of third parties; and
- in order to fund further development and commercialization of new product candidates or programs, we may need to seek out and establish alternative collaboration arrangements with third-party partners; this may not be possible, or we may not be able to do so on terms which are acceptable to us, in which case it may be necessary for us to limit the size or scope of one or more of our programs or increase our expenditures and seek additional funding by other means.

Our efforts to deploy our technology platform in the fine chemicals market may fail.

We have recently begun to use our CodeEvolver® protein engineering technology platform to develop new products in the fine chemicals markets. We do not know if we can successfully compete in this new market. This new market is well established and consists of numerous large, well-funded entrenched market participants who have long and established track records and customer relationships. We have currently developed products in the food sector of this market and these products, or any other products that we may develop in the future for the fine chemicals market may not succeed in displacing current products. If we succeed in commercializing new products for the fine chemicals market, we may not generate significant revenues and cash flows from these activities. The failure to successfully deploy products in the fine chemicals space may limit our growth and have a material adverse effect on our financial condition, operating results and business prospects.

Our business could be adversely affected if our customers' products are not received well in the market, if their products, or the processes used by our customers to manufacture their final products, fail to be approved, or if our customers discontinue their development activities for any reason.

Our enzymes are used by our pharmaceutical customers in the manufacture of intermediates and APIs which are then used in the manufacture of final pharmaceutical products by our existing and potential branded and generic drug customers, and by our fine chemicals customers to manufacture food ingredients. Our business could be adversely affected if these final products do not perform in the market as well as expected, or if our customers encounter competition from new entrants into the market with competing, and possibly superior, products. Additionally, many of these pharmaceutical and food products must be reviewed and approved by the FDA in the United States and similar regulatory bodies in other markets prior to commercialization. If our customers who sell branded drugs, which we refer to as innovators, fail to receive regulatory approval for the drugs, fail to receive regulatory approval for new manufacturing processes for previously approved drugs, or decide for business or other reasons to discontinue their drug development activities, our revenues and prospects will be negatively impacted. The process of producing these drugs, and their generic equivalents, is also subject to regulation by the FDA in the United States and equivalent regulatory bodies in other markets. Similarly, if our food ingredient product and other fine chemical customers were to delay or discontinue development on their products, our revenues and prospects will be negatively impacted. If any pharmaceutical or food manufacturing process that uses our enzymes or enzyme technology does not receive required approval by the appropriate regulatory body or if customers decide not to pursue approval, our business could be adversely affected.

We or our customers may not be able to obtain regulatory approval for the use of our products in food and food ingredients, if required, and, even if approvals are obtained, complying on an ongoing basis with the numerous regulatory requirements applicable to these products will be time-consuming and costly.

The products that we develop for our food and food ingredient customers are, and any other products that we may develop for the food and food ingredients market will likely be, subject to regulation by various government agencies, including the FDA, state and local agencies and similar agencies outside the United States, as well as religious compliance certifying organizations. Food ingredients are regulated by the FDA either as food additives or as substances generally recognized as safe ("GRAS"). A substance can be listed or affirmed as GRAS by the FDA or self-affirmed by its manufacturer upon determination that independent qualified experts would generally agree that the substance is GRAS for a particular use. While we generally self-affirm GRAS status for the products that we develop for the food market, our customer(s) will need to submit a GRAS Notice of Determination for its final commercial product. There can be no assurance that our customer(s) will not receive any objections from the FDA to their Notice of Determination. If the FDA were to disagree with our customer's determination, they could ask our customer to voluntarily withdraw the final commercial product from the market or could initiate legal action to

halt its sale. Such actions by the FDA could have an adverse effect on our business, financial condition, and results of our operations. Food ingredients that are not GRAS are regulated as food additives and require FDA approval prior to commercialization. The food additive petition process is generally expensive and time consuming, with approval, if secured, potentially taking years.

Changes in regulatory requirements, laws and policies, or evolving interpretations of existing regulatory requirements, laws and policies, may result in increased compliance costs, delays, capital expenditures and other financial obligations that could adversely affect our business or financial results.

We expect to encounter regulations in most if not all of the countries in which we may seek to sell our products which are used in food and food ingredients, and we cannot be sure that we or our customers will be able to obtain necessary approvals in a timely manner or at all. If our existing and future products which are used in food and food ingredients do not meet applicable regulatory requirements in a particular country or at all, then we may not be able to commercialize them and our business will be adversely affected. The various regulatory schemes applicable to our products which are used in food and food ingredients will continue to apply following initial approval for sale, including FDA requirements for food safety, mandatory labeling, and certain nutrient content or health claims made about the product. Monitoring regulatory changes and ensuring our ongoing compliance with applicable requirements will be time-consuming and may affect our results of operations. If we fail to comply with such requirements on an ongoing basis, we may be subject to fines or other penalties, or may be prevented from selling our products which are used in food and food ingredients and our business may be harmed.

Our efforts to deploy our technology in the life science tools markets may fail.

We have recently begun to use our CodeEvolver® protein engineering technology platform to develop new products for customers using NGS and PCR/qPCR for*in vitro* molecular diagnostic applications. We do not know if we can successfully compete in this new market. This new market is well established and consists of numerous large, well-funded entrenched market participants who have long and established track records and customer relationships. In December 2019, we licensed our first proprietary enzyme for this market, EvoT4™ DNA ligase, which is designed to improve library preparation for NGS users, to Roche. This enzyme, and any products that we may develop in the future for this market, may not succeed in displacing current products. If we succeed in commercializing new products for this market, we may not generate significant revenues and cash flows from these activities. The failure to successfully deploy products on timely basis in this space may limit our growth and have a material adverse effect on our financial condition, operating results and business prospects.

Interim "top-line" and preliminary data from studies or trials that we announce or publish from time to time may change as more data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publish interim "top-line" or preliminary data from preclinical studies or clinical trials. Interim data are subject to the risk that one or more of the outcomes may materially change as more data become available. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the topline results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Preliminary or "top-line" data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, interim and preliminary data should be viewed with caution until the final data are available. Additionally, interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Adverse differences between preliminary or interim data and final data could significantly harm our business prospects.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure. Any information we determine not to disclose may ultimately be deemed significant by you or others with respect to future decisions, conclusions, views, activities or otherwise regarding a particular product candidate or our business. If the topline data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, product candidates may be harmed, which could significantly harm our business prospects.

The regulatory approval processes of the FDA and comparable foreign authorities are lengthy, time consuming and inherently unpredictable, and if we are ultimately unable to obtain regulatory approval for our product candidates, our business will be substantially harmed.

We and any collaborators are not permitted to commercialize, market, promote or sell any product candidate in the United States without obtaining marketing approval from the FDA. Foreign regulatory authorities impose similar requirements. The time required to obtain approval by the FDA and comparable foreign authorities is unpredictable, but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including substantial discretion of the regulatory authorities. In addition, approval policies, regulations or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions. To date, neither we nor our collaborators have submitted a BLA to FDA or similar drug approval submissions to comparable foreign regulatory authorities for any product candidate. We and any collaborators must complete additional preclinical or nonclinical studies and clinical trials to demonstrate the safety and efficacy of our product candidates in humans to the satisfaction of the regulatory authorities before we will be able to obtain these approvals. Our product candidates could fail to receive regulatory approval for many reasons, including the following:

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our or our collaborators' clinical trials;
- we or our collaborators may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a product candidate is safe and effective for its proposed indication;
- the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval;
- we or our collaborators may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- the FDA or comparable foreign regulatory authorities may disagree with our or our collaborators' interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of product candidates may not be sufficient to support the submission of a BLA to obtain regulatory approval in the United States or elsewhere;
- the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we or our collaborators contract for clinical and commercial supplies;
- the FDA or comparable foreign regulatory authorities may fail to approve the companion diagnostics we contemplate developing with collaborators; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our or our collaborators' clinical data insufficient for approval.

This lengthy approval process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market our product candidates, which would significantly harm our business, results of operations and prospects. In addition, even if we were to obtain approval, regulatory authorities may approve any of our product candidates for fewer or more limited indications than we request, may impose significant limitations in the form of narrow indications, warnings, or a REMS. Regulatory authorities may not approve the price we or our collaborators intend to charge for products we may develop, may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates.

Clinical trials are difficult to design and implement, expensive, time-consuming and involve an uncertain outcome, and the inability to successfully conduct clinical trials and obtain regulatory approval for our product candidates would substantially harm our business.

Clinical testing is expensive and usually takes many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process, and product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through preclinical studies and initial clinical trials. We do not know whether planned clinical trials will begin on time, need to be redesigned, recruit and enroll patients on time or be completed on schedule, or at all. Clinical trials can be delayed, suspended or terminated for a variety of reasons, including in connection with:

- the inability to generate sufficient preclinical, toxicology or other *in vivo* or *in vitro* data to support the initiation of clinical trials;

- applicable regulatory authorities disagreeing as to the design or implementation of the clinical trials;
- obtaining regulatory authorization to commence a trial;
- reaching an agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- obtaining IRB approval at each site;
- developing and validating the companion diagnostic to be used in a clinical trial, if applicable;
- insufficient or inadequate supply or quality of product candidates or other materials necessary for use in clinical trials, or delays in sufficiently developing, characterizing or controlling a manufacturing process suitable for clinical trials;
- recruiting and retaining enough suitable patients to participate in a trial;
- having enough patients complete a trial or return for post-treatment follow-up;
- adding a sufficient number of clinical trial sites;
- inspections of clinical trial sites or operations by applicable regulatory authorities, or the imposition of a clinical hold;
- clinical sites deviating from trial protocol or dropping out of a trial;
- the inability to demonstrate the efficacy and benefits of a product candidate;
- discovering that product candidates have unforeseen safety issues, undesirable side effects or other unexpected characteristics;
- addressing patient safety concerns that arise during the course of a trial; receiving untimely or unfavorable feedback from applicable regulatory authorities regarding the trial or requests from regulatory authorities to modify the design of a trial;
- non-compliance with applicable regulatory requirements by us or third parties or changes in such regulations or administrative actions;
- suspensions or terminations by IRBs of the institutions at which such trials are being conducted, by the Data Safety Monitoring Board, or DSMB, for such trial or by the FDA or other regulatory authorities due to a number of factors, including those described above;
- third parties being unable or unwilling to satisfy their contractual obligations to us; or
- changes in our financial priorities, greater than anticipated costs of completing a trial or our inability to continue funding the trial.

In addition, disruptions caused by the COVID-19 pandemic may increase the likelihood that we encounter such difficulties or delays in initiating, enrolling, conducting or completing our planned and ongoing clinical trials. Many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates. Additionally, we or our collaborators may experience unforeseen events during or resulting from clinical trials that could delay or prevent receipt of marketing approval for or commercialization of product candidates. For example, clinical trials of product candidates may produce negative, inconsistent or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon development programs. Regulators may also revise the requirements for approving the product candidates, or such requirements may not be as we anticipate. If we or our collaborators are required to conduct additional clinical trials or other testing of product candidates beyond those that we or our collaborators currently contemplate, if we or our collaborators are unable to successfully complete clinical trials or other testing of such product candidates, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may:

- incur unplanned costs;
- be delayed in obtaining or fail to obtain marketing approval for product candidates;
- obtain marketing approval in some countries and not in others;
- obtain marketing approval for indications or patient populations that are not as broad as intended or desired;
- obtain marketing approval with labeling that includes significant use or distribution restrictions or safety warnings, including boxed warnings;

- be subject to additional post-marketing testing requirements;
- be subject to changes in the way the product is administered;
- have regulatory authorities withdraw or suspend their approval of the product or impose restrictions on its distribution;
- be sued; or
- experience damage to our reputation.

If we or our collaborators experience delays in the commencement or completion of our clinical trials, or if we or our collaborators terminate a clinical trial prior to completion, we may experience increased costs, have difficulty raising capital and/or be required to slow down the development and approval process timelines. Furthermore, the product candidates that are the subject of such trials may never receive regulatory approval, and their commercial prospects and our ability to generate product revenues from them could be impaired or not realized at all.

We or our collaborators may experience delays or difficulties in enrolling patients in clinical trials, which could delay or prevent receipt of regulatory approvals.

We or our collaborators may not be able to initiate or continue clinical trials on a timely basis or at all for any product candidates we or our collaborators identify or develop if we or our collaborators are unable to locate and enroll a sufficient number of eligible patients to participate in the trials as required by applicable regulations or as needed to provide appropriate statistical power for a given trial. Additionally, some of our competitors may have ongoing clinical trials for product candidates that would treat the same indications as one or more of our product candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in our competitors' clinical trials. Patient enrollment may also be affected by many factors, including:

- severity and difficulty of diagnosing of the disease under investigation;
- size of the patient population and process for identifying subjects;
- eligibility and exclusion criteria for the trial in question;
- our or our collaborators' ability to recruit clinical trial investigators with the appropriate competencies and experience;
- design of the trial protocol;
- availability and efficacy of approved medications or therapies, or other clinical trials, for the disease or condition under investigation;
- perceived risks and benefits of the product candidate under trial or testing, or of the application of genome editing to human indications;
- efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians;
- ability to obtain and maintain subject consent;
- risk that enrolled subjects will drop out before completion of the trial;
- ability to monitor patients adequately during and after treatment; and
- proximity and availability of clinical trial sites for prospective patients.

Disruptions caused by the COVID-19 pandemic may increase the likelihood that we or our collaborators encounter such difficulties or delays in enrolling patients in clinical trials. In addition, we expect that some of our product candidates will focus on diseases with limited patient pools from which to draw for enrollment in clinical trials. The eligibility criteria of our clinical trials will further limit the pool of available trial participants. In addition to the factors identified above, patient enrollment in any clinical trials we or our collaborators may conduct may be adversely impacted by any negative outcomes our competitors may experience, including adverse side effects, clinical data showing inadequate efficacy or failures to obtain regulatory approval. Enrollment delays in clinical trials may result in increased development costs for any of our product candidates, which may cause the value of our company to decline and limit our ability to obtain additional financing. If we or our collaborators have difficulty enrolling a sufficient number of patients to conduct clinical trials as planned, we may need to delay, limit or terminate ongoing or planned clinical trials, any of which may have an adverse effect on our results of operations and prospects.

Results of preclinical studies and early clinical trials of product candidates may not be predictive of results of later studies or trials. Our product candidates may not have favorable results in later clinical trials, if any, or receive regulatory approval.

Preclinical and clinical drug development is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the preclinical study or clinical trial process. Despite promising preclinical or clinical results, any product candidate can unexpectedly fail at any stage of preclinical or clinical development. The historical failure rate for product candidates in our industry is high. The results from preclinical studies or early clinical trials of a product candidate may not be predictive of the results from later preclinical studies or clinical trials, and interim results of a clinical trial are not necessarily indicative of final results. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy characteristics despite having progressed through preclinical studies and initial clinical trials.

Many companies in the biopharmaceutical and biotechnology industries have suffered significant setbacks at later stages of development after achieving positive results in early stages of development, and we may face similar setbacks. These setbacks have been caused by, among other things, preclinical findings made while clinical trials were underway or safety or efficacy observations made in clinical trials, including previously unreported adverse events. Moreover, non-clinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials nonetheless failed to obtain regulatory approval. Even if any product candidates progress to clinical trials, these product candidates may fail to show the safety and efficacy in clinical development required to obtain regulatory approval, despite the observation of positive results in animal studies. Our or our collaborators' failure to replicate positive results from early research programs and preclinical or greenhouse studies may prevent us from further developing and commercializing those or other product candidates, which would limit our potential to generate revenues from them and harm our business and prospects.

For the foregoing reasons, we cannot be certain that any ongoing or future preclinical studies or clinical trials will be successful. Any safety or efficacy concerns observed in any one of our preclinical studies or clinical trials in a targeted area could limit the prospects for regulatory approval of product candidates in that and other areas, which could have a material adverse effect on our business and prospects.

If any of our product candidates do not work as intended or cause undesirable side effects, it could hinder or prevent receipt of regulatory approval or realization of commercial potential for them or our other product candidates and could substantially harm our business.

Our product candidates may be associated with serious adverse events, undesirable side effects or unexpected characteristics. Results of clinical trials could reveal severe or recurring side effects, toxicities or unexpected events. In addition to serious adverse events or side effects caused by product candidates we develop alone or with collaborators, the administration process or related procedures may also cause undesirable side effects. If any such events occur, clinical trials or commercial distribution of any product candidates or products we develop alone or with collaborators could be suspended or terminated, and our business and reputation could suffer substantial harm. Treatment-related side effects could affect patient recruitment and the ability of enrolled patients to complete the trial or result in potential liability claims. Regulatory authorities could order us or our collaborators to cease further development of, deny approval of or require us to cease selling any product candidates or products for any or all targeted indications. If we or our collaborators elect, or are required, to delay, suspend or terminate any clinical trial or commercialization efforts, the commercial prospects of such product candidates or products may be harmed, and our ability to generate product revenues from them or other product candidates that we develop may be delayed or eliminated.

Additionally, if we successfully develop a product candidate alone or with collaborators and it receives marketing approval, the FDA could require us to adopt a REMS to ensure that the benefits of treatment with such product candidate outweigh the risks for each potential patient, which may include, among other things, a communication plan to health care practitioners, patient education, extensive patient monitoring or distribution systems and processes that are highly controlled, restrictive and more costly than what is typical for the industry. We or our collaborators may also be required to adopt a REMS or engage in similar actions, such as patient education, certification of health care professionals or specific monitoring, if we or others later identify undesirable side effects caused by any product that we develop alone or with collaborators. Such identification could also have several additional significant negative consequences, such as:

- regulatory authorities may suspend, withdraw or limit approvals of such product, or seek an injunction against its manufacture or distribution;
- regulatory authorities may require additional warnings on the label, including "boxed" warnings, or issue safety alerts, Dear Healthcare Provider letters, press releases or other communications containing warnings or other safety information about the product;

- we may be required to create a Medication Guide outlining the risks of such side effects for distribution to patients;
- we may be required to change the way a product is administered or conduct additional trials;
- the product may become less competitive;
- we or our collaborators may decide to remove the product from the marketplace;
- we may be subject to fines, injunctions or the imposition of civil or criminal penalties;
- we could be sued and be held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us or our collaborators from achieving or maintaining market acceptance of any potential product.

Even if we obtain regulatory approval for any products that we develop alone or with collaborators, such products will remain subject to ongoing regulatory requirements, which may result in significant additional expense.

Even if products we develop alone or with collaborators receive regulatory approval, they will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, distribution, storage, advertising, promotion, sampling, record-keeping and submission of safety and other post-market information, among other things. Any regulatory approvals received for such products may also be subject to limitations on the approved indicated uses for which they may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing and surveillance studies. For example, the holder of an approved BLA in the United States is obligated to monitor and report adverse events and any failure of a product to meet the specifications in the BLA. In the United States, the holder of an approved BLA must also submit new or supplemental applications and obtain FDA approval for certain changes to the approved product, product labeling or manufacturing process. Similar provisions apply in the European Union. Advertising and promotional materials must comply with FDA rules and are subject to FDA review, in addition to other potentially applicable federal and state laws. Similarly, in the European Union any promotion of medicinal products is highly regulated and, depending on the specific jurisdiction involved, may require prior vetting by the competent national regulatory authority. In addition, product manufacturers and their facilities are subject to payment of user fees and continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP requirements and adherence to commitments made in the BLA or foreign marketing application.

If we, our collaborators or a regulatory agency discovers previously unknown problems with a product such as adverse events of unanticipated severity or frequency or problems with the facility where the product is manufactured or disagrees with the promotion, marketing or labeling of that product, a regulatory agency may impose restrictions relative to that product, the manufacturing facility or us or our collaborators, including requiring recall or withdrawal of the product from the market or suspension of manufacturing.

Moreover, if any of our product candidates are approved, our product labeling, advertising, promotion and distribution will be subject to regulatory requirements and continuing regulatory review. The FDA strictly regulates the promotional claims that may be made about drug products. In particular, a product may not be promoted for uses that are not approved by the FDA as reflected in the product's approved labeling. If we or our collaborators fail to comply with applicable regulatory requirements following approval of any potential products we may develop, authorities may:

- issue an untitled enforcement letter or a warning letter asserting a violation of the law;
- seek an injunction, impose civil and criminal penalties, and impose monetary fines, restitution or disgorgement of profits or revenues;
- suspend or withdraw regulatory approval;
- suspend or terminate any ongoing clinical trials or implement requirements to conduct post-marketing studies or clinical trials;
- refuse to approve a pending BLA or comparable foreign marketing application (or any supplements thereto) submitted by us or our collaborators;
- restrict the labeling, marketing, distribution, use or manufacturing of products;
- seize or detain products or otherwise require the withdrawal or recall of products from the market;
- refuse to approve pending applications or supplements to approved applications that we or our collaborators submit;

- refuse to permit the import or export of products; or
- refuse to allow us or our collaborators to enter into government contracts.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our or our collaborators' ability to commercialize products and our ability to generate revenues.

In addition, the FDA's policies, and policies of foreign regulatory agencies, may change, and additional regulations may be enacted that could prevent, limit or delay regulatory approval of product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. For example, the results of the 2020 U.S. Presidential Election may impact our business and industry. Namely, the Trump administration took several executive actions, including the issuance of a number of Executive Orders, that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. It is difficult to predict whether or how these orders will be implemented, or whether they will be rescinded and replaced under the Biden administration. The policies and priorities of the new administration are unknown and could materially impact the regulations governing our product candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may be subject to enforcement action and we may not achieve or sustain profitability.

Disruptions at the FDA and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire, retain or deploy key leadership and other personnel, or otherwise prevent new or modified products from being developed, approved or commercialized in a timely manner or at all, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, statutory, regulatory and policy changes, the FDA's ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the FDA's ability to perform routine functions. Average review times at the FDA have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies may also slow the time necessary for new biologics or modifications to approved biologics to be reviewed and/or approved by necessary government agencies, which could adversely affect our business. For example, over the last several years, including for 35 days beginning on December 22, 2018, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities.

Separately, in response to the COVID-19 pandemic, on March 10, 2020 the FDA announced its intention to postpone most inspections of foreign manufacturing facilities and products, and on March 18, 2020 the FDA temporarily postponed routine surveillance inspections of domestic manufacturing facilities. Subsequently, on July 10, 2020, the FDA announced its intention to resume certain on-site inspections of domestic manufacturing facilities subject to a risk-based prioritization system. The FDA intends to use this risk-based assessment system to identify the categories of regulatory activity that can occur within a given geographic area, ranging from mission critical inspections to resumption of all regulatory activities. Regulatory authorities outside the United States may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic. If a prolonged government shutdown occurs, or if global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our or our collaborators' regulatory submissions, which could have a material adverse effect on our business.

Our product candidates for which we intend to seek approval as a biologic products may face competition sooner than anticipated.

The BCPIA enacted in the Patient Protection and Affordable Care Act, signed into law on March 23, 2010, created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing the sponsor's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of their product. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty.

We believe that any of our product candidates approved as a biological product under a BLA should qualify for the 12-year period of exclusivity. However, there is a risk that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider our product candidates to be reference products for competing products, potentially creating the opportunity for biosimilar competition sooner than anticipated. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. Moreover, the extent to which a biosimilar, once approved, will be substituted for any one of our reference products in a way that is similar to traditional generic substitution for non-biological products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing.

Our business operations and future relationships with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers will be subject to applicable healthcare regulatory laws, which could expose us to penalties.

Our business operations and future arrangements with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers, may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations. These laws may constrain the business or financial arrangements and relationships through which we will conduct our operations, including how we research, market, sell and distribute our product candidates, if approved. Such laws include:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or providing any remuneration (including any kickback, bribe, or certain rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, lease, order or recommendation of, any good, facility, item or service, for which payment may be made, in whole or in part, under U.S. federal and state healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- the U.S. federal false claims laws, including the civil False Claims Act, which, among other things, impose criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the U.S. federal government, claims for payment or approval that are false or fraudulent, knowingly making, using or causing to be made or used, a false record or statement material to a false or fraudulent claim, or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the U.S. federal government. In addition, the government may assert that a claim including items and services resulting from a violation of the U.S. federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act;
- the U.S. federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), which imposes criminal and civil liability for, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement, in connection with the delivery of, or payment for, healthcare benefits, items or services; similar to the U.S. federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 and its implementing regulations, which also imposes certain obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information without appropriate authorization by covered entities subject to the rule, such as health plans, healthcare clearinghouses and healthcare providers as well as their business associates that perform certain services involving the use or disclosure of individually identifiable health information;
- the U.S. federal Physician Payments Sunshine Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid, or the Children's Health Insurance Program to report annually to the government information related to certain payments and other transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain other healthcare professionals beginning in 2022, and teaching hospitals, as well as ownership and investment interests held by the physicians described above and their immediate family members;
- analogous U.S. state laws and regulations, including: state anti-kickback and false claims laws, which may apply to our future business practices, including but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by any third-party payor, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's

voluntary compliance guidelines and the relevant compliance guidance promulgated by the U.S. federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws and regulations that require drug manufacturers to file reports relating to pricing and marketing information, which requires tracking gifts and other remuneration and items of value provided to healthcare professionals and entities; and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts; and

- similar healthcare laws and regulations in the EU and other jurisdictions, including reporting requirements detailing interactions with and payments to healthcare providers and laws governing the privacy and security of certain protected information, such as the General Data Protection Regulation ("GDPR"), which imposes obligations and restrictions on the collection and use of personal data relating to individuals located in the European Economic Area ("EEA") (including health data).

Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, exclusion from government-funded healthcare programs, such as Medicare and Medicaid or similar programs in other countries or jurisdictions, disgorgement, individual imprisonment, contractual damages, reputational harm, diminished profits and the curtailment or restructuring of our operations.

The successful commercialization of product candidates developed by us or our partners will depend in part on the extent to which governmental authorities and health insurers establish adequate coverage, reimbursement levels and pricing policies. Failure to obtain or maintain coverage and adequate reimbursement for such product candidates, if approved, could limit our or our partners' ability to market those products and decrease our ability to generate revenue.

The availability and adequacy of coverage and reimbursement by governmental healthcare programs such as Medicare and Medicaid, private health insurers and other third-party payors are essential for most patients to be able to afford prescription medications such as our product candidates, assuming FDA approval. Our ability to achieve acceptable levels of coverage and reimbursement for products by governmental authorities, private health insurers and other organizations will have an effect on our ability to successfully commercialize our product candidates. Assuming we obtain coverage for our product candidates by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. We cannot be sure that coverage and reimbursement in the United States, the EU or elsewhere will be available for our product candidates or any product that we may develop, and any reimbursement that may become available may be decreased or eliminated in the future.

Third-party payors increasingly are challenging prices charged for pharmaceutical products and services, and many third-party payors may refuse to provide coverage and reimbursement for particular drugs or biologics when an equivalent generic drug, biosimilar or a less expensive therapy is available. It is possible that a third-party payor may consider our product candidates as substitutable and only offer to reimburse patients for the less expensive product. Even if we show improved efficacy or improved convenience of administration with our product candidates, pricing of existing third-party therapeutics may limit the amount we will be able to charge for our product candidates. These payors may deny or revoke the reimbursement status of a given product or establish prices for new or existing marketed products at levels that are too low to enable us to realize an appropriate return on our investment in our product candidates. For products administered under the supervision of a physician, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such drugs. Additionally, separate reimbursement for the product itself or the treatment or procedure in which the product is used may not be available, which may impact physician utilization. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize our product candidates, and may not be able to obtain a satisfactory financial return on our product candidates.

No uniform policy for coverage and reimbursement for products exists among third-party payors in the United States. Therefore, coverage and reimbursement for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our product candidates to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Furthermore, rules and regulations regarding reimbursement change frequently, in some cases on short notice, and we believe that changes in these rules and regulations are likely.

Outside the United States, international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe and other countries have and will continue to put pressure on the pricing and usage of our product candidates. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. Other countries allow companies to fix their own prices for medical products, but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates. Accordingly, in markets outside the United States, the reimbursement for our product candidates may be reduced compared with the United States and may be insufficient to generate commercially-reasonable revenue and profits.

Moreover, increasing efforts by governmental and third-party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, they may not cover or provide adequate payment for our product candidates. We expect to experience pricing pressures in connection with the sale of our product candidates due to the trend toward managed health care, the increasing influence of health maintenance organizations and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and biologics and surgical procedures and other treatments, has become intense. As a result, increasingly high barriers are being erected to the entry of new products.

Enacted and future healthcare legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and may affect the prices we may set.

In the United States, the EEA and other jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes and proposed changes to the healthcare system that could affect our future results of operations. In particular, there have been and continue to be a number of initiatives at the U.S. federal and state levels that seek to reduce healthcare costs and improve the quality of healthcare. For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively the ACA, was enacted, which substantially changed the way healthcare is financed by both governmental and private insurers. Among the provisions of the ACA, those of greatest importance to the pharmaceutical and biotechnology industries include the following:

- an annual, non-deductible fee payable by any entity that manufactures or imports certain branded prescription drugs and biologic agents (other than those designated as orphan drugs), which is apportioned among these entities according to their market share in certain government healthcare programs;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13.0% of the average manufacturer price for branded and generic drugs, respectively;
- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- extension of a manufacturer's Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations; and
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability.

Since its enactment, there have been judicial and Congressional challenges to certain aspects of the ACA. The U.S. Supreme Court is currently reviewing the constitutionality of the ACA, although it is unclear when a decision will be made or how the Supreme Court will rule. It is also unclear how this decision or other efforts, if any, to challenge, repeal, or replace the ACA will impact the law, our business or financial condition.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. For example, the Budget Control Act of 2011 resulted in aggregate reductions of Medicare payments to providers of 2% per fiscal year, which went into effect in April 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2030, with the exception of a temporary suspension from May 1, 2020 through March 31, 2021, unless additional action is taken by Congress. In January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from

three to five years. These new laws or any other similar laws introduced in the future may result in additional reductions in Medicare and other health care funding, which could negatively affect our future customers and accordingly, our financial operations.

Moreover, payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives. For example, CMS may develop new payment and delivery models, such as bundled payment models. In addition, recently there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products. We expect that additional U.S. federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that the U.S. federal government will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Individual states in the United States have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Legally-mandated price controls on payment amounts by third-party payors or other restrictions could harm our business, results of operations, financial condition and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for our product candidates or put pressure on our product pricing.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action in the United States or any other jurisdiction. If we or any third parties we may engage are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or such third parties are not able to maintain regulatory compliance, our product candidates may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability.

We rely on third parties to conduct our clinical trials and perform some of our research and preclinical studies. If these third parties do not satisfactorily carry out their contractual duties or fail to meet expected deadlines, our development programs may be delayed or subject to increased costs, each of which may have an adverse effect on our business and prospects.

We do not have the ability to conduct all aspects of our preclinical testing or clinical trials ourselves. As a result, we are and expect to remain dependent on third parties to conduct clinical trials of our product candidates. Specifically, we expect CROs, clinical investigators, and consultants to play a significant role in the conduct of these trials and the subsequent collection and analysis of data. However, we will not be able to control all aspects of their activities. Nevertheless, we are responsible for ensuring that each of our trials is conducted in accordance with the applicable protocol and legal, regulatory and scientific standards, and our reliance on the CROs and other third parties does not relieve us of our regulatory responsibilities. We and our CROs are required to comply with GCP requirements, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for all of our product candidates in clinical development. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, clinical trial investigators and clinical trial sites. If we or any of our CROs or clinical trial sites fail to comply with applicable GCP requirements, the data generated in our clinical trials may be deemed unreliable, and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. In addition, our clinical trials must be conducted with product produced under cGMP regulations. Our failure to comply with these regulations may require us to stop and/or repeat clinical trials, which would delay the marketing approval process.

There is no guarantee that any such CROs, clinical trial investigators or other third parties on which we rely will devote adequate time and resources to our development activities or perform as contractually required. If any of these third parties fail to meet expected deadlines, adhere to our clinical protocols or meet regulatory requirements, otherwise performs in a substandard manner, or terminates its engagement with us, the timelines for our development programs may be extended or delayed or our development activities may be suspended or terminated. If any of our clinical trial sites terminates for any reason, we may experience the loss of follow-up information on subjects enrolled in such clinical trials unless we are able to transfer those subjects to another qualified clinical trial site, which may be difficult or impossible. In addition, clinical trial investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and may receive cash or equity compensation in connection with such services. If these relationships and any related compensation result in perceived or actual conflicts of interest, or the FDA or comparable foreign regulatory authorities concludes that the financial relationship may have affected the interpretation of the trial, the integrity of the data generated at the applicable clinical trial site may be questioned and the utility of the clinical trial itself may be jeopardized, which could result in the delay or rejection of any marketing application we submit by the FDA or any comparable foreign regulatory authority. Any such delay or rejection could prevent us from commercializing our product candidates.

We contract with third parties for the manufacturing and supply of product candidates for use in preclinical testing and clinical trials and related services, which supply may become limited or interrupted or may not be of satisfactory quality and quantity.

We do not have any manufacturing facilities. We produce in our laboratory relatively small quantities of products for evaluation in our research programs. We rely, and expect to continue to rely, on third parties for the manufacture of our product candidates for preclinical and clinical testing, as well as for commercial manufacture if any of our product candidates are approved. We currently have limited manufacturing arrangements and expect that each of our product candidates will only be covered by single source suppliers for the foreseeable future. This reliance increases the risk that we will not have sufficient quantities of our product candidates or products, if approved, or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts.

Furthermore, all entities involved in the preparation of therapeutics for clinical trials or commercial sale, including our existing contract manufacturers for our product candidates, are subject to extensive regulation. Components of a finished therapeutic product approved for commercial sale or used in clinical trials must be manufactured in accordance with cGMP requirements. These regulations govern manufacturing processes and procedures, including record keeping, and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Poor control of production processes can lead to the introduction of contaminants, or to inadvertent changes in the properties or stability of our product candidates that may not be detectable in final product testing. We or our contract manufacturers must supply all necessary documentation in support of a BLA on a timely basis and must adhere to the FDA's cGMP regulations enforced by the FDA through its facilities inspection program. Comparable foreign regulatory authorities may require compliance with similar requirements. The facilities and quality systems of our third-party contractor manufacturers must pass a pre-approval inspection for compliance with the applicable regulations as a condition of marketing approval of our product candidates. We do not control the manufacturing activities of, and are completely dependent on, our contract manufacturers for compliance with cGMP regulations.

In the event that any of our manufacturers fails to comply with such requirements or to perform its obligations to us in relation to quality, timing or otherwise, or if our supply of components or other materials becomes limited or interrupted for other reasons, we may be forced to manufacture the materials ourselves, for which we currently do not have the capabilities or resources, or enter into an agreement with another third party, which we may not be able to do on commercially reasonable terms, if at all. In particular, any replacement of our manufacturers could require significant effort and expertise because there may be a limited number of qualified replacements. In some cases, the technical skills or technology required to manufacture our product candidates may be unique or proprietary to the original manufacturer and we may have difficulty transferring such skills or technology to another third party and a feasible alternative may not exist. In addition, certain of our product candidates and our own proprietary methods have never been produced or implemented outside of our company, and we may therefore experience delays to our development programs if and when we attempt to establish new third party manufacturing arrangements for these product candidates or methods. These factors would increase our reliance on such manufacturer or require us to obtain a license from such manufacturer in order to have another third party manufacture our product candidates. If we are required to change manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations and guidelines. The delays associated with the verification of a new manufacturer could negatively affect our ability to develop product candidates in a timely manner or within budget.

Our or a third party's failure to execute on our manufacturing requirements, do so on commercially reasonable terms and comply with cGMP could adversely affect our business in a number of ways, including:

- an inability to initiate or continue clinical trials of our product candidates under development;
- delay in submitting regulatory applications, or receiving marketing approvals, for our product candidates;
- loss of the cooperation of future collaborators;
- subjecting third-party manufacturing facilities or our manufacturing facilities to additional inspections by regulatory authorities;
- requirements to cease development or to recall batches of our product candidates; and
- in the event of approval to market and commercialize our product candidates, an inability to meet commercial demands for our product or any other future product candidates.

Our efforts to prosecute and protect our intellectual property may not be successful.

We will continue to file and prosecute patent applications and maintain trade secrets in an ongoing effort to protect our intellectual property. It is possible that our current patents, or patents which we may later acquire, may be successfully challenged or invalidated in whole or in part. It is also possible that we may not obtain issued patents from our pending patent applications or other inventions we seek to protect. We sometimes permit certain patents or patent applications to lapse or go abandoned under appropriate circumstances. Due to uncertainties inherent in prosecuting patent applications, sometimes patent applications are rejected and we subsequently abandon them. It is also possible that we may develop proprietary products or technologies in the future that are not patentable or that the patents of others will limit or altogether preclude our ability to conduct business. In addition, any patent issued to us or to our licensor may provide us with little or no competitive advantage, in which case we may abandon such patent or license it to another entity, or terminate the license agreement.

Our means of protecting our proprietary rights may not be adequate and our competitors may independently develop technology or products that are similar to ours or that compete with ours. Patent, trademark, copyright and trade secret laws afford only limited protection for our technology platform, services and products. The laws of many countries do not protect our proprietary rights to as great an extent as do the laws of the United States. Despite our efforts to protect our proprietary rights, unauthorized parties have in the past attempted, and may in the future attempt, to operate under aspects of our intellectual property, technology, services or products or to obtain and use information that we regard as proprietary. Third parties may also design around our proprietary rights, which may render our protected technology, services and products less valuable, if the design around is favorably received in the marketplace. In addition, if any of our products, services or technology is covered by third-party patents or other intellectual property rights, we could be subject to various legal actions. We cannot assure you that our technology platform, services and products do not infringe patents held by others or that they will not in the future.

Litigation may be necessary to enforce our intellectual property rights, to protect our trade secrets, to determine the validity and scope of the proprietary rights of others, or to defend against claims of infringement, invalidity, misappropriation, or other claims.

Any such litigation could result in substantial costs and diversion of our resources. Moreover, any settlement of or adverse judgment resulting from litigation relating to intellectual property could require us to obtain a license to continue to make, use or sell the products or technology that is the subject of the claim, or otherwise restrict or prohibit our use of the technology, product or services.

Our ability to compete may decline if we do not adequately protect our proprietary technologies or if we lose some of our intellectual property rights.

Our success depends in part on our ability to obtain patents and maintain adequate protection of our intellectual property for our technologies, services and products in the United States and other countries. We have adopted a strategy of seeking patent protection in the United States and in foreign countries with respect to certain of the technologies used in or relating to our services, products and processes. As such, as of December 31, 2020, we owned or controlled approximately 1,635 issued patents and pending patent applications in the United States and in various foreign jurisdictions. Our patents and patent applications, if issued, as of December 31, 2020, have terms that expire between 2021 and approximately 2041. We also have license rights to a number of issued patents and pending patent applications in the United States and in various foreign jurisdictions. Our owned and licensed patents and patent applications include those directed to our enabling technologies and to the methods and products that support our business in the biotherapeutics, molecular diagnostics, food and other markets. We intend to continue to apply for patents relating to our technologies, methods, services and products as we deem appropriate.

Issuance of claims in patent applications and enforceability of such claims once issued involve complex legal and factual questions and, therefore, we cannot predict with any certainty whether any of our issued patents will survive invalidity claims asserted by third parties. Issued patents and patents issuing from pending applications may be challenged, invalidated, or circumvented. Moreover, the United States Leahy-Smith America Invents Act ("AIA"), enacted in September 2011, brought significant changes to the United States patent system, which include a change to a "first to file" system from a "first to invent" system and changes to the procedures for challenging issued patents and disputing patent applications during the examination process, among other things. While interference proceedings are possible for patent claims filed prior to March 16, 2013, many of our filings will be subject to the post- and pre-grant proceedings set forth in the AIA, including citation of prior art and written statements by third parties, third party pre-issuance submissions, ex parte reexamination, inter partes review, post-grant review, and derivation proceedings. We may need to utilize the processes provided by the AIA for supplemental examination or patent reissuance. These proceedings could result in substantial cost to us even if the outcome is favorable. Even if successful, any interference may result in loss of certain claims. Any litigation or proceedings could divert our management's time and efforts. Even unsuccessful claims brought by third parties could result in significant legal fees and other expenses, diversion of management time, and disruption in our business. Uncertainties resulting from initiation and continuation of any patent or

related litigation could harm our ability to compete. We have not assessed the applicability of the AIA and new regulations on our patent portfolio. These changes could increase the costs and uncertainties surrounding the prosecution of our patent applications and the enforcement or defense of our patent rights.

Additional uncertainty may result from legal precedent handed down by the United States Federal Circuit Court and Supreme Court as they determine legal issues concerning the scope and construction of patent claims and inconsistent interpretation of patent laws by the lower courts. Accordingly, we cannot ensure that any of our pending patent applications will result in issued patents, or even if issued, predict the breadth of the claims upheld in our and other companies' patents. Given that the degree of future protection for our proprietary rights is uncertain, we cannot ensure that: (i) we were the first to invent the inventions covered by each of our pending applications, (ii) we were the first to file patent applications for these inventions, or (iii) the proprietary technologies we develop will be patentable. In addition, unauthorized parties may attempt to copy or otherwise obtain and use our products or technology. Monitoring unauthorized use of our intellectual property is difficult, and we cannot be certain that the steps we have taken will prevent unauthorized use of our technology, particularly in certain foreign countries where the local laws may not protect our proprietary rights as fully as in the United States. Moreover, third parties could practice our inventions in territories where we do not have patent protection. Such third parties may then try to import products made using our inventions into the United States or other countries. If competitors are able to use our technology, our ability to compete effectively could be harmed. In addition, others may independently develop and obtain patents for technologies that are similar to or superior to our technologies. If that happens, we may need to license these technologies, and we may not be able to obtain licenses on reasonable terms, if at all, which could cause harm to our business.

Third parties may claim that we are infringing their intellectual property rights or other proprietary rights, which may subject us to costly and time consuming litigation and prevent us from developing or commercializing our products.

Our commercial success also depends in part on our ability to operate without infringing patents and proprietary rights of third parties, and without breaching any licenses or other agreements that we have entered into with regard to our technologies, services, products and business. We cannot ensure that patents have not been issued to third parties that could block our ability to obtain patents or to operate as we would like. There may be patents in some countries that, if valid, may block our ability to make, use or sell our products in those countries, or import our products into those countries, if we are unsuccessful in circumventing or acquiring rights to these patents. There also may be claims in patent applications filed in some countries that, if granted and valid, may also block our ability to commercialize products or processes in these countries if we are unable to circumvent or license them.

The industries in which we operate and the biotechnology industry, in particular, are characterized by frequent and extensive litigation regarding patents and other intellectual property rights. Many biotechnology companies have employed intellectual property litigation as a way to gain a competitive advantage. Our involvement in litigation or other intellectual property proceedings inside and outside of the United States, to defend our intellectual property rights or as a result of alleged infringement of the rights of others, may divert our management’s time from focusing on business operations and could cause us to spend significant amounts of money. Any potential intellectual property litigation also could force us to do one or more of the following:

- stop selling or using our products or technologies that use the subject intellectual property;
- pay monetary damages or substantial royalties;
- grant cross-licenses to third parties relating to our patents or proprietary rights;
- obtain from the third party asserting its intellectual property rights a license to sell or use the relevant technology, which license may not be available on reasonable terms, or at all; or
- redesign those products or processes that use any allegedly infringing technology, or relocate the operations relating to the allegedly infringing technology to another jurisdiction, which may result in significant cost or delay to us, could be technically infeasible or could prevent us from selling some of our products in the United States or other jurisdictions.

We are aware of some patents and patent applications relating to aspects of our technologies filed by, and issued to, third parties. We cannot assure you that if this third party intellectual property is asserted against us that we would ultimately prevail.

We may be involved in lawsuits to protect or enforce our intellectual property rights, which could be expensive, time-consuming and unsuccessful.

Competitors may infringe our intellectual property rights or those of our licensors. To prevent infringement or unauthorized use, we have in the past filed, and may in the future be required to file, infringement claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that the intellectual property that we own or in-

license is not valid, is unenforceable and/or is not infringed. In addition, in legal proceedings against a third party to enforce a patent directed at one of our technologies, services or products, the defendant could counterclaim that our patent is invalid and/or unenforceable in whole or in part. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a patent validity challenge include an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could include an allegation that someone connected with prosecution of the patent withheld relevant information from the United States Patent and Trademark Office ("USPTO") or made a misleading statement during prosecution. Third parties may also raise similar claims before the USPTO, even outside the context of litigation. The outcome following legal assertions of invalidity and unenforceability is unpredictable, and prior art could render our patents or those of our licensors invalid. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on such product. Such a loss of patent protection would have a material adverse impact on our business.

Even if resolved in our favor, litigation or other legal proceedings relating to our intellectual property rights may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our expenses and reduce the resources available for operations and research and development activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could compromise our ability to compete in the marketplace. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation.

We may not be able to enforce our intellectual property rights throughout the world.

The laws of some foreign countries where we do business do not protect intellectual property rights to the same extent as the laws of the United States. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property, particularly those relating to biotechnology and/or bioindustrial technologies. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate. This could make it difficult for us to stop the infringement of our patents or misappropriation of our other intellectual property rights. Additionally, proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business.

If we lose key personnel, including key management personnel, or are unable to attract and retain additional personnel as needed in the future, it could disrupt the operation of our business, delay our product development programs, harm our research and development efforts, and/or impact our ability to pursue and build collaborations.

Our business involves complex, global operations across a variety of markets and requires a management team and employee workforce that is knowledgeable in the many areas in which we operate. The loss of any key members of our management team or the failure to attract or retain other key employees who possess the requisite expertise for the conduct of our business could prevent us from developing and commercializing our products for our target markets and entering into collaborations or licensing arrangements to execute on our business strategy.

In addition, the loss of any key scientific staff, or the failure to attract or retain other key scientific employees, could prevent us from developing and commercializing our products for our target markets and entering into collaborations or licensing arrangements to execute on our business strategy. We may not be able to attract or retain qualified employees in the future due to the intense competition for qualified personnel among biotechnology and other technology-based businesses or due to the availability of personnel with the qualifications or experience necessary for our business. If we are not able to attract and retain the necessary personnel to accomplish our business objectives, we may experience staffing constraints that will adversely affect our ability to meet the demands of our collaborators and customers in a timely fashion or to support our internal research and development programs. Competition for experienced scientists and other technical personnel from numerous companies and academic and other research institutions may limit our ability to do so on acceptable terms. All of our employees are at-will employees, which mean that either the employee or we may terminate their employment at any time.

Our planned activities will require additional expertise in specific industries and areas applicable to the products and processes developed through our technology platform or acquired through strategic or other transactions, especially in the end markets that we seek to penetrate. These activities will require the addition of new personnel, and the development of additional

expertise by existing personnel. The inability to attract personnel with appropriate skills or to develop the necessary expertise could impair our ability to grow our business.

If our biocatalysts, or the genes that code for our biocatalysts, are stolen, misappropriated or reverse engineered, others could use these biocatalysts or genes to produce competing products.

Third parties, including our contract manufacturers, customers and those involved in shipping our biocatalysts, often have custody or control of our biocatalysts. If our biocatalysts, or the genes that code for our biocatalysts, were stolen, misappropriated or reverse engineered, they could be used by other parties who may be able to reproduce these biocatalysts for their own commercial gain. If this were to occur, it may be difficult for us to challenge this type of use, especially in countries with limited intellectual property protection or in countries in which we do not have patents covering the misappropriated biocatalysts.

Confidentiality agreements with employees and others may not adequately prevent disclosures of trade secrets and other proprietary information.

We rely in part on trade secret and confidentiality protection to protect our confidential and proprietary information and processes. However, trade secrets and confidential information are difficult to protect. We have taken measures to protect our trade secrets and confidential and proprietary information, but these measures may not be effective. We require employees and consultants to execute confidentiality agreements upon the commencement of an employment or consulting arrangement with us. These agreements generally require that all confidential information developed by the individual or made known to the individual by us during the course of the individual's relationship with us be kept confidential and not disclosed to third parties. These agreements also generally provide that inventions conceived by the individual in the course of rendering services to us shall be our exclusive property. Nevertheless, our confidential and proprietary information may be disclosed, third parties could reverse engineer our biocatalysts and others may independently develop substantially equivalent confidential and proprietary information and techniques or otherwise gain access to our trade secrets. Costly and time-consuming litigation could be necessary to enforce and determine the scope of our confidential and proprietary rights, and failure to obtain or maintain trade secret protection could adversely affect our competitive business position.

We may need additional capital in the future in order to expand our business.

Our future capital requirements may be substantial, particularly as we continue to develop our business. Although we believe that, based on our current level of operations, our existing cash, cash equivalents and equity securities will provide adequate funds for ongoing operations, planned capital expenditures and working capital requirements for at least the next 12 months, we may need additional capital if our current plans and assumptions change. Our need for additional capital will depend on many factors, including the financial success of our biocatalysis business, our spending to develop and commercialize new and existing products and the amount of collaboration funding we may receive to help cover the cost of such expenditures, the effect of any acquisitions of other businesses, technologies or facilities that we may make or develop in the future, our spending on new market opportunities, including opportunities in the fine chemicals markets, and the filing, prosecution, enforcement and defense of patent claims. If our capital resources are insufficient to meet our capital requirements, and we are unable to enter into or maintain collaborations with partners that are able or willing to fund our development efforts or commercialize any products that we develop or enable, we will have to raise additional funds to continue the development of our technology and products and complete the commercialization of products, if any, resulting from our technologies. In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. We may seek to obtain such additional capital through equity offerings, debt financings, credit facilities and/or strategic collaborations. If future financings involve the issuance of equity securities, our existing stockholders would suffer dilution. If we raise debt financing or enter into credit facilities, we may be subject to restrictive covenants that limit our ability to conduct our business. Strategic collaborations may also place restrictions on our business. We may not be able to raise sufficient additional funds on terms that are favorable to us, if at all. If we fail to raise sufficient funds and fail to generate sufficient revenues to achieve planned gross margins and to control operating costs, our ability to fund our operations, take advantage of strategic opportunities, develop products or technologies, or otherwise respond to competitive pressures could be significantly limited. If this happens, we may be forced to delay or terminate research or development programs or the commercialization of products resulting from our technologies, curtail or cease operations or obtain funds through collaborative and licensing arrangements that may require us to relinquish commercial rights, or grant licenses on terms that are not favorable to us. If adequate funds are not available, we will not be able to successfully execute our business plan or continue our business.

If we are unable to comply with the terms of our credit facility, our business and financial condition would be materially and adversely affected.

On June 30, 2017 we entered into a credit facility ("Credit Facility") financing arrangement with Western Alliance Bank which is secured by a lien on substantially all of our personal property other than our intellectual property. Although we have made no loans or draws under the Credit Facility as of December 31, 2020, the Credit Facility includes affirmative and negative covenants including, among others, covenants requiring us to achieve consolidated product revenues at minimum levels and restricting our ability to transfer collateral, incur additional indebtedness, engage in mergers or acquisitions, pay dividends or make other distributions, make investments, create liens and sell assets. The Credit Facility also includes events of default including, among other things, our failure to pay any amounts due under the Credit Facility, a breach of covenants under the Credit Facility, our insolvency, a material adverse change, the occurrence of any default under certain other indebtedness in an amount greater than $250,000 and a final judgment against us in an amount greater than $250,000. If an event of default occurs, it could cause our obligations to become immediately due and payable and our lender would be entitled to foreclose against the collateral securing the indebtedness, including our cash. If our indebtedness were to be accelerated, we may be unable to repay such debt and, therefore, such acceleration could materially and adversely affect our business and financial condition. For more information regarding our compliance with our financial covenants, see "Management's Discussion and Analysis of Financial Condition and Results of Operations."

Debt service obligation may place us at a competitive disadvantage in our industry.

Draws under the Credit Facility would create debt service obligations for us. Although we have not drawn on the Credit Facility to date, any future draws under the Credit Facility and the related debt service requirements could adversely affect our ability to operate our business and may limit our ability to take advantage of potential business opportunities. For example, the Credit Facility presents the following risks, certain of which apply regardless of whether we draw on the Credit Facility:

- we may be required to use a portion of our cash flow from operations to make debt service payments, thereby reducing the availability of our cash flow to fund working capital, capital expenditures, product development efforts, research and development, and other general corporate requirements;
- our interest expense could increase if prevailing interest rates increase, because a portion of draws which could be made under the Credit Facility bear interest at floating rates;
- the Credit Facility could reduce our flexibility to adjust to changing business conditions or obtain additional financing to fund working capital, capital expenditures, product development efforts, research and development, and other general corporate requirements; and
- restrictive covenants in our Credit Facility, which apply regardless of whether we draw down under the facility, limit our ability to, among other things, transfer collateral, incur additional indebtedness, engage in mergers or acquisitions, pay dividends or make other distributions, make investments, create liens and sell assets.

Our revenues, financial condition and results of operations may also be adversely affected if one or more of our customers is delayed in paying, or becomes unable to pay, for our delivered products on a timely basis.

Certain of our customers may become subject to financial and other challenges that affect their cash flow. If these customers fail to pay us on a timely basis it may cause our financial results to fluctuate. Failure by such customers to pay us on timely basis, or at all, would adversely impact our financial condition.

If goodwill or other long-lived assets become impaired, we may be required to record a significant charge to earnings.

Our total assets reflect goodwill of $3.2 million and other long-lived assets of $31.2 million as of December 31, 2020. Under accounting principles generally accepted in the United States ("GAAP"), we review goodwill for impairment on at least an annual basis and at any interim date whenever events or changes in circumstances indicate that the carrying value may not be recoverable. We review our long lived assets with finite lives for impairment whenever events or changes in circumstances indicate that the carrying amount of the assets may not be recoverable. Events or changes in circumstances (i.e., information that indicates an impairment might exist) could include: a significant decrease in the market price of our common stock; current period cash flow losses or operating losses combined with a history of losses or a forecast of continuing losses associated with the use of the assets; slower growth rates in our industry; significant adverse changes in the business climate or legal factors; accumulation of costs significantly in excess of the amount originally expected for the acquisition or construction of the assets; loss of significant customers or partners; or the current expectation that the assets will more likely than not be sold or disposed of significantly before the end of their estimated useful life. We tested goodwill for impairment as of December 31, 2020. Based on our analysis, we determined that the fair value of goodwill at the reporting unit level exceeded their carrying value and that no impairment was necessary as of December 31, 2020. Nevertheless, we may experience additional events or changes

in circumstances in the future that we determine to be indicators of impairment and that may in turn require us to undertake impairment analysis in future periods. Depending on the circumstances and judgments made at such future time, the outcome of the analysis may require us to recognize impairment.

We may be required to record a significant charge to earnings in our financial statements during the period in which any impairment of our goodwill or other long-lived assets is determined, resulting in an adverse impact on our financial position and results of operations.

We have investments in non-marketable securities, which may subject us to significant impairment charges.

We have investments in illiquid non-marketable equity and debt securities acquired in private transactions. At December 31, 2020, 1.1% of our consolidated assets were comprised of investment securities, which are illiquid investments. Investments in illiquid, or non-marketable, securities are inherently risky and difficult to value. We account for our non-marketable equity securities under the measurement alternative. Under the measurement alternative, the carrying value of our non-marketable equity investments is adjusted to fair value for observable transactions for identical or similar investments of the same issuer or impairment. Adjustments are determined primarily based on a market approach as of the transaction date and are recorded as a component of other income (expense), net. We measure investments in non-marketable equity securities without a readily determinable fair value using a measurement alternative that measures these securities at the cost method minus impairment, if any, plus or minus changes resulting from observable price changes on a non-recurring basis. We measure available for sale investments in non-marketable debt at fair value. Unrealized gains and losses on these securities are recognized in other comprehensive income until realized. We evaluate our investment in non-marketable securities when circumstances indicate that we may not be able to recover the carrying value. We may impair these securities and establish an allowance for a credit loss when we determine that there has been an "other-than-temporary" decline in estimated fair value of the debt or equity security compared to its carrying value. The impairment analysis requires significant judgment to identify events or circumstances that would likely have a material adverse effect on the fair value of the investment. Because a portion amount of our assets are comprised of non-marketable investment securities, any future impairment charges from the write down in value of these securities could have a material adverse effect on our financial condition or results of operations.

If we are unable to maintain effective internal control over financial reporting in the future, the accuracy and timeliness of our financial reporting may be adversely affected.

Section 404 of the Sarbanes-Oxley Act of 2002 requires companies to conduct a comprehensive evaluation of their disclosure controls and procedures over financial reporting. At the end of each fiscal year, we must perform an evaluation of our disclosure controls and procedures over financial reporting, include in our annual report the results of the evaluation, and have our external auditors publicly attest to such evaluation.

We have identified material weaknesses and other control deficiencies in the past, and while the material weaknesses have since been remediated, we cannot assure you that in the future additional material weaknesses or significant deficiencies will not exist or otherwise be discovered. If other deficiencies are discovered in the future, our ability to accurately report our financial position, results of operations or cash flows on timely basis could be impaired, which could result in late filings of our annual and quarterly reports under the Exchange Act, restatements of our consolidated financial statements, a decline in our stock price, suspension or delisting of our common stock by the Nasdaq Stock Market, or other material adverse effects on our business, reputation, results of operations, financial condition or liquidity.

We are dependent on information technology systems, infrastructure and data, and any failure of these systems could harm our business. Security breaches, loss of data, and other disruptions could compromise sensitive information related to our business or prevent us from accessing critical information and expose us to liability, which could adversely affect our business, results of operations and financial condition.

Information technology helps us operate efficiently, interface with customers, maintain financial accuracy and efficiency, and accurately produce our financial statements. If we do not allocate and effectively manage the resources necessary to build and sustain the proper technology infrastructure, we could be subject to transaction errors, processing inefficiencies, the loss of customers, business disruptions, or the loss of or damage to intellectual property through security breach. If our data management systems do not effectively collect, store, process, and report relevant data for the operation of our business, whether due to equipment malfunction or constraints, software deficiencies, or human error, our ability to effectively plan, forecast, and execute our business plan and comply with applicable laws and regulations will be impaired, perhaps materially. Any such impairment could materially and adversely affect our financial condition, results of operations, cash flows, and the timeliness with which we report our internal and external operating results.

Our business may require us to use and store customer, employee, and business partner personally identifiable information ("PII"). This may include names, addresses, phone numbers, email addresses, contact preferences, tax identification numbers, and payment account information. We require usernames and passwords in order to access our information technology systems. We also use encryption and authentication technologies to secure the transmission and storage of data. These security measures may be compromised as a result of security breaches by unauthorized persons, employee error, malfeasance, faulty password management, or other irregularity, and result in persons obtaining unauthorized access to our data or accounts. Third parties may attempt to fraudulently induce employees or customers into disclosing usernames, passwords, or other sensitive information, which may in turn be used to access our information technology systems. For example, our employees have received "phishing" emails and phone calls attempting to induce them to divulge passwords and other sensitive information.

In addition, unauthorized persons may attempt to hack into our products or systems to obtain personal data relating to employees and other individuals, our confidential or proprietary information or confidential information we hold on behalf of third parties. If the unauthorized persons successfully hack into or interfere with our connected products or services, they may create issues with product functionality that could pose a risk of loss of data. We have programs in place to detect, contain, and respond to data security incidents, and we make ongoing improvements to our information-sharing products in order to minimize vulnerabilities, in accordance with industry and regulatory standards. However, because the techniques used to obtain unauthorized access to or sabotage systems change frequently and may be difficult to detect, we may not be able to anticipate and prevent these intrusions or mitigate them when and if they occur.

We also rely on external vendors to supply and/or support certain aspects of our information technology systems. The systems of these external vendors may contain defects in design or manufacture or other problems that could unexpectedly compromise information security of our own systems, and we are dependent on these third parties to deploy appropriate security programs to protect their systems.

While we devote significant resources to network security, data encryption, and other security measures to protect our systems and data, these security measures cannot provide absolute security. We may experience a breach of our systems and may be unable to protect sensitive data. The costs to us to eliminate or alleviate network security problems, bugs, viruses, worms, malicious software programs, and security vulnerabilities could be significant. Our efforts to address these problems may not be successful and could result in unexpected interruptions, delays, cessation of service, and harm to our business operations. Moreover, if a computer security breach affects our systems or results in the unauthorized release of PII, our reputation and brand could be materially damaged and use of our products and services could decrease. We would also be exposed to a risk of loss or litigation and potential liability, which could have a material adverse impact on our business, financial condition, results of operations, or cash flows.

Our business is subject to complex and evolving laws and regulations regarding privacy, data protection and other matters relating to information collection.

There are numerous state, federal and foreign laws, regulations, decisions, and directives regarding privacy and the collection, storage, transmission, use, processing, disclosure and protection of different types of personal data and personal information ("Personal Information") and other personal, customer, or other data, the scope of which is continually evolving and subject to differing interpretations. We may be subject to significant consequences, including penalties and fines, for any failure to comply with such laws, regulations and directives.

For example, the GDPR is in effect across the EEA, which imposes several stringent requirements for controllers and processors of personal data and increased our obligations, for example, by imposing higher standards when obtaining consent from individuals to process their personal data, requiring more robust disclosures to individuals, strengthening individual data rights, shortening timelines for data breach notifications, limiting retention periods and secondary use of information, increasing requirements pertaining to health data as well as pseudonymized (i.e., key-coded) data, and imposing additional obligations when we contract third-party processors in connection with the processing of personal data. The GDPR provides that European Union member states may make their own further laws and regulations limiting the processing of genetic, biometric, or health data, which could limit our ability to use and share personal data or could cause our costs to increase and harm our business and financial condition. Failure to comply with the requirements of the GDPR and the applicable national data protection laws of the European Union member states may result in fines of up to the greater of EUR20 million and 4% of the total worldwide annual turnover of the preceding financial year and other administrative penalties. If we are required to comply with the new data protection rules imposed by GDPR, such compliance may be onerous and adversely affect our business, financial condition, and results of operations.

To the extent applicable to our business, compliance with the new data protection rules imposed by GDPR may be onerous and adversely affect our business, financial condition, and results of operations.

In addition, recent legal developments in Switzerland and Europe have created complexity and compliance uncertainty regarding certain transfers of information from Switzerland and the European Union to the United States. For example, the EU-US Privacy Shield Framework is regularly reviewed, and there is current litigation challenging the adequacy of EU-specified standard contractual clauses (another data transfer mechanism). It is uncertain whether the Privacy Shield Framework and/or the standard contractual clauses will be invalidated by the European courts or legislature. We rely on a mixture of mechanisms to transfer personal data from our European Union business to the U.S. and could be impacted by changes in law as a result of a future review of these transfer mechanisms by European regulators under the GDPR as well as current challenges to these mechanisms in the European courts. If one or more of the legal bases for transferring Personal Information from Europe to the U.S. is invalidated, or if we are unable to transfer Personal Information between and among countries and regions in which we operate, it could affect the manner in which we provide our services or could adversely affect our financial results.

California has also recently passed the California Consumer Privacy Act (the "CCPA"), which is the most far-reaching data privacy law introduced in the United States to date, and introduces new compliance burdens on organizations doing business in California who collect Personal Information about California residents. The CCPA's definition of Personal Information is very broad and specifically includes biometric information. It went into effect in 2020 and allows for fines on a dramatic scale, as well as a private right of action from individuals in relation to certain security breaches. The CCPA is also prompting a wave of similar legislative developments in other U.S. states and creating the potential for a patchwork of overlapping but different laws. These developments increase our compliance burden and our risk, including risks of regulatory fines, litigation and associated reputational harm.

Furthermore, any failure, or perceived failure, by us to comply with or make effective modifications to our policies, or to comply with any federal, state or international privacy, data-retention or data-protection-related laws, regulations, orders or industry self-regulatory principles could result in proceedings or actions against us by governmental entities or others, a loss of customer confidence, damage to our brand and reputation and a loss of customers, any of which could have an adverse effect on our business. In addition, various federal, state and foreign legislative or regulatory bodies may enact new or additional laws and regulations concerning privacy, data-retention and data-protection issues, including laws or regulations mandating disclosure to domestic or international law enforcement bodies, which could adversely impact our business or our reputation with customers. For example, some countries have adopted laws mandating that some Personal Information regarding customers in their country be maintained solely in their country. Having to maintain local data centers and redesign product, service and business operations to limit Personal Information processing to within individual countries could increase our operating costs significantly.

Our product gross margins are variable and may decline from quarter to quarter.

Our product gross margins have varied significantly in the past and may continue to fluctuate from quarter to quarter and year to year in the future due to a variety of factors, including product mix, pricing pressure from our pharmaceutical customers and competition from other products or technologies. This variability may have a material adverse impact on our operating results and financial condition and cause our stock price to decline.

We face risks associated with our international business.

While we have a limited number of employees located outside of the United States, we are and will continue to be dependent upon contract manufacturers located outside of the United States. In addition, we have customers and partners located outside of the United States. Conducting business internationally exposes us to a variety of risks, including:

- changes in or interpretations of foreign regulations that may adversely affect our ability to sell our products, repatriate profits to the United States or operate our foreign-located facilities;
- the imposition of tariffs;
- the imposition of limitations on, or increase of, withholding and other taxes on remittances and other payments by foreign subsidiaries or joint ventures;
- the imposition of limitations on genetically-engineered products or processes and the production or sale of those products or processes in foreign countries;
- currency exchange rate fluctuations;
- uncertainties relating to foreign laws, regulations and legal proceedings including tax, import/export, anti-corruption and exchange control laws;
- the availability of government subsidies or other incentives that benefit competitors in their local markets that are not available to us;

- increased demands on our limited resources created by our operations may constrain the capabilities of our administrative and operational resources and restrict our ability to attract, train, manage and retain qualified management, technicians, scientists and other personnel;
- economic or political instability in foreign countries;
- difficulties associated with staffing and managing foreign operations; and
- the need to comply with a variety of United States and foreign laws applicable to the conduct of international business, including import and export control laws and anti-corruption laws.

Compliance with European Union chemical regulations could be costly and adversely affect our business and results of operations.

Some of our products are subject to the European Union regulatory regime known as The Registration, Evaluation and Authorization of Chemicals ("REACH"). REACH mandates that certain chemicals manufactured in, or imported into, the European Union be registered and evaluated for their potential effects on human health and the environment. Under REACH, we and our contract manufacturers located in the European Union are required to register certain of our products based on the quantity of such product imported into or manufactured in the European Union and on the product's intended end-use. The registration, evaluation and authorization process under REACH can be costly and time consuming. Problems or delays in the registration, evaluation or authorization process under REACH could delay or prevent the manufacture of some of our products in, or the importation of some of our products into, the European Union, which could adversely affect our business and results of operations. In addition, if we or our contract manufacturers fail to comply with REACH, we may be subject to penalties or other enforcement actions, which could have a material adverse effect on our business and results of operations.

Competitors and potential competitors who have greater resources and experience than we do may develop products and technologies that make ours obsolete or may use their greater resources to gain market share at our expense.

The biocatalysis industry and each of our target markets are characterized by rapid technological change. Our future success will depend on our ability to maintain a competitive position with respect to technological advances. In addition, as we enter new markets, we will face new competition and will need to adapt to competitive factors that may be different from those we face today.

We are aware that other companies, including Royal DSM, N.V. ("DSM"), BASF, Bayer and Novozymes have alternative methods for obtaining and generating genetic diversity or use mutagenesis techniques to produce genetic diversity. Academic institutions such as the California Institute of Technology, the Max Planck Institute and the Austrian Centre of Industrial Biotechnology are also working in this field. Technological development by others may result in our products and technologies, as well as products developed by our customers using our biocatalysts, becoming obsolete.

Our primary competitors in the biocatalysis for pharmaceutical productsare companies marketing either conventional, non-enzymatic processes or biocatalytic enzymes to manufacturers of pharmaceutical intermediates and APIs, and also existing in-house technologies (both biocatalysts and conventional catalysts) within our client and potential client companies. The principal methods of competition and competitive differentiation in this market are price, product quality and performance, including manufacturing yield, safety and environmental benefits, and speed of delivery of product. Pharmaceutical manufacturers that use biocatalytic processes can face increased competition from manufacturers that use more conventional processes and/or manufacturers that are based in regions (such as India and China) with lower regulatory, safety and environmental costs.

The market for the manufacture and supply of APIs and intermediates is large with many established companies. These companies include many of our large innovator and generic pharmaceutical customers, such as Merck, GSK, Novartis, Pfizer, Bristol-Myers, Kyorin, Urovant and Teva which have significant internal research and development efforts directed at developing processes to manufacture APIs and intermediates. The processes used by these companies include classical conventional organic chemistry reactions, chemo catalytic reactions, biocatalytic reactions or combinations thereof. Our biocatalytic based manufacturing processes must compete with these internally developed routes. Additionally, we also face competition from companies developing and marketing conventional catalysts such as Solvias Inc., BASF and Takasago International Corporation.

The market for supplying enzymes for use in pharmaceutical manufacturing is quite fragmented. There is competition from large industrial enzyme companies, such as Novozymes, and Dupont, as well as subsidiaries of larger contract research/contract manufacturing organizations ("CRO/CMO"), such as DSM, Cambrex Corporation, Lonza, WuXi STA, and Almac Group Ltd. Some fermentation pathway design companies, like Ginkgo Bioworks and Zymergen, whose traditional focus has been to design microorganisms that express small molecule chemicals, could extend into designing organisms that express enzymes.

There is also competition in the enzyme customization and optimization area from several smaller companies, such as BRAIN AG, Arzeda, c-LEcta GmbH and Evocatal GmbH.

We entered the fine chemicals market in 2013, by applying our protein engineering technology in the food market. We face similar forms of competition in this market as in the pharmaceutical markets with the exception that the risk of losing opportunities to larger competitors in fine chemicals is greater given the larger scale of opportunities available in the fine chemicals market compared to the pharmaceutical market. Our significant competitors in the fine chemicals markets include companies that have been in these marketplaces for many years, such as DuPont Industrial Biosciences (DuPont Genencor), DSM, Novozymes and A.B. Enzymes. These companies have greater resources in these markets than we do and have long-term supply arrangements already in place with customers. Our ability to compete in these markets may be limited by our relatively late entrance. We also face competition in both the fine chemicals and pharmaceutical markets from emerging companies offering whole cell metabolic pathway approaches to these markets.

There are numerous companies that participate in the biotherapeutics market generally and the PKU market specifically. Many of these companies are large, successful and well-capitalized. BioMarin Pharmaceutical Inc. ("BioMarin") and Daiichi Sankyo Company market Kuvan® in the United States, Europe and Japan for the treatment of a certain type of PKU. In addition, BioMarin gained US FDA approval in 2018 and began commercial sales of Palynziq™ as an injectable enzyme substitution therapy for the potential treatment of PKU. Several companies, i.e., Synlogic, Homology Medicines, and Rubius have reported clinical efforts to develop biotherapeutic candidates for PKU. Beyond targeting PKU, Takeda (who recently acquired Shire Plc), Genzyme / Sanofi S.A., BioMarin, and other companies market or are actively developing new enzyme therapeutics. There are numerous companies that are developing other forms of therapeutics, such as small molecules, gene therapies, as well as therapies based on gene editing, which could compete with biotherapeutics.

Our ability to compete successfully in any of these markets will depend on our ability to develop proprietary products that reach the market in a timely manner and are technologically superior to and/or are less expensive than other products on the market. Many of our competitors have substantially greater production, financial, research and development, personnel and marketing resources than we do. They also started developing products earlier than we did, which may allow them to establish blocking intellectual property positions or bring products to market before we can. In addition, certain of our competitors may also benefit from local government subsidies and other incentives that are not available to us. As a result, our competitors may be able to develop competing and/or superior technologies and processes, and compete more aggressively and sustain that competition over a longer period of time than we could. Our technologies and products may be rendered obsolete or uneconomical by technological advances or entirely different approaches developed by one or more of our competitors. We cannot be certain that any products we develop in the future will compare favorably to products offered by our competitors or that our existing or future products will compare favorably to any new products that are developed by our competitors. As more companies develop new intellectual property in our markets, the possibility of a competitor acquiring patent or other rights that may limit our products or potential products increases, which could lead to litigation.

Our limited resources relative to many of our competitors may cause us to fail to anticipate or respond adequately to new developments and other competitive pressures. This failure could reduce our competitiveness and market share, adversely affect our results of operations and financial position, and prevent us from obtaining or maintaining profitability.

We must rely on our suppliers, contract manufacturers and customers to deliver timely and accurate information in order to accurately report our financial results in the time frame and manner required by law.

We need to receive timely, accurate and complete information from a number of third parties in order to accurately report our financial results on a timely basis. We rely on suppliers and certain contract manufacturers to provide us with timely and accurate information regarding our inventories and manufacturing cost information, and we rely on current and former collaborators to provide us with product sales and cost saving information in connection with royalties owed to us. Any failure to receive timely information from one or more of these third parties could require that we estimate a greater portion of our revenues and other operating performance metrics for the period, which could cause our reported financial results to be incorrect. Moreover, if the information that we receive is not accurate, our financial statements may be materially incorrect and may require restatement, and we may not receive the full amount of revenues that we are entitled to under these arrangements. Although we typically have audit rights with these parties, performing such an audit could be harmful to our collaborative relationships, expensive and time consuming and may not be sufficient to reveal any discrepancies in a timeframe consistent with our reporting requirements.

Our results of operations may be adversely affected by the results of regulatory tax examinations.

We are subject to value added tax, customs tax, sales and use tax, withholding tax, payroll tax, income tax and other taxes in connection with the operation of our business. Regulators from the various jurisdictions in which we operate periodically

perform audits, and we are regularly subject to, and are currently undergoing, audits and assessments by tax authorities in the United States and foreign jurisdictions for prior tax years. Although we believe our tax estimates are reasonable, and we intend to defend our positions if necessary, the final outcome of tax audits and related proceedings is inherently uncertain and could be materially different than that reflected in our historical income tax provisions and accruals. Moreover, we could be subject to assessments of substantial additional taxes and/or fines or penalties relating to ongoing or future audits. The adverse resolution of any audits or related proceedings could have an adverse effect on our financial position and results of operations.

Business interruptions resulting from disasters or other disturbances could delay us in the process of developing our products and could disrupt our sales. Our business continuity and disaster recovery plans may not adequately protect us from a serious disaster or other disturbance.

Our headquarters and other facilities are located in the San Francisco Bay Area, which in the past has experienced both severe earthquakes and wildfires. Earthquakes, wildfires or other natural disasters could severely disrupt our operations, and have a material adverse effect on our business, results of operations, financial condition and prospects. We are also vulnerable to other types of disasters and other events that could disrupt our operations, such as riot, civil disturbances, war, terrorist acts, infections in our laboratory or production facilities or those of our customers or contract manufacturers and other events beyond our control. If a natural disaster or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as our enterprise financial systems or manufacturing resource planning and enterprise quality systems, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible, for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place currently are limited and are unlikely to prove adequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans. We do not carry insurance for earthquakes and we may not carry sufficient business interruption insurance to compensate us for losses that may occur. Any losses or damages we incur could have a material adverse effect on our cash flows and success as an overall business.

Ethical, legal and social concerns about genetically engineered products and processes could limit or prevent the use of our products, processes, and technologies and limit our revenues.

Some of our products and processes are genetically engineered or involve the use of genetically engineered products or genetic engineering technologies. If we and/or our collaborators are not able to overcome the ethical, legal, and social concerns relating to genetic engineering, our products and processes may not be accepted. Any of the risks discussed below could result in increased expenses, delays, or other impediments to our programs or the public acceptance and commercialization of products and processes dependent on our technologies or inventions. Our ability to develop and commercialize one or more of our technologies, products, or processes could be limited by the following factors:

- public attitudes about the safety and environmental hazards of, and ethical concerns over, genetic research and genetically engineered products and processes, which could influence public acceptance of our technologies, products and processes;
- public attitudes regarding, and potential changes to laws governing ownership of genetic material, which could harm our intellectual property rights with respect to our genetic material and discourage collaborators from supporting, developing, or commercializing our products, processes and technologies; and
- governmental reaction to negative publicity concerning genetically modified organisms, which could result in greater government regulation of genetic research and derivative products. The subject of genetically modified organisms has received negative publicity, which has aroused public debate. This adverse publicity could lead to greater regulation and trade restrictions on imports of genetically altered products. The biocatalysts that we develop have significantly enhanced characteristics compared to those found in naturally occurring enzymes or microbes. While we produce our biocatalysts only for use in a controlled industrial environment, the release of such biocatalysts into uncontrolled environments could have unintended consequences. Any adverse effect resulting from such a release could have a material adverse effect on our business and financial condition, and we may have exposure to liability for any resulting harm.

If we engage in any acquisitions, we will incur a variety of costs and may potentially face numerous risks that could adversely affect our business and operations.

We have made acquisitions in the past, and if appropriate opportunities become available, we expect to acquire additional businesses, assets, technologies, or products to enhance our business in the future. For example, in October 2010, we acquired substantially all of the patents and other intellectual property rights associated with Maxygen's directed evolution technology.

In connection with any future acquisitions, we could:

- issue additional equity securities, which would dilute our current stockholders;
- incur substantial debt to fund the acquisitions;
- use our cash to fund the acquisitions; or
- assume significant liabilities including litigation risk.

Acquisitions involve numerous risks, including problems integrating the purchased operations, technologies or products, unanticipated costs and other liabilities, diversion of management's attention from our core businesses, adverse effects on existing business relationships with current and/or prospective collaborators, customers and/or suppliers, risks associated with entering markets in which we have no or limited prior experience and potential loss of key employees. We do not have extensive experience in managing the integration process and we may not be able to successfully integrate any businesses, assets, products, technologies, or personnel that we might acquire in the future without a significant expenditure of operating, financial and management resources, if at all. The integration process could divert management's time from focusing on operating our business, result in a decline in employee morale and cause retention issues to arise from changes in compensation, reporting relationships, future prospects or the direction of the business. Acquisitions may also require us to record goodwill and non-amortizable intangible assets that will be subject to impairment testing on a regular basis and potential periodic impairment charges, incur amortization expenses related to certain intangible assets, and incur large and immediate write offs and restructuring and other related expenses, all of which could harm our operating results and financial condition. In addition, we may acquire companies that have insufficient internal financial controls, which could impair our ability to integrate the acquired company and adversely impact our financial reporting. If we fail in our integration efforts with respect to any of our acquisitions and are unable to efficiently operate as a combined organization, our business and financial condition may be adversely affected.

We use hazardous materials in our business and we must comply with environmental laws and regulations. Any claims relating to improper handling, storage or disposal of these materials or noncompliance of applicable laws and regulations could be time consuming and costly and could adversely affect our business and results of operations.

Our research and development and commercial processes involve the use of hazardous materials, including chemical, radioactive, and biological materials. Our operations also produce hazardous waste. We cannot eliminate entirely the risk of accidental contamination or discharge and any resultant injury from these materials. Federal, state, local and foreign laws and regulations govern the use, manufacture, storage, handling and disposal of, and human exposure to, these materials. We may be sued for any injury or contamination that results from our use or the use by third parties of these materials, and our liability may exceed our total assets. Although we believe that our activities comply in all material respects with environmental laws, there can be no assurance that violations of environmental, health and safety laws will not occur in the future as a result of human error, accident, equipment failure or other causes. Compliance with applicable environmental laws and regulations may be expensive, and the failure to comply with past, present, or future laws could result in the imposition of fines, third party property damage, product liability and personal injury claims, investigation and remediation costs, the suspension of production, or a cessation of operations, and our liability may exceed our total assets. Liability under environmental laws can be joint and several and without regard to comparative fault. Environmental laws could become more stringent over time imposing greater compliance costs and increasing risks and penalties associated with violations, which could impair our research, development or production efforts and harm our business. In addition, we may have to indemnify some of our customers or suppliers for losses related to our failure to comply with environmental laws, which could expose us to significant liabilities.

We may be sued for product liability.

The design, development, manufacture and sale of our products involve an inherent risk of product liability claims and the associated adverse publicity. For example, we may be named directly in product liability suits relating to drugs that are produced using our enzymes or that incorporate our intermediates and APIs. The biocatalysts, pharmaceutical intermediates and APIs that we produce or are produced for us by our manufacturing partners could be subject to quality control or contamination issues of which we are not aware. Claims could be brought by various parties, including customers who are purchasing products directly from us, other companies who purchase products from our customers or by the end users of the drugs. We could also be named as co-parties in product liability suits that are brought against our contract manufacturers who manufacture our enzymes, pharmaceutical intermediates and APIs. Insurance coverage is expensive and may be difficult to obtain, and may not be available in the future on acceptable terms, or at all. We cannot assure you that any contract manufacturer that we have used in the past or shall use in the future has or will have adequate insurance coverage to cover against potential claims. In addition, although we currently maintain product liability insurance for our products in amounts we believe to be commercially reasonable, if the coverage limits of these insurance policies are not adequate, a claim brought against us, whether covered by

insurance or not, could have a material adverse effect on our business, results of operations, financial condition and cash flows. This insurance may not provide adequate coverage against potential losses, and if claims or losses exceed our liability insurance coverage, we may go out of business. Moreover, we have agreed to indemnify some of our customers for certain claims that may arise out of the use of our products, which could expose us to significant liabilities.

Our ability to use our net operating loss carryforwards to offset future taxable income may be subject to certain limitations.

In general, under Section 382 of the Internal Revenue Code of 1986, as amended (the "Code"), a corporation that undergoes an "ownership change" is subject to limitations on its ability to utilize its pre-change net operating loss carryforwards ("NOLs"), to offset future taxable income. If the Internal Revenue Service challenges our analysis that our existing NOLs are not subject to limitations arising from previous ownership changes, our ability to utilize NOLs could be limited by Section 382 of the Code. Future changes in our stock ownership, some of which are outside of our control, could result in an ownership change under Section 382 of the Code. Furthermore, our ability to utilize NOLs of companies that we may acquire in the future may be subject to limitations. For these reasons, we may not be able to utilize a material portion of the NOLs reflected in our financial statements, even if we attain profitability.

Risks Related to Owning our Common Stock

We are subject to anti-takeover provisions in our certificate of incorporation and bylaws and under Delaware law that could delay or prevent an acquisition of our company, even if the acquisition would be beneficial to our stockholders.

Provisions in our amended and restated certificate of incorporation and our bylaws may delay or prevent an acquisition of us. Among other things, our amended and restated certificate of incorporation and bylaws provide for a board of directors which is divided into three classes, with staggered three-year terms and provide that all stockholder action must be effected at a duly called meeting of the stockholders and not by a consent in writing, and further provide that only our board of directors, the chairman of the board of directors, our chief executive officer or president may call a special meeting of the stockholders. In addition, our amended and restated certificate of incorporation allows our board of directors, without further action by our stockholders, to issue up to 5,000,000 shares of preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions thereof. These provisions may also frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors, who are responsible for appointing the members of our management team. Furthermore, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law which prohibits, with some exceptions, stockholders owning in excess of 15% of our outstanding voting stock from merging or combining with us. Finally, our charter documents establish advanced notice requirements for nominations for election to our board of directors and for proposing matters that can be acted upon at stockholder meetings. Although we believe these provisions together provide for an opportunity to receive higher bids by requiring potential acquirers to negotiate with our board of directors, they would apply even if an offer to acquire our company may be considered beneficial by some stockholders.

Concentration of ownership among our existing officers, directors and principal stockholders may prevent other stockholders from influencing significant corporate decisions and depress our stock price.

Based on the number of shares outstanding as of December 31, 2020, our officers, directors and stockholders who hold at least 5% of our stock together beneficially own approximately 39% of our outstanding common stock. If these officers, directors and principal stockholders or a group of our principal stockholders act together, they will be able to exert a significant degree of influence over our management and affairs and control matters requiring stockholder approval, including the election of directors and approval of mergers or other business combination transactions. The interests of this concentration of ownership may not always coincide with our interests or the interests of other stockholders. For instance, officers, directors and principal stockholders, acting together, could cause us to enter into transactions or agreements that we would not otherwise consider. Similarly, this concentration of ownership may have the effect of delaying or preventing a change in control of our company otherwise favored by our other stockholders. As of December 31, 2020, one stockholder beneficially owned approximately 9% of our common stock.

Sales of a substantial number of shares of our common stock in the public market could cause our stock price to fall.

If our existing stockholders sell, or indicate an intention to sell, substantial amounts of our common stock in the public market, the trading price of our common stock could decline. As of December 31, 2020, we had approximately 64.3 million shares of common stock outstanding. Of those shares, approximately 1.7 million shares were held by current directors, executive officers and other affiliates, or may otherwise be subject to Rule 144 under the Securities Act of 1933, or the Securities Act.

As of December 31, 2020, approximately 0.3 million shares of common stock issuable upon vesting of outstanding restricted stock units and performance stock units and up to approximately 4.6 million shares of common stock issuable upon exercise of outstanding options were eligible for sale in the public market to the extent permitted by the provisions of the applicable vesting schedules, and Rule 144 and Rule 701 under the Securities Act. If these additional shares of common stock are issued and sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

Our share price may be volatile which may cause the value of our common stock to decline and subject us to securities class action litigation.

The market price of shares of our common stock could be subject to wide fluctuations in response to many risk factors listed in this section, and others beyond our control, including:

- actual or anticipated fluctuations in our financial condition and operating results;
- the position of our cash, cash equivalents and equity securities;
- actual or anticipated changes in our growth rate relative to our competitors;
- actual or anticipated fluctuations in our competitors' operating results or changes in their growth rate;
- announcements of technological innovations by us, our collaborators or our competitors;
- announcements by us, our collaborators or our competitors of significant acquisitions or dispositions, strategic partnerships, joint ventures or capital commitments;
- additions or losses of one or more significant pharmaceutical products;
- announcements or developments regarding pharmaceutical products manufactured using our biocatalysts and intermediates;
- the entry into, modification or termination of collaborative arrangements;
- additions or losses of customers;
- additions or departures of key management or scientific personnel;
- competition from existing products or new products that may emerge;
- issuance of new or updated research reports by securities or industry analysts;
- fluctuations in the valuation of companies perceived by investors to be comparable to us;
- disputes or other developments related to proprietary rights, including patent litigation and our ability to obtain patent protection for our technologies;
- contractual disputes or litigation with our partners, customers or suppliers;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders or our other stockholders;
- share price and volume fluctuations attributable to inconsistent trading volume levels of our shares;
- general market conditions in our industry; and
- general economic and market conditions.

Furthermore, the stock markets have experienced extreme price and volume fluctuations that have affected and continue to affect the market prices of equity securities of many companies. These fluctuations often have been unrelated or disproportionate to the operating performance of those companies. These broad market and industry fluctuations, as well as general economic, political and market conditions such as recessions, interest rate changes or international currency fluctuations, may negatively impact the market price of shares of our common stock. In the past, companies that have experienced volatility in the market price of their stock have been subject to securities class action litigation. We may be the target of this type of litigation in the future. Securities litigation against us could result in substantial costs and divert our management's attention from other business concerns, which could seriously harm our business.

We may incur losses associated with currency fluctuations and may not be able to effectively hedge our exposure.

Our operating results and cash flows are subject to volatility due to fluctuations in foreign currency exchange rates. Our primary exposure to fluctuations in foreign currency exchange rates relates to cash denominated in currencies other than the United States dollar ("USD"). The weakening of foreign currencies relative to the USD adversely affects our foreign currency-denominated cash. In periods when the USD declines in value as compared to the foreign currencies in which we incur

expenses, our foreign-currency based cash decrease when translated into United States dollars. Conversely, the strengthening of foreign currencies relative to the USD will generally be beneficial to our foreign currency-denominated cash when translated into USD.

The effect of a 10% unfavorable change in exchange rates on foreign denominated receivables and cash as of December 31, 2020 would have had foreign exchange losses of approximately $0.1 million recognized as a component of other expense in our consolidated statement of operations.

We do not engage in foreign currency hedging transactions, and as a result, unfavorable movements in foreign currency exchange rates may have an adverse financial impact, which could materially adversely affect our financial condition or results of operations. See “Item 7A. Quantitative and Qualitative Disclosures About Market Risk” for additional discussion on the impact of foreign exchange risk.

General Risk Factors

Changes in financial accounting standards or practices may cause adverse, unexpected financial reporting fluctuations and affect our reported results of operations.

Financial accounting standards may change or their interpretation may change. A change in accounting standards or practices can have a significant effect on our reported results and may even affect our reporting of transactions completed before the change becomes effective. Changes to existing rules or the re-examining of current practices may adversely affect our reported financial results or the way we conduct our business. In particular, in order to be able to comply with the requirements of the revenue recognition standard under Accounting Standards Update (ASU) 2014-09 *Revenue from Contracts with Customers (Topic 606)* and related amendments (“ASC 606”), we have updated and enhanced our internal accounting processes and our internal controls over financial reporting. This has required, and will continue to require, additional investments by us, and may require incremental resources that could increase our operating costs in future periods. Further, the timing of recognition for our product sales under certain license and supply agreements and research and development revenues, on or after January 1, 2018, have been changed as a result of ASC 606.

We incur significant costs as a result of operating as a public company, and our management is required to devote substantial time to compliance initiatives.

As a public company, we incur significant legal, accounting and other expenses. In addition, the Sarbanes-Oxley Act and the Dodd-Frank Wall Street Reform and Consumer Protection Act, as well as related rules implemented by the Securities and Exchange Commission and the Nasdaq Stock Market, impose various requirements on public companies that require our management and other personnel to devote a substantial amount of time to compliance initiatives.

In addition, the Sarbanes-Oxley Act requires, among other things, that we maintain effective internal control over financial reporting and disclosure controls and procedures. In particular, we must perform system and process evaluation and testing of our internal control over financial reporting to allow management and our independent registered public accounting firm to report on the effectiveness of our internal control over financial reporting, as required by Section 404 of the Sarbanes-Oxley Act. Our compliance with Section 404 requires that we incur substantial accounting expense and expend significant management time on compliance-related issues. Moreover, if we are not able to maintain compliance with the requirements of Section 404, our stock price could decline, and we could face sanctions, delisting or investigations by the Nasdaq Global Market, or other material adverse effects on our business, reputation, results of operations, financial condition or liquidity.

We may also be subject to more stringent state law requirements. For example, in September 2018, California Governor Jerry Brown signed into law Senator Bill 826 (SB 826), which generally requires public companies with principal executive offices in California to have a minimum number of females on the company's board of directors. As of December 31, 2019, each public company with principal executive offices in California was required to have at least one female on its board of directors. By December 31, 2021, each public company will be required to have at least two females on its board of directors if the company has at least five directors, and at least three females on its board of directors if the company has at least six directors. The new law does not provide a transition period for newly listed companies. Similarly, in January 2020, New York enacted a new law that mandates a study on the number of female directors on the board of corporations doing business in New York.

Additionally, on September 30, 2020, California Governor Gavin Newsom signed into law Assembly Bill 979 (AB 979), which generally requires public companies with principal executive offices in California to include specified numbers of directors from "underrepresented communities." A director from an "underrepresented community" means a director who self-identifies as Black, African American, Hispanic, Latino, Asian, Pacific Islander, Native American, Native Hawaiian, Alaska Native, gay, lesbian, bisexual or transgender. By December 31, 2021, each public company with principal executive offices in California is

required to have at least one director from an underrepresented community. By December 31, 2022, a public company with more than four but fewer than nine directors will be required to have a minimum of two directors from underrepresented communities, and a public company with nine or more directors will need to have a minimum of three directors from underrepresented communities. Similar to SB 826, AB 979 does not provide a transition period for newly listed companies.

If we fail to comply with either SB 826 or AB 979, we could be fined by the California Secretary of State, with a $100,000 fine for the first violation and a $300,000 fine for each subsequent violation of either law, and our reputation may be adversely affected.

If securities or industry analysts do not publish research or reports about our business, or publish negative reports about our business, our stock price and trading volume could decline.

The trading market for our common stock will be influenced by the research and reports that securities or industry analysts publish about us or our business. We do not have any control over these analysts. If one or more of the analysts who cover us downgrade our stock or change their opinion of our stock in a negative manner, our stock price would likely decline. If one or more of these analysts cease coverage of our company or fail to regularly publish reports on us, we could lose visibility in the financial markets, which could cause our stock price or trading volume to decline.

Epidemic diseases, or the perception of their effects, could have a material adverse effect on our business, financial condition, results of operations or cash flows.

Outbreaks of epidemic, pandemic, or contagious diseases, such as the COVID-19 pandemic or, historically, the Ebola virus, Middle East Respiratory Syndrome, Severe Acute Respiratory Syndrome or the H1N1 virus, could disrupt our business. Business disruptions could include disruptions or restrictions on our ability to travel or to distribute our products, as well as temporary closures of the facilities of our customers, partners, suppliers or contract manufacturers. Any disruption of our customers, partners, suppliers or contract manufacturers would likely impact our sales and operating results. In addition, a significant outbreak of epidemic, pandemic, or contagious diseases in the human population could result in a widespread health crisis that could adversely affect the economies and financial markets of many countries, resulting in an economic downturn that could affect demand for our products and services. Any of these events could have a material adverse effect on our business, financial condition, results of operations, or cash flows.

ITEM 1B. UNRESOLVED STAFF COMMENTS

Not applicable.

ITEM 2. PROPERTIES

Facilities

Our headquarters are located in Redwood City, California, where we lease approximately 77,300 square feet of office and laboratory space.

Our lease ("RWC Lease") with Metropolitan Life Insurance Company ("MetLife") includes approximately 28,200 square feet of space located at 200 and 220 Penobscot Drive, Redwood City, California (the "200/220 Penobscot Space"), approximately 37,900 square feet of space located at 400 Penobscot Drive, Redwood City, California (the "400 Penobscot Space") (the 200/220 Penobscot Space and the 400 Penobscot Space are collectively referred to as the "Penobscot Space"), and approximately 11,200 square feet of space located at 501 Chesapeake Drive, Redwood City, California (the "Chesapeake Space"). Until the end of January 2020, we also leased approximately 29,900 square feet of space located at 101 Saginaw Drive, Redwood City, California (the "Saginaw Space"). During January 2020, we subleased approximately 26,500 square feet of the Saginaw Space to Minerva Surgical, Inc. Both the lease and sublease for the Saginaw Space expired at the end of January 2020. From February through April 2020, we subleased approximately 3,400 square feet 101 Saginaw Drive from Minerva Surgical, Inc. The sublease expired at the end of April 2020.

We entered into the initial lease with MetLife for our facilities in Redwood City in 2004 and the RWC lease has been amended multiple times since then to adjust the leased space and terms of the RWC Lease. In February 2019, we entered into an Eighth Amendment to the RWC Lease (the "Eighth Amendment") with MetLife with respect to the Penobscot Space and the 501 Chesapeake Space to extend the term of the RWC Lease for additional periods. Pursuant to the Eighth Amendment, the term of the lease of the Penobscot Space has been extended through May 2027. The lease term for the 501 Chesapeake Space has been extended to May 2029. We have one (1) option to extend the term of the lease for the Penobscot Space for five (5) years, and one (1) separate option to extend the term of the lease for the 501 Chesapeake Space for five (5) years.

In the first quarter of 2021, we entered into lease agreement with ARE-San Francisco No. 63, LLC ("ARE") to lease a portion of a facility comprising approximately 36,593 rentable square feet in San Carlos, California to serve as additional office and research and development laboratory space (the "San Carlos Space"). We expect to commence occupancy of the San Carlos Space in November 2021 once tenant improvements are substantially completed by ARE in accordance with the construction plan.

We believe that the facilities that we currently lease in Redwood City, California and the San Carlos, California facility we plan to lease are adequate for our needs for the immediate future and that, should it be needed, additional space can be leased to accommodate any future growth.

ITEM 3. LEGAL PROCEEDINGS

We are not currently a party to any material pending litigation or other material legal proceedings.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Market Information

Our common stock is quoted on the Nasdaq Global Select Market ("Nasdaq"), under the symbol "CDXS."

As of February 26, 2021, there were approximately 130 stockholders of record. A substantially greater number of stockholders may be "street name" or beneficial holders, whose shares are held of record by banks, brokers and other financial institutions.

Dividend Policy

We have never declared or paid cash dividends on our common stock, and we currently do not plan to declare dividends on shares of our common stock in the foreseeable future. We expect to retain our future earnings, if any, for use in the operation and expansion of our business. In addition, unless waived, the terms of our Credit Facility prohibit us from paying any cash dividends or making other distributions. The payment of cash dividends in the future, if any, will be at the discretion of our board of directors and will depend upon such factors as earnings levels, capital requirements, our overall financial condition and any other factors deemed relevant by our board of directors.

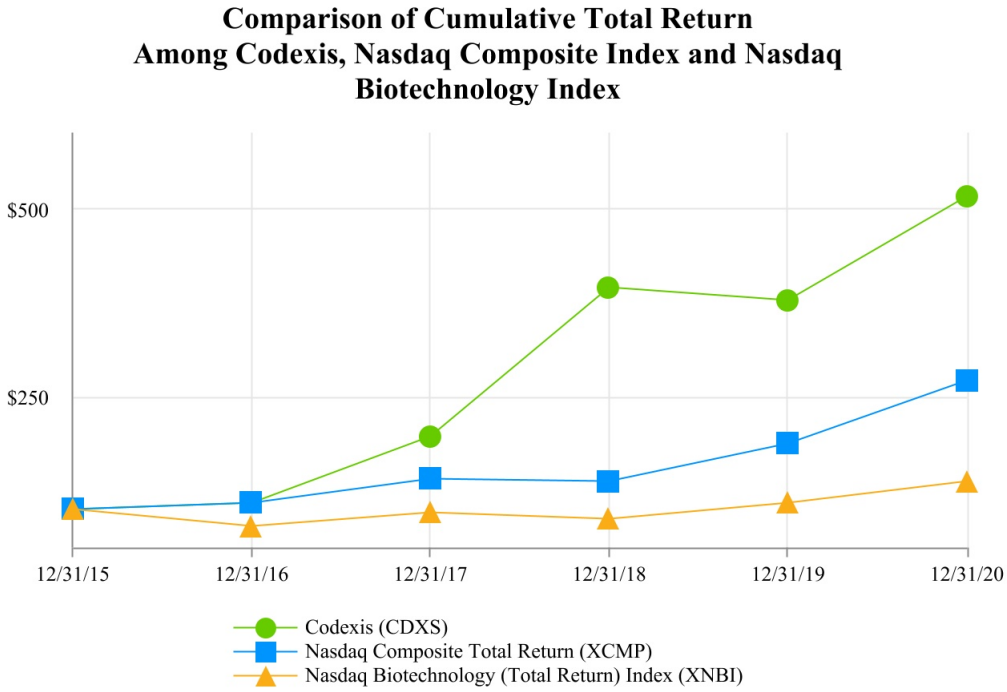
Securities Authorized for Issuance under Equity Compensation Plans

The information required by this item concerning securities authorized for issuance under equity compensation plans is incorporated by reference from the information that will be set forth in the Definitive Proxy Statement to be filed with the Securities and Exchange Commission in connection with the Annual Meeting of Stockholders to be held in 2021 (the "2021 Proxy Statement") under the heading "Executive Compensation—Equity Compensation Plan Information."

Stock Price Performance Graph

The following tabular information and graph compare our total common stock return with the total return for (i) the Nasdaq Composite Index and (ii) the Nasdaq Biotechnology Index for the period December 31, 2015 through December 31, 2020. The figures represented below assume an investment of $100 in our common stock at the closing price on December 31, 2015 and in the Nasdaq Composite Index and the Nasdaq Biotechnology Index on December 31, 2015 and the reinvestment of dividends into shares of common stock. The comparisons in the table and graph are required by the SEC and are not intended to forecast or be indicative of possible future performance of our common stock. The tabular information and graph shall not be deemed "soliciting material" or to be "filed" for purposes of Section 18 of the Exchange Act or otherwise subject to the liabilities under that Section, and shall not be deemed to be incorporated by reference into any of our filings under the Securities Act or the Exchange Act.

		December 31,					
$100 investment in stock or index	**Ticker**	**2015**	**2016**	**2017**	**2018**	**2019**	**2020**
Codexis, Inc.	CDXS	$ 100.00	$ 108.75	$ 197.40	$ 394.80	$ 378.01	$ 516.08
Nasdaq Composite Total Return	XCMP	$ 100.00	$ 108.87	$ 141.13	$ 137.12	$ 187.44	$ 271.64
Nasdaq Biotechnology (Total Return) Index	XNBI	$ 100.00	$ 78.65	$ 95.67	$ 87.19	$ 109.08	$ 137.90



Unregistered Sales of Equity Securities and Use of Proceeds

Unregistered Sales of Equity Securities

During the year ended December 31, 2020, we did not issue or sell any unregistered securities not previously disclosed in a Quarterly Report on Form 10-Q or in a Current Report on Form 8-K.

Issuer Purchases of Equity Securities

None.

ITEM 6. SELECTED FINANCIAL DATA

The following selected consolidated financial data should be read together with our Consolidated Financial Statements and accompanying Notes and "Management's Discussion and Analysis of Financial Condition and Results of Operations" appearing elsewhere in this Annual Report on Form 10-K. The selected consolidated financial data in this section is not intended to replace our Consolidated Financial Statements and the accompanying Notes. Our historical results are not necessarily indicative of our future results.

We derived the consolidated statements of operations data for the fiscal years ended December 31, 2020, 2019, and 2018 and the consolidated balance sheets data as of December 31, 2020 and 2019 from our audited Consolidated Financial Statements appearing elsewhere in this filing. The consolidated statements of operations data for the fiscal years ended December 31, 2017 and 2016 and the consolidated balance sheets data as of December 31, 2018, 2017 and 2016 have been derived from our audited Consolidated Financial Statements not included in this filing. The data should be read in conjunction with the Consolidated Financial Statements, related Notes and other financial information included herein.

SELECTED CONSOLIDATED FINANCIAL DATA

	Year Ended December 31,				
	2020	2019	2018	2017	2016
	(1) (2)	(1) (2)	(1)		
	(In Thousands, Except Per Share Amounts)				
Consolidated Statements of Operations Data:					
Revenues:					
Product revenue	$ 30,220	$ 29,465	$ 25,590	$ 26,685	$ 15,321
Research and development revenue	38,836	38,993	35,004	23,339	33,516
Total revenues	69,056	68,458	60,594	50,024	48,837
Costs and operating expenses:					
Cost of product revenue	13,742	15,632	12,620	14,327	9,753
Research and development	44,185	33,873	29,978	29,659	22,229
Selling, general and administrative	35,049	31,502	29,291	29,008	25,419
Total costs and operating expenses	92,976	81,007	71,889	72,994	57,401
Loss from operations	(23,920)	(12,549)	(11,295)	(22,970)	(8,564)
Interest income	405	1,287	671	147	60
Other expenses, net	(156)	(656)	(291)	(92)	(94)
Loss before income taxes	(23,671)	(11,918)	(10,915)	(22,915)	(8,598)
Provision for (benefit from) income taxes	339	17	(37)	81	(40)
Net loss	$ (24,010)	$ (11,935)	$ (10,878)	$ (22,996)	$ (8,558)
Net loss per share, basic and diluted	$ (0.40)	$ (0.21)	$ (0.21)	$ (0.50)	$ (0.21)
Weighted average common stock shares used in computing net loss per share, basic and diluted	59,360	56,525	52,205	46,228	40,629

(1) Financial results for years ended December 31, 2020, 2019 and 2018 as compared to the years ended December 31, 2017 and 2016 reflect the effects of adopting Accounting Standards Update ("ASU") 2014-09, *Revenue from Contracts with Customers (Topic 606)* and the related amendments ("ASC 606"), which provided a new basis of accounting for our revenue arrangements beginning in the 2018 fiscal year 2018 and continuing thereafter. The adoption of ASC 606 limits the comparability of revenue and certain expenses, including revenues and costs and operating expenses, presented in the results of operations for the years ended December 31, 2020, 2019 and 2018 when compared to the years ended December 31, 2017 and 2016.

(2) Lease costs for the years ended December 31, 2020 and 2019 as compared to years ended December 31, 2018, 2017 and 2016 reflect the effects of adopting ASU 2016-02 and the related amendments, *Leases (Topic 842)* ("ASC 842") which provided a new basis of accounting for leases beginning in our 2019 fiscal year. The adoption of ASC 842 limited the comparability of lease costs included in operating expenses, presented in the results of operations for the years ended December 31, 2020 and 2019 when compared to the years ended December 31, 2018, 2017 and 2016.

	December 31,				
	2020	2019	2018	2017	2016
	(1) (2)	(1) (2)	(1)		
Consolidated Balance Sheets Data:			(In Thousands)		
Cash, cash equivalents and restricted cash	$ 150,817	$ 92,221	$ 54,485	$ 32,776	$ 20,864
Working capital	159,442	98,817	50,085	20,087	14,860
Total assets	221,646	149,073	79,283	53,625	35,648
Total liabilities	51,543	43,556	22,977	29,078	16,549
Total stockholders' equity	170,103	105,517	56,306	24,547	19,099

(1) Financial results for years ended December 31, 2020, 2019 and 2018 as compared to the years ended December 31, 2017 and 2016 reflected the effects of adopting ASU 2014-09, *Revenue from Contracts with Customers* ("ASC 606"), which provided a new basis of accounting for our revenue arrangements during our 2020, 2019 and 2018 fiscal years. We recognized the cumulative effect of applying ASC 606 and recognized a $4.1 million increase to the opening balance of the accumulated deficit in 2018. The comparative information for the years ended December 31, 2017 and 2016 has not been restated and continues to be reported under the accounting standards in effect for the periods presented.

(2) Financial results for years ended December 31, 2020 and 2019 as compared to the years ended December 31, 2018, 2017 and 2016 reflected the effects of adopting ASU 2016-02 and the related amendments, *Leases (Topic 842)* ("ASC 842"), which established a right-of-use ("ROU") model requiring lessees to record a ROU asset and lease obligations on the balance sheet for all leases with terms longer than 12 months. On adoption of ASC 842 in 2019, for operating leases, we recognized $26.6 million of ROU assets and $27.6 million of lease obligations, and for finance leases, we recognized $0.5 million of ROU assets and $0.3 million of lease obligations in our consolidated balance sheet.

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

The following discussion and analysis should be read in conjunction with our audited Consolidated Financial Statements and the related Notes that appear elsewhere in this Annual Report on Form 10-K. This Annual Report on Form 10-K contains "forward-looking statements" within the meaning of Section 21E of the Exchange Act. These statements are often identified by the use of words such as "may," "will," "expect," "believe," "anticipate," "intend," "could," "should," "estimate," or "continue," and similar expressions or variations. Such forward-looking statements are subject to risks, uncertainties and other factors that could cause actual results and the timing of certain events to differ materially from future results expressed or implied by such forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in the section titled "Risk Factors," set forth in Part I, Item 1A of this Annual Report on Form 10-K and elsewhere in this report. The forward-looking statements in this Annual Report on Form 10-K represent our views as of the date of this Annual Report on Form 10-K. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so except to the extent required by applicable law. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this Annual Report on Form 10-K.

Business Overview

We discover, develop and sell enzymes and other proteins that deliver value to our clients in a growing set of industries. We view proteins as a vast, largely untapped source of value-creating products, and we are using our proven technologies, which we have been continuously improving since our inception in 2002, to commercialize an increasing number of novel enzymes, both as proprietary Codexis products and in partnership with our customers.

We are a pioneer in harnessing computational technologies to drive biology advancements. Since 2002, we have made substantial investments in the development of our CodeEvolver® protein engineering technology platform, the primary source of our competitive advantage. Our technology platform is powered by proprietary, artificial intelligence-based, computational algorithms that rapidly mine the structural and performance attributes of our large and continuously growing library of protein variants. These computational outputs enable increasingly reliable predictions for next generation protein variants to be engineered, enabling time- and cost-efficient delivery of the targeted performance enhancements. In addition to its computational prowess, our CodeEvolver® protein engineering technology platform integrates additional modular competencies, including robotic high-throughput screening and genomic sequencing, organic chemistry and bioprocess development which are all coordinated to rapidly innovate novel, fit-for-purpose products.

The core historical application of the technology has been in developing commercially viable biocatalytic manufacturing processes for more sustainable production of complex chemicals. It begins by conceptually designing the most cost-effective and practical process for a targeted product. We then develop optimized biocatalysts to enable the designed process, using our CodeEvolver® platform. Engineered biocatalyst candidates, numbering many thousands for each project, are then rapidly screened and validated using high throughput methods under process-relevant operating conditions. This approach results in an optimized biocatalyst that enables cost-efficient processes that are relatively simple to run in conventional manufacturing equipment. This also allows for efficient technical transfer of our processes to our manufacturing partners.

The successful embodiment of our CodeEvolver® protein engineering technology platform in commercial manufacturing processes requires well-integrated expertise in a number of technical disciplines. In addition to those competencies directly integrated in our CodeEvolver® protein engineering platform, such as molecular biology, enzymology, microbiology, cellular engineering, metabolic engineering, bioinformatics, biochemistry and high throughput analytical chemistry, our process development projects also involve integrated expertise in organic chemistry, chemical process development, chemical engineering, bioprocess development and fermentation engineering. Our integrated, multi-disciplinary approach to product and process development is a critical success factor for the Company.

We initially commercialized our CodeEvolver® protein engineering technology platform and products in the manufacture of small molecule pharmaceuticals, which remains a primary business focus. Our customers, which include many large, global pharmaceutical companies, use our technology, products and services in their process development and in manufacturing. Additionally, we have licensed our proprietary CodeEvolver® protein engineering technology platform to global pharmaceutical companies enabling them to use this technology, in house, to engineer enzymes for their own businesses. Most recently, in May 2019, we entered into a Platform Technology Transfer and License Agreement (the "Novartis CodeEvolver® Agreement") with Novartis. The Novartis CodeEvolver® Agreement (Codexis' third such agreement with large pharma companies) allows Novartis to use our proprietary CodeEvolver® protein engineering platform technology in the field of human healthcare.

As evidence of our strategy to extend our technology beyond pharmaceutical manufacturing, we have also used the technology to develop biocatalysts and enzyme products for use in a broader set of industrial markets, including several large verticals, such as food, feed, consumer care and fine chemicals. In addition, we are using our technology to develop enzymes for various life science related applications, such as next generation sequencing ("NGS") and polymerase chain reaction ("PCR/qPCR") for in vitro molecular diagnostic and genomic research applications. In December 2019, we entered into a license agreement to provide Roche Sequencing Solutions, Inc. with our first enzyme for this target market: the Company's EvoT4™ DNA ligase.
In June 2020, we also entered into a Master Collaboration and Research Agreement with MAI (the "MAI Agreement") pursuant to which we are leveraging our CodeEvolver® platform technology to improve the DNA polymerase enzymes that are critical for enzymatic DNA synthesis. Concurrently with the MAI Agreement, we entered into a Stock Purchase Agreement with Molecular Assemblies, Inc ("MAI") pursuant to which we purchased 1,587,050 shares of MAI's Series A preferred stock for $1.0 million and, in connection with the transaction, John Nicols, our President and Chief Operating Officer, also joined MAI's board of directors.

Approximately five years ago, we began using the CodeEvolver® protein engineering technology platform to develop early stage, novel biotherapeutic product candidates, both in partnership with customers and for our own proprietary Codexis drug candidates. Our first program was for the potential treatment of phenylketonuria ("PKU") in humans. PKU is an inherited metabolic disorder in which the enzyme that converts the essential amino acid phenylalanine into tyrosine is deficient. In October 2017, we entered into a Global Development, Option and License Agreement (the "Nestlé License Agreement") with Societé des Produits Nestlé S.A., formerly known as Nestec Ltd. ("Nestlé Health Science") to advance CDX-6114, our enzyme biotherapeutic product candidate for the potential treatment of PKU. In February 2019, Nestlé Health Science exercised its option to obtain an exclusive license to develop and commercialize CDX-6114. Also in October 2017, we entered into the Nestlé SCA pursuant to which we and Nestlé Health Science are collaborating to leverage the CodeEvolver® platform technology to develop other novel enzymes for Nestlé Health Science's established Consumer Care and Medical Nutrition business areas. In January 2020, we entered into a development agreement with Nestlé Health Science to advance a new lead candidate discovered under the Nestlé SCA, CDX-7108, into preclinical development and early clinical studies as a potential treatment for a gastro-intestinal disorder. In parallel, the Nestlé SCA was extended through December 2021 to support the discovery of therapeutic candidates for additional disorders. In March 2020, we entered into a Strategic Collaboration and License Agreement ("Takeda Agreement") with Shire Human Genetic Therapies, Inc., a wholly-owned subsidiary of Takeda Pharmaceutical Company Limited ("Takeda"), for the research and development of novel gene therapies for certain disease indications, including the treatment of lysosomal storage disorders and a blood factor deficiency.

Business Segments

We manage our business as two business segments: Performance Enzymes and Novel Biotherapeutics. See Note 15,*"Segment, Geographical and Other Revenue Information*" in the Notes to the Consolidated Financial Statements set forth in Item 8 of this Annual Report on Form 10-K.

Performance Enzymes

We initially commercialized our CodeEvolver® protein engineering technology platform and products in the manufacture of small molecule pharmaceuticals and, to date, this continues to be our largest market served. Our customers, which include many large global pharmaceutical companies, use our technology, products and services in their manufacturing processes and process development. We have also used the technology to develop customized enzymes for use in other industrial markets. These markets consist of several large industrial verticals, including food, feed, consumer care, and fine chemicals. We also use our technology in the life sciences markets to develop enzymes for customers using NGS and PCR/qPCR for in vitro molecular diagnostic and molecular biology research applications, as well DNA/RNA synthesis and health monitoring applications.

Novel Biotherapeutics

We are also targeting new opportunities in the pharmaceutical industry to discover, improve, and/or develop biotherapeutic drug candidates. We believe that our CodeEvolver® protein engineering platform technology can be used to discover novel biotherapeutic drug candidates that will target human diseases that are in need of improved therapeutic interventions. Similarly, we believe that we can deploy our platform technology to improve specific characteristics of a customer's pre-existing biotherapeutic drug candidate, such as its activity, stability or immunogenicity. Our first lead program was for the potential treatment of hyperphenylalaninemia ("HPA") (also referred to as PKU) in humans. PKU is an inherited metabolic disorder in which the enzyme that converts the essential amino acid phenylalanine into tyrosine is deficient. In October 2017, we announced a global development, option and license agreement with Nestlé Health Science to advance CDX-6114, our own novel orally administrable enzyme therapeutic candidate for the potential treatment of PKU. In July 2018, we announced that we had dosed the first subjects in a first-in-human Phase 1a dose-escalation trial with CDX-6114, which was conducted in

Australia. The initiation of the trial triggered a $4.0 million milestone payment from Nestlé Health Science. The $1.0 million milestone payment that was triggered by the achievement of a formulation relating to CDX-6114 was received in February 2019. In January 2019, we received notice from the FDA that it had completed its review of our IND for CDX-6114 and concluded that we may proceed with the proposed Phase 1b multiple ascending dose study in healthy volunteers in the United States. In February 2019, Nestlé Health Science exercised its option to obtain an exclusive, worldwide, royalty-bearing, sub-licensable license for the global development and commercialization of CDX-6114 for the management of PKU. As a result of the option exercise, we earned a milestone and recognized $3.0 million in revenues in the first quarter of 2019. Upon exercising its option, Nestlé Health Science assumed all responsibilities for future clinical development and commercialization of CDX-6114. During 2020, Nestlé Health Science completed a safety, tolerability and PK/PD study of CDX-6114 in PKU patients that demonstrated CDX-6114 was well tolerated and safe at all doses tested. In addition, an increase in blood levels of cinnamic acid, a biomarker of enzyme activity, was observed which is consistent with the intended mode of action for CDX-6114.

In October 2017, we separately entered into the Nestlé SCA with Nestlé Health Science pursuant to which we and Nestlé Health Science are collaborating to leverage the CodeEvolver® platform technology to develop other novel enzymes for Nestlé Health Science's established Consumer Care and Medical Nutrition business areas. In January 2020, we and Nestlé Health Science entered into a development agreement pursuant to which we and Nestlé Health Science are collaborating to advance into pre-clinical and early clinical studies a lead candidate targeting a gastro-intestinal disorder, CDX-7108, discovered through the Nestlé SCA. The Nestlé SCA was extended through December 2021. During 2020, we, together with Nestlé Health Science, continued to advance CDX-7108 towards initiation of a Phase 1 clinical trial which we anticipate will begin in 2021. Additionally, the parties initiated two new programs under the Nestlé SCA targeting a gastro-intestinal disorder.

In March 2020, we entered into the Takeda Agreement with Takeda pursuant to which we are collaborating to research and develop protein sequences for use in gene therapy products for certain disease indications in accordance with the respective program plans for Fabry Disease, Pompe Disease, and an undisclosed blood factor deficiency. In March 2020, we received a one-time, non-refundable cash payment of $8.5 million. Of these programs, the Fabry disease program is the most advanced, with multiple sequences, including CDX-6311, having been provided to Takeda.

For further description of our business segments, see Note 15, "Segment, Geographical and Other Revenue Information," in the Notes to Consolidated Financial Statements set forth in Item 8 of this Annual Report on Form 10-K.

Business Update Regarding COVID-19

We are subject to risks and uncertainties as a result of the current COVID-19 pandemic. The COVID-19 pandemic has presented a substantial public health and economic challenge around the world and is affecting our employees, communities and business operations, as well as the U.S. economy and other economies worldwide. The full extent to which the COVID-19 pandemic will directly or indirectly impact our business, results of operations and financial condition will depend on future developments that are highly uncertain and may not be accurately predicted, including the duration and severity of the pandemic and the extent and severity of the impact on our customers, new information that may emerge concerning COVID-19, the actions taken to contain it or treat its impact and the economic impact on local, regional, national and international markets.

To date, we and our collaboration partners have been able to continue to supply our enzymes to our customers worldwide. However, we are dependent on our manufacturing and logistics partners and consequently, disruptions in operations of our partners and customers may affect our ability to supply enzymes to our customers. Furthermore, our ability to provide future research and development ("R&D") services will continue to be impacted as a result of governmental orders and any disruptions in operations of our customers with whom we collaborate. We believe that these disruptions have had a negative impact on revenue for the year ended December 31, 2020, although we are unable to fully determine and quantify the extent to which this pandemic has affected the amount and timing of our total revenues. The extent to which the pandemic may impact our business operations and operating results will continue to remain highly dependent on future developments, which are uncertain and cannot be predicted with confidence.

In the U.S., the impact of COVID-19, including governmental orders ("Orders") governing the operation of businesses during the pandemic, caused the temporary closure of our Redwood City, California facilities and has disrupted our R&D operations. R&D operations for several projects were temporarily suspended from mid-March 2020 through the end of April 2020 in accordance with these Orders. In May 2020, we re-initiated limited R&D operations and have ramped up operations such that we are currently utilizing the majority of our normal R&D capacity while following county, state and federal COVID-19 guidance for the protection of our employees. Additionally, we resumed small scale manufacturing at our Redwood City pilot plant in May 2020.

Our future results of operations and liquidity could be adversely impacted by delays in payments of outstanding receivable amounts beyond normal payment terms, supply chain disruptions and uncertain demand, and the impact of any initiatives or programs that we may undertake to address financial and operations challenges faced by our customers. The extent to which the COVID-19 pandemic may materially impact our financial condition, liquidity, or results of operations in the future is uncertain.

For additional information on the various risks posed by the COVID-19 pandemic, please read Item 1A. Risk Factors included in this Annual Report on Form 10-K.

Recent Investing Activities

In June 2020, we entered into a Stock Purchase Agreement with MAI pursuant to which we purchased 1,587,050 shares of MAI's Series A preferred stock for $1.0 million. In connection with the transaction, John Nicols, our President and Chief Operating Officer, also joined MAI's board of directors. Concurrently with our initial equity investment, we entered into the MAI Agreement, pursuant to which we are performing services utilizing our CodeEvolver® protein engineering platform technology to improve DNA polymerase enzymes in exchange for compensation in the form of additional shares of MAI's Series A preferred stock. We received 714,171 shares of MAI's Series A preferred stock from research and development activities in the year ended December 31, 2020, and recognized $0.9 million in research and development revenue from these activities with MAI in the year ended December 31, 2020. At December 31, 2020, we had $0.5 million of financial assets due from MAI for services rendered.

In November 2020, we announced the SynBio Innovation Accelerator ("Accelerator") collaboration with Casdin Capital, LLC ("Casdin"). The goal of the Accelerator is to fund the early-stage companies with disruptive technology platforms or unique product development capabilities in the field of synthetic and industrial biotechnology. There is no commitment under the Accelerator collaboration for either party to make any specific investments or any volume of investments. The first investment by Codexis associated with the Accelerator collaboration was made in Arzeda Corp., a privately-held computational protein design company that focuses on computational approaches to designing novel enzyme functionality. We invested $1.0 million in Arzeda and received a convertible subordinated note issued by Arzeda Corp. The note is an available-for-sale non-marketable interest-bearing debt security which will mature in July 2021.

In December 2020, we completed an underwritten public offering of 4,928,572 shares of our common stock, including the exercise in full by the underwriters of their option to purchase an additional 642,857 of our shares, at a public offering price of $17.50 per share. After deducting the underwriting discounts, commissions, and estimated offering expenses, net proceeds were approximately $80.8 million.

Results of Operations Overview

Revenues were $69.1 million in 2020, a 1% increase from $68.5 million in 2019. Product revenue, which consists primarily of sales of biocatalysts, pharmaceutical intermediates, and Codex® biocatalyst panels and kits, was $30.2 million in 2020, an increase of 3% compared with $29.5 million in 2019. The increase in product revenue was primarily due to higher customer demand for enzymes for the manufacture of branded pharmaceuticals products.

Research and development revenues, which include license, technology access and exclusivity fees, research service fees, milestone payments, royalties, and optimization and screening fees, totaled $38.8 million in 2020, with a nominal decrease compared with $39.0 million in 2019. The decrease in research and development revenue was primarily due to lower revenues from Novartis CodeEvolver® Agreement, a prior year functional license fee revenue from Nestlé Health Science, and a prior year milestone payment from GSK under GSK CodeEvolver® Agreement, partially offset by the recognition of license fees from Takeda under the Takeda Agreement, and recognition of functional license fees revenue from Porton.

Our products' profitability is affected by many factors including the margin of profit on products we sell. Our profit margins are affected by many factors including the costs of internal and third-party fixed and variable costs, including materials and supplies, labor, facilities and other overhead costs. Profit margin data is used as a management performance measure to provide additional information regarding our results of operations on a consolidated basis. Product gross margins increased to 55% in 2020, compared to 47% in 2019 due to improved product mix due to higher demand for enzymes for the manufacture of branded pharmaceutical products.

Research and development expenses were $44.2 million in 2020, an increase of 30% from $33.9 million in 2019. The increase was primarily due to an increase in costs associated with outside services relating to Chemistry, Manufacturing and Controls ("CMC") and regulatory expenses, higher headcount, higher allocable expenses, higher outside services, higher in depreciation expense and were partially offset by lower lab supply expenses.

Selling, general and administrative expenses were $35.0 million in 2020, an increase of 11% compared to $31.5 million in 2019. The increase was primarily due to an increase in costs associated with headcount, stock compensation expense, consultants, legal and accounting fees, facilities, outside and temporary services, and licensed technology, which were partially offset by lower allocable expenses and travel expenses.

Net loss was $24.0 million, or a net loss of $0.40 per share, in 2020 compared to a net loss of $11.9 million, or a net loss of $0.21 per share, in 2019. The increase in net loss was primarily related to higher operating expenses composed of increases in costs associated headcount, higher outside services, higher stock compensation expenses, and higher facility expense.

Cash and cash equivalents increased to $149.1 million as of December 31, 2020 compared to $90.5 million as of December 31, 2019. In addition, net cash used in operations was $16.5 million in 2020, as compared to net cash used in operations of $12.6 million in 2019. We believe that based on our current level of operations, our existing cash and cash equivalents will provide adequate funds for ongoing operations, planned capital expenditures and working capital requirements for at least the next 12 months.

In June 2017, we entered into a loan and security agreement with Western Alliance Bank that allows us to borrow up to $10.0 million under a term loan, and up to $5.0 million under a revolving credit facility with 80% of certain eligible accounts receivable as a borrowing base (the "Credit Facility"). Obligations under the Credit Facility are secured by a lien on substantially all of our personal property other than our intellectual property. In September 2020, we entered into an Eighth Amendment to the Credit Facility whereby we may draw on the term debt and the Revolving Line of Credit at any time prior to October 1, 2021 and October 1, 2024, respectively. Draws on the term debt are subject to customary conditions for funding including, among others, that no event of default exists. As of December 31, 2020, no amounts were borrowed under the Credit Facility and we were in compliance with the covenants for the Credit Facility. See Note 13, *"Commitments and Contingencies"* in the Notes to the Consolidated Financial Statements set forth in Item 8 of this Annual Report on Form 10-K.

Below is an overview of our results of operations by business segments:

Performance Enzymes

Revenues decreased by $10.1 million, or 17%, to $48.1 million in 2020, compared to $58.2 million in 2019. The increase in product revenue of $0.8 million, or 3%, to $30.2 million in 2020, compared to $29.5 million in 2019 was primarily due to higher customer demand for enzymes for the manufacture of branded pharmaceuticals products. The decrease in research and development revenue of $10.8 million, or 38%, to $17.9 million in 2020, compared to $28.7 million in 2019 was primarily due to lower revenues from Novartis CodeEvolver® Agreement, a prior year milestone payment from GSK under the GSK CodeEvolver® Agreement, and lower license fees and revenues from Merck, partially offset by the recognition of functional license fees revenue from Porton.

Product gross margins were 55% in 2020, compared to 47% in the corresponding period in 2019. The increase in product gross margins was primarily due to improved product mix due to higher demand for enzymes for the manufacture of branded pharmaceutical products.

Research and development expense increased $1.5 million, or 8%, to $20.9 million in 2020, compared to $19.4 million in 2019, The increase was primarily due to an increase in costs associated with higher headcount, higher stock compensation expense, and higher repairs and maintenance expense, which were partially offset by lower lab supply expenses and lower allocable expenses.

Selling, general and administrative expense increased by $1.1 million, or 13%, to $9.6 million in 2020, compared to $8.5 million in 2019, due primarily to an increase in costs associated with licensed technology, outside services, stock compensation expense, and higher allocable expenses which were partially offset by lower travel expenses.

Novel Biotherapeutics

Research and development revenue increased by $10.6 million, or 103%, to $21.0 million in 2020, compared to $10.3 million in 2019. The increase in research and development revenue was primarily due to recognition of license fees from Takeda under the Takeda Agreement, partially offset by a decrease in prior year functional license fee revenue from Nestlé Health Science.

Research and development expense increased $8.4 million, or 63%, to $21.7 million in 2020, compared to $13.3 million in 2019. The increase was primarily due to an increase in costs associated with outside services relating to CMC and regulatory expenses for CDX-7108 which we are developing pursuant to our development agreement with Nestlé Health Science, higher headcount, higher outside services, and higher allocable expenses which were partially offset by lower expenses for lab supplies and consultants.

Selling, general and administrative expense increased by $0.1 million, or 6%, to $2.4 million in 2020, compared to $2.2 million in 2019. The increase was primarily due to an increase in costs associated with headcount, licensed technology, consultants and stock compensation expense which were partially offset by lower allocable expenses, outside services, and travel expenses.

GSK Platform Technology Transfer, Collaboration and License Agreement

In July 2014, we entered into a CodeEvolver® protein engineering platform technology transfer collaboration and license agreement (the "GSK CodeEvolver® Agreement") with GSK. Pursuant to the terms of the agreement, we granted GSK a non-exclusive license to use the CodeEvolver® protein engineering platform technology to develop novel enzymes for use in the manufacture of GSK's pharmaceutical and health care products. We received an upfront fee upon the execution of the agreement in July 2014 and milestone payments in each of the years from 2014 through April 2016. We completed the transfer of the CodeEvolver® protein engineering platform technology to GSK in April 2016 and all revenues relating to the technology transfer have been recognized as of April 2016. We have the potential to receive additional cumulative contingent payments that range from $5.75 million to $38.5 million per project based on GSK's successful application of the licensed technology. We are also eligible to receive royalties, based on net sales of GSK's sales of licensed enzyme products, that are currently not being recognized.

In 2019, we received a $2.0 million milestone payment relating to the advancement of an enzyme developed by GSK using our CodeEvolver® protein engineering platform technology. We recognized research and development revenue of nil, $2.0 million and nil in 2020, 2019, and 2018, respectively.

Merck Platform Technology Transfer and License Agreement

In August 2015, we entered into a CodeEvolver® platform technology transfer collaboration and license agreement (the "Merck CodeEvolver® Agreement") with Merck, Sharp & Dohme ("Merck") which allows Merck to use the CodeEvolver® protein engineering technology platform in the field of human and animal healthcare.

We received an upfront license fee upon execution of the Merck CodeEvolver® Agreement, and milestone payments in September 2015 and in September 2016, when we completed the transfer of the engineering platform technology. Additionally, we recognized research and development revenues of $3.1 million, $4.0 million, and $4.1 million in the years ended December 31, 2020, 2019 and 2018, respectively, for various research projects under our collaborative arrangement.

We have the potential to receive payments of up to a maximum of $15.0 million for each commercial active pharmaceutical ingredient ("API") that is manufactured by Merck using one or more novel enzymes developed by Merck using the CodeEvolver® protein engineering technology platform. The API payments are based on the quantity of API developed and manufactured by Merck and will be recognized as usage-based royalties.

In October 2018, we entered into an amendment to the Merck CodeEvolver® Agreement whereby we amended certain licensing provisions and one exhibit. In January 2019, we entered into an amendment to the Merck CodeEvolver® Agreement whereby we installed certain CodeEvolver® protein engineering technology upgrades into Merck's platform license installation and we will maintain those upgrades for a multi-year term expiring in January 2022. The license installation was completed in 2019 and we recognized $0.9 million as license fee revenue accordingly in 2019 under the amendment. Pursuant to the agreement, Merck has options to future technology enhancements for a specified fee. As of December 31, 2020, Merck has not exercised its option for technology enhancements. We recognized $0.1 million and $0.9 million in research and development revenues under the terms of the amendment in the years ended December 31, 2020 and 2019, respectively.

Merck Sitagliptin Catalyst Supply Agreement

In February 2012, we entered into a five-year Sitagliptin Catalyst Supply Agreement ("Sitagliptin Catalyst Supply Agreement") with Merck whereby Merck may obtain commercial scale enzyme for use in the manufacture of Januvia®, its product based on the active ingredient sitagliptin. In December 2015, Merck exercised its option under the terms of the Sitagliptin Catalyst Supply Agreement to extend the agreement for an additional five years through February 2022.

Effective as of January 2016, we and Merck amended the Sitagliptin Catalyst Supply Agreement to prospectively provide for variable pricing based on the cumulative volume of sitagliptin catalyst purchased by Merck and to allow Merck to purchase a percentage of its requirements for sitagliptin catalyst from a specified third-party supplier. Merck received a distinct, functional license to manufacture a portion of its demand beginning January 1, 2018, which we recognized as research and development revenue. We recognized research and development revenues of nil, nil and $1.3 million of research and development revenues in the years ended December 31, 2020, 2019 and 2018, respectively.

We have determined that the variable pricing, which provides a discount based on the cumulative volume of sitagliptin catalyst purchased by Merck, provides Merck material rights and we are recognizing product revenues using the alternative method.

Under the alternative approach, we estimate the total expected consideration and allocate it proportionately with the expected sales.

The Sitagliptin Catalyst Supply Agreement requires Merck to pay an annual fee for the rights to the sitagliptin technology each year for the term of the Sitagliptin Catalyst Supply Agreement. Amounts of annual license fees are based on contractually agreed prices and are on a declining scale over the term of the contract.

Pursuant to the terms of the Sitagliptin Catalyst Supply Agreement, Merck may purchase supply from us for a fee based on contractually stated prices. We recognized $13.4 million, $15.1 million and $12.3 million in product revenues for the years ended December 31, 2020, 2019 and 2018, respectively. Revenues from Merck under the Sitagliptin Catalyst Supply Agreement comprised 19%, 22%, and 22% of our total revenues for the years ended December 31, 2020, 2019 and 2018, respectively.

The Sitagliptin Catalyst Supply Agreement will terminate in February 2022 unless extended and we have not received an amendment to extend the agreement.

As of December 31, 2020, we recorded revenue of $6.8 million from sitagliptin products that were recognized over time based on the progress of the manufacturing process. These products will be shipped within the six month period following the end of the quarter. The contract asset balances were partially offset by contract liabilities as they are under the same contract.

Global Development, Option and License Agreement and Strategic Collaboration Agreement

In October 2017, we entered into the Nestlé License Agreement with Societé des Produits Nestlé S.A., formerly known as Nestec Ltd. ("Nestlé Health Science") and, solely for the purpose of the integration and the dispute resolution clauses of the Nestlé License Agreement, Nestlé Health Science S.A., to advance CDX-6114, our enzyme biotherapeutic product candidate for the potential treatment of PKU.

We received an upfront cash payment of $14.0 million upon the execution of the Nestlé License Agreement, a $4.0 million milestone payment after dosing the first subjects in a first-in-human Phase 1a dose-escalation trial with CDX-6114, and a $1.0 million milestone payment upon achievement of a milestone relating to formulation of CDX-6114. The $4.0 million milestone payment that was triggered by the initiation of the trial was received in September 2018 and the $1.0 million milestone payment that was triggered by the achievement of a formulation relating to CDX-6114 was received in February 2019. The upfront payment and the variable consideration relating to the progress payment of $4.0 million and milestone payment of $1.0 million were recognized over time as the development work was performed. Revenue was recognized using a single measure of progress that depicted our performance in transferring control of the services, which was based on the ratio of level of effort incurred to date compared to the total estimated level of effort required to complete all performance obligations under the agreement. We recognized development fees of $13 thousand, $1.9 million, and $9.9 million in research and development revenue in 2020, 2019, and 2018, respectively.

In January 2019, we received notice from the FDA that it had completed its review of our IND for CDX-6114 and concluded that we may proceed with the proposed Phase 1b multiple ascending dose study in healthy volunteers in the United States. In February 2019, Nestlé Health Science exercised its option to obtain an exclusive, worldwide, royalty-bearing, sub-licensable license for the global development and commercialization of CDX-6114 for the management of PKU. The option payment of $3.0 million was recognized in the first quarter of 2019 as research and development revenue. Upon exercising its option, Nestlé Health Science assumed all responsibilities for future clinical development and commercialization of CDX-6114. We are also eligible to receive payments from Nestlé Health Science under the Nestlé License Agreement that include (i) development and approval milestones of up to $85.0 million, (ii) sales-based milestones of up to $250.0 million in the aggregate, which aggregate amount is achievable if net sales exceed $1.0 billion in a single year, and (iii) tiered royalties, at percentages ranging from the middle single digits to low double-digits, of net sales of product.

In October 2017, we entered into the Nestlé SCA pursuant to which we and Nestlé Health Science are collaborating to leverage the CodeEvolver® protein engineering technology platform to develop novel enzymes for Nestlé Health Science's established Consumer Care and Medical Nutrition business areas. Under the Strategic Collaboration Agreement, we received an upfront payment of $1.2 million in 2017 and an incremental $0.6 million payment in September 2018 for additional services. The Nestlé SCA has been extended through December 2021.

In January 2020, we entered into a development agreement with Nestlé Health Science pursuant to which we and Nestlé Health Science are collaborating to advance a lead candidate, CDX-7108, targeting a gastro-intestinal disorder discovered through our Nestlé SCA into pre-clinical and early clinical studies.

Under the Nestlé SCA and the development agreement, we recognized research and development fees of $7.9 million, $5.4 million, and $3.6 million in 2020, 2019 and 2018 respectively.

Strategic Collaboration Agreement

In April 2018, we entered into a Strategic Collaboration Agreement (the "Porton Agreement") with Porton Pharma Solutions Ltd. ("Porton") to license key elements of our biocatalyst technology for use in Porton's global custom intermediate and API development and manufacturing business. Under the Porton Agreement, we are eligible to receive annual collaboration fees and research and development revenues. We received initial collaboration payments of $0.5 million within 30 days of the effective date of the Porton Agreement, $1.5 million upon the first anniversary of the effective date of the agreement, and $1.0 million upon the second anniversary of the effective date of the agreement and we are eligible to receive $1.0 million on the third anniversary of the effective date of the agreement. We completed the technical transfer in the fourth quarter of 2018 and recognized $2.8 million in research and development revenue. We recognized revenue related to the functional license provided to Porton at a point in time when control of the license was transferred to the customer. We recognized research and development revenue related to the Porton Agreement of $1.1 million, nil, and $2.8 million in 2020, 2019 and 2018, respectively.

Platform Technology Transfer and License Agreement

In May 2019, we entered into a Platform Technology Transfer and License Agreement (the "Novartis CodeEvolver® Agreement") with Novartis. The Agreement allows Novartis to use our proprietary CodeEvolver® protein engineering platform technology in the field of human healthcare. Under the Novartis CodeEvolver® Agreement, we are transferring our proprietary CodeEvolver® protein engineering platform technology to Novartis over approximately 25 months starting with the date on which we commenced the technology transfer (the "Technology Transfer Period"). As a part of this technology transfer, the Company provided to Novartis our proprietary enzymes, proprietary protein engineering protocols and methods, and proprietary software algorithms. In addition, teams of the Company and Novartis scientists participated in technology training sessions and collaborative research projects at our laboratories in Redwood City, California and at a designated Novartis laboratory in Basel, Switzerland. Upon completion of technology transfer, Novartis will have the CodeEvolver® protein engineering platform technology installed at its designated laboratory.

Pursuant to the agreement, we received an upfront payment of $5.0 million shortly after the effective date of the Novartis CodeEvolver® Agreement. In the second quarter of 2020, we completed the second technology milestone transfer under the agreement and became eligible to receive a milestone payment of $4.0 million, which we subsequently received in July 2020.
We have also billed $3.4 million for partial completion of the third technology milestone and we expect to receive payment in the first quarter of 2021. In addition to this payment we are eligible for an additional payment of $1.6 million for completion of the third technology milestone transfer, which would bring total cash payment for this milestone to $5 million as specified in the Novartis CodeEvolver® Agreement. In consideration for the continued disclosure and license of improvements to the our technology and materials during a multi-year period that begins on the conclusion of the Technology Transfer Period ("Improvements Term"), Novartis will pay Codexis annual payments which amount to an additional $8.0 million. The Company also has the potential to receive quantity-dependent, usage payments for each API that is manufactured by Novartis using one or more enzymes that have been developed or are in development using the CodeEvolver® protein engineering platform technology during the period that begins on the conclusion of the Technology Transfer Period and ends on the expiration date of the last to expire licensed patent. These product-related usage payments, if any, will be paid by Novartis to the Company for each quarter that Novartis manufactures API using a CodeEvolver®-developed enzyme. The usage payments will be based on the total volume of API produced using the CodeEvolver®-developed enzyme. These usage payments can begin in the clinical stage and will extend throughout the commercial life of each API. Revenue for the combined initial license and technology transfer performance obligation, which is expected to occur over twenty-three months, is being recognized using a single measure of progress that depicts our performance in transferring control of the services, which is based on the ratio of level of effort incurred to date compared to the total estimated level of effort required to complete the performance obligation relating to the combined initial license and technology transfer. Revenue allocated to future improvements will be recognized during the Improvement Term. We recognized $6.2 million and $11.3 million in research and development revenue in 2020 and 2019, respectively, from the Novartis CodeEvolver® Agreement.

Strategic Collaboration and License Agreement

In March 2020, we entered into a Strategic Collaboration and License Agreement (the "Takeda Agreement") with Shire Human Genetic Therapies, Inc., a wholly-owned subsidiary of Takeda Pharmaceutical Co. Ltd. ("Takeda"), under which we are collaborating to research and develop protein sequences for use in gene therapy products for certain diseases. On execution of the Takeda Agreement, we received an upfront non-refundable cash payment of $8.5 million. Revenue relating to the functional licenses provided to Takeda was recognized at a point in time when the control of the license transferred to the customer.

Other potential payments from Takeda include (i) reimbursement of research and development fees and pre-clinical approval milestones for initial programs to earn $15.4 million, (ii) development and commercialization-based milestones, per target gene, of up to $100.0 million, the modulation of which leads to treatment of certain diseases by the applicable product, and (iii) tiered royalties based on net sales of applicable products at percentages ranging from the middle-single digits to low single-digits. We recognized research and development revenue related to the Takeda Agreement of $13.2 million in 2020. As of December 31, 2020, we had $1.5 million in deferred revenue.

Master Collaboration and Research Agreement and Stock Purchase Agreement

In June 2020, we entered into a Stock Purchase Agreement with Molecular Assemblies, Inc. (“MAI”) pursuant to which we purchased 1,587,050 shares of MAI's Series A preferred stock for $1.0 million. In connection with the transaction, John Nicols, our President and Chief Operating Officer, also joined MAI’s board of directors. Concurrently with our initial equity investment, we entered into a Master Collaboration and Research Agreement with MAI (the “MAI Agreement”), pursuant to which we are performing services utilizing our CodeEvolver® protein engineering platform technology to improve DNA polymerase enzymes in exchange for compensation in the form of additional shares of MAI's Series A preferred stock. Based on these services, the Company is eligible to earn additional shares of MAI's Series A preferred stock. MAI will combine its advanced chemistries with our enzymes to drive the process to commercialization. We are eligible to earn such non-monetary payments over ten to thirteen months, and any such shares would be issued thirty days in arrears after each calendar quarter-end. We are also eligible to receive amounts for bonuses, targets and milestones on achievement of timeline and project goals specified in the statement of work ("SOW"). Payments for bonuses, targets and milestones on achievement of timeline and project goals are to be issued thirty days after the Company provides notification of completion. We recognized research and development revenue of $0.9 million in 2020.

Recent Accounting Pronouncements

For information on recent accounting pronouncements, see Note 2, *“Summary of Significant Accounting Policies*”, in the Notes to the Consolidated Financial Statements set forth in Item 8 of this Annual Report on Form 10-K.

Results of Operations

The following table shows the amounts from our consolidated statements of operations for the periods presented (in thousands, except percentages):

	Year Ended December 31,			% of Total Revenues		
	2020	2019	2018	2020	2019	2018
Revenues:						
Product revenue	$ 30,220	$ 29,465	$ 25,590	44 %	43 %	42 %
Research and development revenue	38,836	38,993	35,004	56 %	57 %	58 %
Total revenues	69,056	68,458	60,594	100 %	100 %	100 %
Costs and operating expenses:						
Cost of product revenue	13,742	15,632	12,620	20 %	23 %	21 %
Research and development	44,185	33,873	29,978	64 %	49 %	50 %
Selling, general and administrative	35,049	31,502	29,291	51 %	46 %	48 %
Total costs and operating expenses	92,976	81,007	71,889	135 %	118 %	119 %
Loss from operations	(23,920)	(12,549)	(11,295)	(35)%	(18)%	(19)%
Interest income	405	1,287	671	1 %	2 %	1 %
Other expense, net	(156)	(656)	(291)	— %	(1)%	— %
Loss before income taxes	(23,671)	(11,918)	(10,915)	(34)%	(17)%	(18)%
Provision for (benefit from) income taxes	339	17	(37)	— %	— %	— %
Net loss	$ (24,010)	$ (11,935)	$ (10,878)	(34)%	(17)%	(18)%

Revenues

Our revenues are comprised of product revenue and research and development revenue as follows:

- Product revenue consist of sales of biocatalysts, pharmaceutical intermediates, and Codex® biocatalyst panels and kits.
- Research and development revenue include license, technology access and exclusivity fees, research services fees, milestone payments, royalties, optimization and screening fees.

Revenues are as follows (in thousands, except percentages):

	Year Ended December 31,			Change			
				2020		2019	
	2020	2019	2018	$	%	$	%
Product revenue	$ 30,220	$ 29,465	$ 25,590	$ 755	3 %	$ 3,875	15 %
Research and development revenue	38,836	38,993	35,004	(157)	— %	3,989	11 %
Total revenues	$ 69,056	$ 68,458	$ 60,594	$ 598	1 %	$ 7,864	13 %

Revenues typically fluctuate on a quarterly basis due to the variability in our customers' manufacturing schedules and the timing of our customers' clinical trials. In addition, we have limited internal capacity to manufacture enzymes. As a result, we are dependent upon the performance and capacity of third party manufacturers for the commercial scale manufacturing of the enzymes used in our pharmaceutical and fine chemicals business.

We accept purchase orders for deliveries covering periods from one day up to approximately 14 months from the date on which the order is placed. However, a majority of the purchase orders can be revised or cancelled by the customer without penalty. Considering these industry practices and our experience, we do not believe the total of customer purchase orders outstanding (backlog) provides meaningful information that can be relied on to predict actual sales for future periods.

2020 compared to 2019

Total revenues increased by $0.6 million in 2020 to $69.1 million, as compared to 2019. The increase was driven by growth in product revenue of $0.8 million, or 3%, offset by decrease in research and development revenue of $157 thousand, or nominal percent.

Product revenue, which consist primarily of sales of biocatalysts, pharmaceutical intermediates, and Codex® biocatalyst panels and kits, were $30.2 million in 2020, an increase of 3% compared with $29.5 million in 2019. The increase in product revenue is primarily due to higher customer demand for enzymes for the manufacture of branded pharmaceuticals products.

Research and development revenue decreased by $157 thousand in 2020 to $38.8 million, or nominal percent compared with $39.0 million in 2019, primarily due to lower revenues from the Novartis CodeEvolver® Agreement, a prior year functional license fee revenue from Nestlé Health Science, and a prior year milestone payment from GSK under the GSK CodeEvolver® Agreement, partially offset by the recognition of license fees from Takeda under the Takeda Agreement, and recognition of functional license fees revenue from Porton.

2019 compared to 2018

Total revenues increased by $7.9 million in 2019 to $68.5 million, as compared to 2018. The increase was driven by growth in product revenue of $3.9 million, or 15%, and research and development revenue of $4.0 million, or 11%.

Product revenue, which consist primarily of sales of biocatalysts, pharmaceutical intermediates, and Codex® biocatalyst panels and kits, were $29.5 million in 2019, an increase of 15% compared with $25.6 million in 2018. The increase in product revenue is primarily due to higher customer demand for enzymes for the manufacture of both branded and generic pharmaceuticals products.

Research and development revenue increased by $4.0 million in 2019 to $39.0 million, or 11% compared with $35.0 million in 2018, primarily due to revenues from Novartis under the Novartis CodeEvolver® Agreement and a milestone payment from GSK under the GSK CodeEvolver® Agreement partially offset by lower revenue from Tate & Lyle due to the prior year completion of services and lower development fees from Nestlé Health Science.

Cost and Operating Expenses (in thousands, except percentages):

	Year Ended December 31,			Change			
				2020		2019	
	2020	2019	2018	$	%	$	%
Cost of product revenue	$ 13,742	$ 15,632	$ 12,620	$ (1,890)	(12)%	$ 3,012	24 %
Research and development	44,185	33,873	29,978	10,312	30 %	3,895	13 %
Selling, general and administrative	35,049	31,502	29,291	3,547	11 %	2,211	8 %
Total costs and operating expenses	$ 92,976	$ 81,007	$ 71,889	$ 11,969	15 %	$ 9,118	13 %

Cost of Product Revenue and Product Gross Margin

Our revenues from product revenue are derived entirely from our Performance Enzymes segment. Revenues from the Novel Biotherapeutics segment are from collaborative research and development activities and not from product revenue.

The following table shows the amounts of our product revenue, cost of product revenue, product gross profit and product gross margin from our consolidated statements of operations for the years ended (in thousands, except percentages):

	Year Ended December 31,		Change		Year Ended December 31,		Change	
	2020	2019	$	%	2019	2018	$	%
Product revenue	$ 30,220	$ 29,465	$ 755	3 %	$ 29,465	$ 25,590	$ 3,875	15 %
Cost of product revenue [1]	13,742	15,632	(1,890)	(12)%	15,632	12,620	3,012	24 %
Product gross profit	$ 16,478	$ 13,833	$ 2,645	19 %	$ 13,833	$ 12,970	$ 863	7 %
Product gross margin (%) [2]	55 %	47 %			47 %	51 %		

[1] Cost of product revenue comprises both internal and third-party fixed and variable costs, including materials and supplies, labor, facilities and other overhead costs associated with our product revenue.

[2] Product gross margin is used as a performance measure to provide additional information regarding our results of operations on a consolidated basis.

2020 compared to 2019

Cost of product revenue decreased by $1.9 million in 2020 to $13.7 million, as compared to 2019. The decrease was primarily due to lower costs compared to costs associated with prior year product revenue. Product gross margin increased to 55% in 2020 as compared to 47% in 2019 due to improved product mix.

2019 compared to 2018

Cost of product revenue increased by $3.0 million in 2019 to $15.6 million, as compared to 2018. The increase was primarily due to an increase in costs associated with the higher level of product revenue. Product gross margin decreased to 47% in 2019 as compared to 51% in 2018 due to the variations in product mix.

Research and Development Expenses

Research and development expenses consist of costs incurred for internal projects as well as collaborative research and development activities. These costs primarily consist of (i) employee-related costs, which include salaries and other personnel-related expenses (including stock-based compensation), (ii) various allocable expenses, which include occupancy-related costs, supplies, depreciation of facilities and laboratory equipment, and (iii) external costs. Research and development expenses are expensed when incurred.

2020 compared to 2019

Research and development expenses were $44.2 million in 2020 compared to $33.9 million in 2019, an increase of $10.3 million, or 30%. The increase was primarily due to $5.0 million in costs associated with outside services relating to CMC and regulatory expenses, $3.4 million in costs associated with higher headcount, $1.5 million in higher allocable expenses which include occupancy-related costs and supplies, $0.4 million in higher outside services, $0.3 million in higher depreciation expense and were partially offset by a decrease of $0.4 million in lab supply expenses.

2019 compared to 2018

Research and development expenses were $33.9 million in 2019 compared to $30.0 million in 2018, an increase of $3.9 million, or 13%. The increase was primarily due to $2.1 million in costs associated with higher headcount, $2.1 million in higher allocable expenses which include occupancy-related costs and supplies, and increases of $0.8 million in lab supplies, which were partially offset by a decrease of $0.5 million in outside services and a decrease of $0.6 million in stock compensation expense.

Selling, General and Administrative Expenses

Selling, general and administrative expenses consist of employee-related costs, which include salaries and other personnel-related expenses (including stock-based compensation), hiring and training costs, consulting and outside services expenses (including audit and legal counsel related costs), marketing costs, building lease costs, and depreciation expenses and amortization expense.

2020 compared to 2019

Selling, general and administrative expenses were $35.0 million in 2020 compared to $31.5 million in 2019, an increase of $3.5 million, or 11%. The increase was primarily due to increases of $1.7 million in salaries and personnel costs associated with higher headcount, $0.6 million in stock compensation expense, $0.8 million in consultants, $0.8 million in legal and accounting fees, $0.7 million in facilities, $0.7 million in outside and temporary services, $0.4 million in licensed technology, which were partially offset by decreases of $1.6 million in allocable expenses and $0.8 million in travel expenses.

2019 compared to 2018

Selling, general and administrative expenses were $31.5 million in 2019 compared to $29.3 million in 2018, an increase of $2.2 million, or 8%. The increase was primarily due to increases of $2.2 million in facility expense, $2.6 million in salaries and personnel costs associated with higher headcount, which were partially offset by decreases of $2.1 million in allocable expenses and $0.5 million in outside services.

Other Income (Expense), net (in thousands, except percentages):

	Year Ended December 31,			Change			
				2020		2019	
	2020	2019	2018	$	%	$	%
Interest income	$ 405	$ 1,287	$ 671	$ (882)	(69)%	$ 616	92 %
Other expense, net	(156)	(656)	(291)	500	76 %	(365)	(125)%
Total other income (expense), net	$ 249	$ 631	$ 380	$ (382)	(61)%	$ 251	66 %

Interest Income

Interest income decreased by $0.9 million in 2020 compared to 2019, primarily due to lower average interest rates on declining average cash balances. Interest income increased by $0.6 million in 2019 compared to 2018, primarily due to higher interest rates on higher levels of cash and cash equivalents.

Other Expense

Other expense decreased by $0.5 million in 2020 compared to 2019 primarily due to prior year write-down of $0.5 million of our investment in CQ Solutions and fluctuations in foreign currency. Other expense increased by $0.4 million in 2019 compared to 2018, primarily due to $0.5 million write-down in the fair value of our investment in CO_2 Solutions partially offset by gains from fluctuations in foreign currency.

Provision for (benefit from) Income Taxes (in thousands, except percentages):

	Year Ended December 31,			Change			
				2020		2019	
	2020	2019	2018	$	%	$	%
Provision for (benefit from) income taxes	$ 339	$ 17	$ (37)	$ 322	1,894 %	$ 54	146 %

The provision for income taxes for 2020 was primarily due to foreign withholding taxes on certain sales to non-U.S. customers. The provision for income taxes in 2019 was primarily due to the accrual of interest and penalties on historic uncertain tax positions. The benefit from income taxes in 2018 was primarily related to a net loss from our foreign operations and a reduction in the deferred tax liability for accrued future withholding taxes on dividends.

Net Loss

Net loss for 2020 was $24.0 million, or a net loss per basic and diluted share of $0.40. This compared to a net loss of $11.9 million, or a net loss per basic and diluted share of $0.21 for 2019. The increase in net loss was primarily related to increase in costs associated with outside services relating to CMC and regulatory expenses, higher headcount, higher consultants, higher stock compensation expenses and higher facility expense.

The net loss for 2019 was $11.9 million, or a net loss per basic and diluted share of $0.21, for 2019. This compared to a net loss of $10.9 million, or a net loss per basic and diluted share of $0.21 for 2018. The increases in net loss was primarily attributable to higher operating expenses due to increases in costs associated with headcount, outside services, higher allocable expenses, and higher facility expense.

Results of Operations by Segment (in thousands, except percentages)

Revenues by segment

	Year Ended December 31, 2020			Year Ended December 31, 2019			Change			
	Performance Enzymes	Novel Biotherapeutics	Total	Performance Enzymes	Novel Biotherapeutics	Total	Performance Enzymes		Novel Biotherapeutics	
							$	%	$	%
Revenues:										
Product revenue	$ 30,220	$ —	$ 30,220	$ 29,465	$ —	$ 29,465	$ 755	3%	$ —	—%
Research and development revenue	17,886	20,950	38,836	28,691	10,302	38,993	(10,805)	(38)%	10,648	103%
Total revenues	$ 48,106	$ 20,950	$ 69,056	$ 58,156	$ 10,302	$ 68,458	$ (10,050)	(17)%	$ 10,648	103%

	Year Ended December 31, 2019			Year Ended December 31, 2018			Change			
	Performance Enzymes	Novel Biotherapeutics	Total	Performance Enzymes	Novel Biotherapeutics	Total	Performance Enzymes		Novel Biotherapeutics	
							$	%	$	%
Revenues:										
Product revenue	$ 29,465	$ —	$ 29,465	$ 25,590	$ —	$ 25,590	$ 3,875	15%	$ —	—%
Research and development revenue	28,691	10,302	38,993	21,483	13,521	35,004	7,208	34%	(3,219)	(24)%
Total revenues	$ 58,156	$ 10,302	$ 68,458	$ 47,073	$ 13,521	$ 60,594	$ 11,083	24%	$ (3,219)	(24)%

2020 compared to 2019

Revenues from the Performance Enzymes segment decreased by $10.1 million, or 17%, to $48.1 million in 2020, compared to $58.2 million in 2019. The increase in product revenue of $0.8 million, or 3%, to $30.2 million in 2020, compared to $29.5 million in 2019 was primarily due to higher customer demand for enzymes for the manufacture of branded pharmaceuticals products. The decrease in research and development revenue of $10.8 million, or 38%, to $17.9 million in 2020, compared to $28.7 million in 2019 was primarily due to lower revenues from Novartis CodeEvolver® Agreement, a prior year milestone payment from GSK under the GSK CodeEvolver® Agreement, and lower license fees and revenues from Merck, partially offset by the recognition of functional license fees revenue from Porton.

Revenues from the Novel Biotherapeutics segment increased by $10.6 million, or 103%, to $21.0 million in 2020, compared to $10.3 million in 2019. The increase in revenue was primarily due to recognition of license fees from Takeda under the Takeda Agreement, partially offset by a decrease in prior year functional license fee revenue from Nestlé Health Science.

2019 compared to 2018

Revenues from the Performance Enzymes segment increased by $11.1 million, or 24%, to $58.2 million in 2019, compared to $47.1 million in 2018. The increase in product revenue was primarily due to higher customer demand for enzymes for the manufacture of both branded and generic pharmaceuticals products. The increase in research and development revenues was primarily due to revenues from Novartis under the Novartis CodeEvolver® Agreement and a milestone payment from GSK under the GSK CodeEvolver® Agreement, partially offset by less revenue due to the prior year completion of services to Tate & Lyle.

Revenues from the Novel Biotherapeutics segment decreased by $3.2 million, or 24%, to $10.3 million in 2019, compared to $13.5 million in 2018. Revenues in the Novel Biotherapeutics segment are derived entirely from research and development revenue from Nestlé Health Science relating to the development of the CDX-6114 product candidate under the Nestlé License Agreement and to services under the Nestlé SCA. The decrease was primarily due to lower development fees from Nestlé Health Science as an extension study was substantially completed in 2019.

Costs and operating expenses by segment

	Year Ended December 31, 2020			Year Ended December 31, 2019			Change			
	Performance Enzymes	Novel Biotherapeutics	Total	Performance Enzymes	Novel Biotherapeutics	Total	Performance Enzymes		Novel Biotherapeutics	
							$	%	$	%
Cost of product revenue	$ 13,742	$ —	$ 13,742	$ 15,632	$ —	$ 15,632	$ (1,890)	(12)%	$ —	—%
Research and development[(1)]	20,923	21,705	42,628	19,380	13,278	32,658	1,543	8%	8,427	63%
Selling, general and administrative[(1)]	9,597	2,355	11,952	8,462	2,222	10,684	1,135	13%	133	6%
Total segment costs and operating expenses	$ 44,262	$ 24,060	68,322	$ 43,474	$ 15,500	58,974	$ 788	2%	$ 8,560	55%
Corporate costs			22,555			20,255				
Depreciation and amortization			2,099			1,778				
Total costs and operating expenses			$ 92,976			$ 81,007				

[(1)] Research and development expenses and Selling, general and administrative expenses exclude depreciation and amortization of finance leases.

	Year Ended December 31, 2019			Year Ended December 31, 2018			Change			
	Performance Enzymes	Novel Biotherapeutics	Total	Performance Enzymes	Novel Biotherapeutics	Total	Performance Enzymes		Novel Biotherapeutics	
							$	%	$	%
Cost of product revenue	$ 15,632	$ —	$ 15,632	$ 12,620	$ —	$ 12,620	$ 3,012	24%	$ —	—%
Research and development[1]	19,380	13,278	32,658	18,924	10,185	29,109	456	2%	3,093	30%
Selling, general and administrative[1]	8,462	2,222	10,684	7,538	771	8,309	924	12%	1,451	188%
Total segment costs and operating expenses	$ 43,474	$ 15,500	58,974	$ 39,082	$ 10,956	50,038	$ 4,392	11%	$ 4,544	41%
Corporate costs			20,255			20,704				
Depreciation and amortization			1,778			1,147				
Total costs and operating expenses			$ 81,007			$ 71,889				

[1] Research and development expenses and Selling, general and administrative expenses exclude depreciation.

For a discussion of product cost of revenue, see *"Results of Operations"*.

2020 compared to 2019

Research and development expense in the Performance Enzymes segment increased by $1.5 million, or 8%, to $20.9 million in 2020, compared to $19.4 million in 2019. The increase was primarily due to an increase in costs associated with higher headcount, higher stock compensation expense, higher repairs and maintenance expense, and were partially offset by lower lab supply expenses and lower allocable expenses.

Selling, general and administrative expense in the Performance Enzymes segment increased by $1.1 million, or 13%, to $9.6 million in 2020, compared to $8.5 million in 2019. The increase was primarily due to an increase in costs associated with licensed technology, outside services, stock compensation expense, and higher allocable expenses which were partially offset by lower travel expenses.

Research and development expense in the Novel Biotherapeutics segment increased by $8.4 million, or 63%, to $21.7 million in 2020, compared to $13.3 million in 2019. The increase was primarily due to an increase in costs associated with outside services relating to CMC and regulatory expenses for CDX-7108 which we are developing pursuant to our development agreement with Nestlé Health Science, higher headcount, higher outside services, and higher allocable expenses and were partially offset by lower lab supply expenses and consultant expense.

Selling, general and administrative expense in the Novel Biotherapeutics segment increased by $0.1 million, or 6%, to $2.4 million in 2020, compared to $2.2 million in 2019. The increase was primarily due to an increase in costs associated with headcount, licensed technology, consultants and stock compensation expense which were partially offset by lower allocable expenses, outside services, and travel expenses.

2019 compared to 2018

Research and development expense in the Performance Enzymes segment increased by $0.5 million, or 2%, to $19.4 million in 2019, compared to $18.9 million in 2018. The increase was primarily due to $2.2 million associated with higher headcount which was partially offset by a decrease of $1.2 million in allocable expenses, which included occupancy-related costs, supplies, and depreciation expense, and a decrease of $0.5 million in stock compensation expense.

Selling, general and administrative expense in the Performance Enzymes segment increased by $0.9 million, or 12%, to $8.5 million in 2019, compared to $7.5 million in 2018. The increase was primarily due to $0.5 million in higher costs associated with increased headcount, $0.2 million in higher stock compensation expense, and $0.1 million in higher allocable expenses.

Research and development expense in the Novel Biotherapeutics segment increased by $3.1 million, or 30%, to $13.3 million in 2019, compared to $10.2 million in 2018. The increase was primarily due to $3.2 million increase in allocable expenses which was partially offset by a decrease of $0.1 million in stock compensation expense.

Selling, general and administrative expense in the Novel Biotherapeutics segment increased by $1.5 million, or 188%, to $2.2 million in 2019, compared to $0.8 million in 2018. The increase was primarily due to an increase of $1.0 million in higher costs associated with increased headcount and $0.5 million in higher stock compensation expense.

Income (loss) from operations by segment

	Year Ended December 31, 2020			Year Ended December 31, 2019			Change			
	Performance Enzymes	Novel Biotherapeutics	Total	Performance Enzymes	Novel Biotherapeutics	Total	Performance Enzymes		Novel Biotherapeutics	
							$	%	$	%
Income (loss) from operations	$ 3,844	$ (3,110)	$ 734	$ 14,682	$ (5,198)	$ 9,484	$ (10,838)	(74)%	$ 2,088	40%

	Year Ended December 31, 2019			Year Ended December 31, 2018			Change			
	Performance Enzymes	Novel Biotherapeutics	Total	Performance Enzymes	Novel Biotherapeutics	Total	Performance Enzymes		Novel Biotherapeutics	
							$	%	$	%
Income (loss) from operations	$ 14,682	$ (5,198)	$ 9,484	$ 7,991	$ 2,565	$ 10,556	$ 6,691	84%	$ (7,763)	(303)%

2020 compared to 2019

Income from operations in the Performance Enzymes segment decreased by $10.8 million, or 74%, to $3.8 million, in 2020, compared to $14.7 million in 2019. The decrease in income from operations was primarily due to decrease in research and development revenue and increases in research and development costs and selling, general and administrative expense.

Loss from operations in the Novel Biotherapeutics segment decreased by $2.1 million, or 40%, to $3.1 million in 2020 compared to a loss from operations of $5.2 million in 2019. The decrease in loss from operations was primarily due to the recognition of license fees from Takeda under the Takeda Agreement, partially offset by a decrease in prior year functional license fee revenue from Nestlé Health Science, an increase in costs associated with outside services relating to CMC and regulatory expenses, higher headcount, higher outside services, and higher allocable expenses.

2019 compared to 2018

Income from operations in the Performance Enzymes segment increased $6.7 million, or 84%, to $14.7 million, in 2019, compared to $8.0 million in 2018. The increase in income from operations was primarily due to increases in product revenue and research and development revenue and were partially offset by increases in product costs, research and development costs and selling, general and administrative expense.

Loss from operations in the Novel Biotherapeutics segment increased $7.8 million, or 303%, to $5.2 million in 2019 compared to an income from operations of $2.6 million in 2018. The decrease in income from operation was primarily due to a decrease of $3.2 million in revenue from the development of our CDX-6114 product candidate and the Strategic Collaboration Agreement with Nestlé Health Science, and increase in the outside research and development services used in the CDX-6114 product candidate development and selling, general and administrative expense.

Liquidity and Capital Resources

Liquidity is the measurement of our ability to meet working capital needs and to fund capital expenditures. We have historically funded our operations primarily through cash generated from operations, stock option exercises and public and private offerings of our common stock. We also have the ability to borrow up to $15.0 million under our Credit Facility. We actively manage our cash usage and investment of liquid cash to ensure the maintenance of sufficient funds to meet our working capital needs. The majority of our cash and cash equivalents are held in U.S. banks, and our foreign subsidiaries maintain a limited amount of cash in their local banks to cover their short-term operating expenses.

The following summarizes our cash and cash equivalents balance and working capital as of December 31, 2020, 2019 and 2018 (in thousands):

	December 31,		
	2020	2019	2018
Cash and cash equivalents	$ 149,117	$ 90,498	$ 53,039
Working capital	$ 159,442	$ 98,817	$ 50,085

In addition to our existing cash and cash equivalents, we are eligible to earn milestone and other contingent payments for the achievement of defined collaboration objectives and certain royalty payments under our collaboration agreements. Our ability to earn these milestone and contingent payments and the timing of achieving these milestones is primarily dependent upon the outcome of our collaborators' research and development activities and is uncertain at this time. In the third quarter of 2016, we completed the final phase in the transfer of CodeEvolver® technology to Merck under the Merck CodeEvolver® Agreement. Following the completion of the technology transfer to Merck, we are now eligible to receive payments of up to $15.0 million for each commercial API that is manufactured by Merck using one or more novel enzymes developed by Merck using the CodeEvolver® technology. In addition, depending upon GSK's successful application of the licensed technology, we have the potential to receive additional contingent payments that range from $5.75 million to $38.5 million per project. In May 2019, we entered into a Platform Technology Transfer and License Agreement with Novartis. The Novartis CodeEvolver® Agreement allows Novartis to use Codexis' proprietary CodeEvolver® protein engineering platform technology in the field of human healthcare. Pursuant to the agreement, we received an upfront payment of $5.0 million shortly after the effective date of the Novartis CodeEvolver® Agreement. In the second quarter of 2020, we completed the second technology milestone transfer under the agreement and became eligible to receive a milestone payment of $4.0 million, which we subsequently received in July 2020. We have also recognized $3.4 million for partial completion of the third technology milestone and we expect to receive payment in the first quarter of 2021. Additionally, we are eligible to receive an additional $1.6 million upon satisfactory completion of the third technology transfer milestone. In consideration for the continued disclosure and license of improvements to our technology and materials during a multi-year period that begins on the conclusion of the Technology Transfer Period ("Improvements Term"), Novartis will pay Codexis annual payments which amount to an additional $8.0 million.

We are actively collaborating with new and existing customers in the pharmaceutical and food industries. We believe that we can utilize our current products and services, and develop new products and services, to increase our revenues and gross margins in future periods.

We have historically experienced negative cash flows from operations as we continue to invest in key technology development projects and improvements to our CodeEvolver® protein engineering technology platform, and expand our business development and collaboration with new customers. Our cash flows from operations will continue to be affected principally by sales and gross margins from licensing our technology to major pharmaceutical companies, product sales and collaborative research and development services provided to customers, as well as our headcount costs, primarily in research and development. Our primary source of cash flows from operating activities is cash receipts from our customers for purchases of products, collaborative research and development services, and licensing our technology to major pharmaceutical companies. Our largest uses of cash from operating activities are for employee-related expenditures, rent payments, inventory purchases to support our product sales and non-payroll research and development costs.

In April 2018, we completed an underwritten public offering of 4.3 million shares of our common stock at a public offering price of $9.25 per share resulting in net proceeds of approximately $37.5 million after deducting the underwriting discounts and commissions.

In June 2019, we entered into a Securities Purchase Agreement with an affiliate of Casdin Capital, LLC ("Casdin") pursuant to which we issued and sold to Casdin 3,048,780 shares of our common stock at a purchase price of $16.40 per share resulting in net proceeds of approximately $49.9 million after deducting related issuance costs.

In December 2020, we completed an underwritten public offering of approximately 4,928,572 shares of our common stock, par value $0.0001 per share, at an offering price of $17.50 per share. The net proceeds to us were approximately $80.8 million after deducting offering costs and the underwriting discounts and commissions and other offering expenses of $5.5 million.

In June 2017, we entered into the Credit Facility with Western Alliance Bank which consists of term debt for loans that allow us to borrow up to $10.0 million and a revolving credit facility that allows us to borrow up to $5.0 million with a certain eligible accounts receivable borrowing base of 80% of eligible accounts receivable. In January 2019, we entered into a Fifth Amendment to the Credit Facility to allow for Codexis to obtain a letter of credit of up to $1.1 million to secure its obligations under the Lease with MetLife. In July 2019, we entered into a Sixth Amendment to the Credit Facility to increase permitted indebtedness to $0.7 million for financing insurance premiums in the ordinary course of business. In September 2020, we entered into an Eighth Amendment to the Credit Facility whereby we may draw on the Term Debt and the Revolving Line of Credit at any time prior to October 1, 2021 and October 1, 2024, respectively, subject to customary conditions for funding including, among others, that no event of default exists. Draws on the Credit Facility are secured by a lien on substantially all of our personal property other than our intellectual property. On October 1, 2024 loans drawn under the Term Debt mature and the Revolving Line of Credit terminate. No amounts were drawn under the credit facility as of December 31, 2020. At December 31, 2020, we were in compliance with the covenants for the Credit Facility. The Credit Facility requires us to maintain compliance with certain financial covenants including attainment of certain lender-approved projections or maintenance of certain minimum cash levels. Restrictive covenants in the Credit Facility restrict the payment of dividends or other distributions. For additional information about our contractual obligations, see Note 13, *"Commitments and Contingencies"* in the Notes to the Consolidated Financial Statements set forth in Item 8 of this Annual Report on Form 10-K.

In October 2017, we entered into the Nestlé SCA with Nestlé Health Science. Pursuant to the Nestlé License Agreement, Nestlé Health Science paid us an upfront cash payment of $14.0 million. In July 2018, we announced that we had dosed the first subjects in a first-in-human Phase 1a dose-escalation trial with CDX-6114 for the potential treatment of PKU. The initiation of the trial triggered a $4.0 million milestone payment from Nestlé Health Science which was paid in September 2018 and the $1.0 million milestone payment that was triggered by the achievement of a formulation relating to CDX-6114 was received in February 2019. In January 2019, we received notice from the FDA that it had completed its review of our IND for CDX-6114 and concluded that we may proceed with the proposed Phase 1b multiple ascending dose study in healthy volunteers in the United States. In February 2019, Nestlé Health Science exercised its option to obtain an exclusive, worldwide, royalty-bearing, sub-licensable license for the global development and commercialization of CDX-6114 for the management of PKU. The option payment of $3.0 million was recognized in the first quarter of 2019 as research and development revenue. Upon exercising its option, Nestlé Health Science assumed all responsibilities for future clinical development and commercialization of CDX-6114, with the exception of the completion of an extension study, CDX-6114-004, which was substantially completed in the fourth quarter of 2019. Other potential payments from Nestlé Health Science to us under the Nestlé License Agreement include (i) development and approval milestones of up to $85.0 million, (ii) sales-based milestones of up to $250.0 million in the aggregate, which aggregate amount is achievable if net sales exceed $1.0 billion in a single year, and (iii) tiered royalties, at percentages ranging from the middle single digits to low double-digits, of net sales of Product.

We are subject to risks and uncertainties as a result of the current COVID-19 pandemic. The COVID-19 pandemic has presented a substantial public health and economic challenge around the world and is affecting our employees, communities and business operations, as well as the U.S. economy and other economies worldwide. The full extent to which the COVID-19 pandemic will directly or indirectly impact our business, results of operations and financial condition will depend on future developments that are highly uncertain and may not be accurately predicted, including the duration and severity of the pandemic and the extent and severity of the impact on our customers, new information that may emerge concerning COVID-19, the actions taken to contain it or treat its impact and the economic impact on local, regional, national and international markets. To date, we and our collaboration partners have been able to continue to supply our enzymes to our customers worldwide. However, we are dependent on our manufacturing and logistics partners and consequently, disruptions in operations of our partners and customers may affect our ability to supply enzymes to our customers. Furthermore, our ability to provide future research and development ("R&D") services will continue to be impacted as a result of governmental orders and any disruptions in operations of our customers with whom we collaborate. We believe that these disruptions had a negative impact on revenue for the year ended December 31, 2020, although we are unable to fully determine and quantify the extent to which this pandemic has affected the amount and timing of our total revenues. The extent to which the pandemic may impact our business operations and operating results will continue to remain highly dependent on future developments, which are uncertain and cannot be predicted with confidence. In the U.S., the impact of COVID-19, including governmental orders ("Orders") governing the operation of businesses during the pandemic, caused the temporary closure of our Redwood City, California facilities and has disrupted our R&D operations. R&D operations for several projects were temporarily suspended from mid-

March 2020 through the end of April 2020 in accordance with these Orders. In May 2020, we re-initiated limited R&D operations and have ramped up operations such that we are currently utilizing the majority of our normal R&D capacity while following county, state and federal COVID-19 guidance for the protection of our employees. Additionally, we have resumed small scale manufacturing at our Redwood City pilot plant in May 2020. Our future results of operations and liquidity could be adversely impacted by delays in payments of outstanding receivable amounts beyond normal payment terms, supply chain disruptions and uncertain demand, and the impact of any initiatives or programs that we may undertake to address financial and operations challenges faced by our customers. While we believe we have adequate cash on hand to manage through the disruptions being caused by the COVID-19 pandemic, the extent to which the pandemic may materially impact our financial condition, liquidity, or results of operations in the future is uncertain. For additional information on the various risks posed by the COVID-19 pandemic, please read Item 1A. Risk Factors included in this Annual Report on Form 10-K.

As of December 31, 2020, we had cash and cash equivalents of $149.1 million and $15.0 million available to borrow under our Credit Facility. Our liquidity is dependent upon our cash and cash equivalents, cash flows provided by operating activities and the continued availability of borrowings under our Credit Facility. We may need additional capital if our current plans and assumptions change. Our need for additional capital will depend on many factors, including the financial success of our business, the spending required to develop and commercialize new and existing products, the effect of any acquisitions of other businesses, technologies or facilities that we may make or develop in the future, our spending on new market opportunities, and the potential costs for the filing, prosecution, enforcement and defense of patent claims, if necessary.

We believe that, based on our current level of operations, our existing cash and cash equivalents will provide adequate funds for ongoing operations, planned capital expenditures and working capital requirements for at least the next 12 months.

However, we may need additional capital if our current plans and assumptions change. Our need for additional capital will depend on many factors, including the financial success of our business, the spending required to develop and commercialize new and existing products, the effect of any acquisitions of other businesses, technologies or facilities that we may make or develop in the future, our spending on new market opportunities, and the potential costs for the filing, prosecution, enforcement and defense of patent claims, if necessary. If our capital resources are insufficient to meet our capital requirements, and we are unable to enter into or maintain collaborations with partners that are able or willing to fund our development efforts or commercialize any products that we develop or enable, we will have to raise additional funds to continue the development of our technology and products and complete the commercialization of products, if any, resulting from our technologies. If future financings involve the issuance of equity securities, our existing stockholders would suffer dilution. If we raise debt financing or enter into credit facilities, we may be subject to restrictive covenants that limit our ability to conduct our business. We may not be able to raise sufficient additional funds on terms that are favorable to us, if at all. If we fail to raise sufficient funds and fail to generate sufficient revenues to achieve planned gross margins and to control operating costs, our ability to fund our operations, take advantage of strategic opportunities, develop products or technologies, or otherwise respond to competitive pressures could be significantly limited. If this happens, we may be forced to delay or terminate research or development programs or the commercialization of products resulting from our technologies, curtail or cease operations or obtain funds through collaborative and licensing arrangements that may require us to relinquish commercial rights, or grant licenses on terms that are not favorable to us. If adequate funds are not available, we will not be able to successfully execute our business plan or continue our business.

Cash Flows

The following is a summary of cash flows for the years ended December 31, 2020, 2019 and 2018 (in thousands):

	Year Ended December 31,		
	2020	2019	2018
Net cash used in operating activities	$ (16,464)	$ (12,560)	$ (14,094)
Net cash used in investing activities	(5,748)	(3,665)	(2,766)
Net cash provided by financing activities	80,808	53,961	38,569
Net increase in cash, cash equivalents and restricted cash	$ 58,596	$ 37,736	$ 21,709

Cash Flows from Operating Activities

Cash used in operating activities was $16.5 million in 2020, which resulted from a net loss of $24.0 million adjusted for non-cash depreciation of $2.0 million, right-of-use ("ROU") lease asset amortization expense of $2.6 million, stock-based compensation of $7.7 million, offset by equity securities earned from research and development activities of $0.9 million as well as changes in operating assets and liabilities. The net change in operating assets and liabilities included decreases in other

long-term liabilities of $2.6 million and combined increases in financial assets of $8.7 million, prepaid expenses and other assets of $1.0 million, as well as accrued liabilities of $6.2 million and deferred revenue of $2.7 million.

Cash used in operating activities was $12.6 million in 2019, which resulted from a net loss of $11.9 million adjusted for non-cash depreciation of $1.6 million, ROU lease asset amortization expense of $3.0 million and stock-based compensation of $6.9 million, as well as changes in operating assets and liabilities. The net change in operating assets and liabilities included decreases in deferred revenue of $6.2 million and in other long-term liabilities of $1.2 million, and combined increases in financial assets of $5.9 million, prepaid expenses and other assets of $1.3 million, as well as accrued liabilities of $2.2 million.

Cash used in operating activities was $14.1 million in 2018, which resulted from a net loss of $10.9 million adjusted for non-cash depreciation of $1.1 million and stock-based compensation of $7.9 million, as well as changes in operating assets and liabilities. The net change in operating assets and liabilities included decreases in deferred revenue of $10.6 million primarily related to the Nestlé License Agreement, a decrease in other long-term liabilities of $0.9 million and a combined increase in financial assets of $1.4 million as well as accrued liabilities of $0.5 million.

Cash Flows from Investing Activities

Cash used in investing activities was $5.7 million in 2020 primarily due to the purchase of property and equipment of $3.7 million, and investments in non-marketable equity securities of $1.0 million and in non-marketable debt security of $1.0 million. We expect our capital spending including replacement and upgrades of lab equipment and information technology equipment will be higher in 2021 as compared to 2020.

Cash used in investing activities was $3.7 million in 2019 primarily due to the purchase of property and equipment of $3.7 million and partially offset by proceeds from sale of CO_2 investment securities of $62 thousand.

Cash used in investing activities was $2.8 million in 2018, primarily due to the purchase of property and equipment.

Cash Flows from Financing Activities

Cash provided by financing activities was $80.8 million in 2020, primarily due to $80.8 million net proceeds from our offering of common stock after deducting underwriting discounts and commission and related costs and proceeds from the exercises of employee stock options which were partially offset by the payment of taxes related to the net share settlement of equity awards.

Cash provided by financing activities was $54.0 million in 2019, primarily due to net proceeds from our private offering of common stock after deducting underwriting discounts and commission and related costs and proceeds from the exercises of employee stock options which were partially offset by the payment of taxes related to the net share settlement of equity awards.

Cash provided by financing activities was $38.6 million in 2018, primarily due to net proceeds from our offering of common stock after deducting underwriting discounts and commission and related costs and proceeds from the exercises of employee stock options which were partially offset by the payment of taxes related to the net share settlement of equity awards.

Contractual Obligations

The following table summarizes our significant contractual obligations at December 31, 2020 (in thousands):

	Payments due by period				
	Total	**Less than 1 year**	**1 to 3 years**	**4 to 5 years**	**More than 5 years**
Operating leases obligations [1]	$ 31,291	$ 4,197	$ 8,874	$ 9,594	$ 8,626

[1] Represents future minimum lease payments under non-cancellable operating leases in effect as of December 31, 2020 for our facilities in Redwood City, California. The minimum lease payments above do not include common area maintenance charges or real estate taxes. In February 2019, we have entered into an Eighth Amendment to the Lease (the "Eighth Amendment") with MetLife for our facilities, extending the lease terms from May 2027 to May 2029. For additional information see Note 13, *"Commitments and Contingencies"* in the Notes to the Consolidated Financial Statements set forth in Item 8 of this Annual Report on Form 10-K.

Other Commitments

We have other commitments related to supply and service arrangements entered into in the normal course of business. For additional information about other commitments, see Note 13, "*Commitments and Contingencies*" in the Notes to the Consolidated Financial Statements set forth in Item 8 of this Annual Report on Form 10-K. Future minimum payments reflect

amounts those obligations are expected to have on our liquidity and cash flows in future period and include obligations subject to risk of cancellation by us (in thousands):

Other Commitment Agreement Type	Agreement Date	Future Minimum Payment
Manufacture and supply agreement with expected future payment date of December 2022	April 2016	$ 320
Development and manufacturing services agreements	September 2019	2,341
Total other commitments		$ 2,661

Credit Facility

In June 2017, we entered into a credit facility ("Credit Facility") financing arrangement with Western Alliance Bank consisting of term loans ("Term Debt") up to $10.0 million, and advances ("Advances") under a revolving line of credit ("Revolving Line of Credit") up to $5.0 million with an accounts receivable borrowing base of 80% of eligible accounts receivable. At December 31, 2020, we have not drawn from the Credit Facility. We may draw on the Term Debt and the Revolving Line of Credit at any time prior to October 1, 2021 and October 1, 2024, respectively. Term loans drawn under the Term Debt mature and the Revolving Line of Credit terminates on October 1, 2024. Term loans made under the Term Debt bear interest at variable rate through maturity at the greater of (i) 3.75% or (ii) the sum of (A) Index Rate (prime rate published in the Money Rates section of the Western Edition of The Wall Street Journal plus (B) 0.50%. Advances made under the Revolving Line of Credit bear interest at a variable annual rate equal to the greater of (i) 4.25% or (ii) the sum of (A) the prime rate plus (B) 1.00%.

Our obligations under the Credit Facility are secured by a lien on substantially all of our personal property other than our intellectual property. The Credit Facility includes a number of customary covenants and restrictive financial covenants including meeting minimum product revenues levels and maintaining certain minimum cash levels with the lender. The Credit Facility's financial covenants restrict the ability of the Company to transfer collateral, incur additional indebtedness, engage in mergers or acquisitions, pay dividends or make other distributions, make investments, create liens, sell assets, or sell certain assets held at foreign subsidiaries. A failure to comply with these covenants could permit the lender to exercise remedies against us and the collateral securing the Credit Facility, including foreclosure of our properties securing the Credit Facilities and our cash. At December 31, 2020, we were in compliance with the covenants for the Credit Facility.

For additional information about our credit facility, see Note 13, *"Commitments and Contingencies"* in the Notes to the Consolidated Financial Statements set forth in Item 8 of this Annual Report on Form 10-K.

Subsequent Event

In the first quarter of 2021, we entered into a new lease facility agreement for 36,593 square feet in San Carlos, California to serve as additional office and research and development laboratory space. The lease commences on or around November 1, 2021 once tenant improvements are substantially completed by the contractors in accordance with the construction plan. For additional information see Note 17, *"Subsequent Events"* in the Notes to the Consolidated Financial Statements set forth in Item 8 of this Annual Report on Form 10-K. The following table summarizes the estimated contractual obligation entered into after December 31, 2020 (in thousands):

	Payments due by period				
	Total	Less than 1 year	1 to 3 years	4 to 5 years	More than 5 years
Operating leases obligations [1]	$ 27,969	$ 208	$ 4,673	$ 5,398	$ 17,690

[1] Represents estimated future minimum lease payments under non-cancellable operating leases entered into after December 31, 2020 for additional facilities in San Carlos, California. The estimated minimum lease payments above do not include common area maintenance charges or real estate taxes.

Off-Balance Sheet Arrangements

As of December 31, 2020, we had no off-balance sheet arrangements as defined in Item 303(a)(4) of Regulation S-K as promulgated by the SEC.

Critical Accounting Policies and Estimates

Management's discussion and analysis of our financial condition and results of operations are based upon our consolidated financial statements. The consolidated financial statements have been prepared in conformity with generally accepted accounting principles in the United States and include our accounts and the accounts of our wholly owned subsidiaries. The preparation of our consolidated financial statements requires our management to make estimates, assumptions, and judgments that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements, and the reported amounts of revenues and expenses during the applicable periods. Management bases its estimates, assumptions and judgments on historical experience and on various other factors that are believed to be reasonable under the circumstances. Different assumptions and judgments would change the estimates used in the preparation of our consolidated financial statements, which, in turn, could change the results from those reported. Our management evaluates its estimates, assumptions and judgments on an ongoing basis.

The critical accounting policies requiring estimates, assumptions, and judgments that we believe have the most significant impact on our consolidated financial statements are described below.

Revenue Recognition

Our revenues are derived primarily from product revenue and collaborative research and development agreements. The majority of our contracts with customers typically contain multiple products and services. We account for individual products and services separately if they are distinct-that is, if a product or service is separately identifiable from other items in the contract and if a customer can benefit from it on its own or with other resources that are readily available to the customer.

In determining the appropriate amount of revenue to be recognized as we fulfill our obligations under our product revenue and collaborative research and development agreements, we perform the following steps: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations, including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations based on estimated selling prices; and (v) recognition of revenue when (or as) we satisfy each performance obligation.

The majority of our collaborative contracts contain multiple revenue streams such as upfront and/or annual license fees, research and development services, contingent milestone payments upon achievement of contractual criteria, and royalty fees based on the licensees' product revenue or usage, among others. We determine the stand-alone selling price ("SSP") and allocate consideration to distinct performance obligations. Typically, we base our SSPs on our historical sales. If an SSP is not directly observable, then we estimate the SSP taking into consideration market conditions, forecasted sales, entity-specific factors and available information about the customer. We estimate the SSP for license rights by using a discounted cash flow method which includes the following key assumptions: the development timelines, revenue forecasts, commercialization expenses, discount rate, and the probability of technical and regulatory success. For licenses that have been previously sold to other customers, we use historical information to determine SSP.

We account for a contract with a customer when there is approval and commitment from both parties, the rights of the parties are identified, payment terms are identified, the contract has commercial substance and collectability of consideration is probable. Non-cancellable purchase orders received from customers to deliver a specific quantity of product, when combined with our order confirmation, in exchange for future consideration, create enforceable rights and obligations on both parties and constitute a contract with a customer.

We measure revenue based on the consideration specified in the contract with each customer, net of any sales incentives and taxes collected on behalf of government authorities. We recognize revenue in a manner that best depicts the transfer of promised goods or services to the customer, when control of the product or service is transferred to a customer. We make significant judgments when determining the appropriate timing of revenue recognition.

The following is a description of principal activities from which we generate revenue:

Product Revenue

Product revenue consist of sales of biocatalysts, pharmaceutical intermediates and Codex® biocatalyst panels and kits. A majority of our product revenue is made pursuant to purchase orders or supply agreements and is recognized at a point in time when the control of the product has been transferred to the customer typically upon shipment. For some of the products that we develop, we recognize revenue over time as the product is manufactured because we have a right to payment from the customer under a binding, non-cancellable purchase order, and there is no alternate use of the product for us as it is specifically made for the customer's use.

Certain of our agreements provide options to customers which they can exercise at a future date, such as the option to purchase our product during the contract duration at discounted prices and an option to extend their contract, among others. In accounting for customer options, we determine whether an option is a material right and this requires us to exercise significant judgment. If a contract provides the customer an option to acquire additional goods or services at a discount that exceeds the range of discounts that we typically give for that product or service, or if the option provides the customer certain additional goods or services for free, the option may be considered a material right. If the contract gives the customer the option to acquire additional goods or services at their normal SSPs, we would likely determine that the option is not a material right and, therefore, account for it as a separate performance obligation when the customer exercises the option. We primarily account for options which provide material rights using the alternative approach available under ASC 606, as we concluded we meet the criteria for using the alternative approach. Therefore, the transaction price is calculated as the expected consideration to be received for all the goods and services we expect to provide. We update the transaction price for expected consideration, subject to constraint, each reporting period if our estimate of future goods to be ordered by customers change.

Research and Development Revenues

We perform research and development activities as specified in each respective customer agreement. We identify each performance obligation in our research and development agreements at contract inception. We allocate the consideration to each distinct performance obligation based on the estimated SSP of each performance obligation. Performance obligations included in our research and services agreements typically include research and development services for a specified term, periodic reports and small samples of enzyme produced.

The majority of our research and development agreements are based on a contractual rate per dedicated project team working on the project. The underlying product that we develop for customers does not create an asset with an alternative use to us and the customer receives benefits as we perform the work towards completion. Thus, our performance obligations are generally satisfied over time as the service is performed. We utilize an appropriate method of measuring progress towards the completion of our performance obligations to determine the timing of revenue recognition. For each performance obligation that is satisfied over time, we recognize revenue using a single measure of progress, typically based on hours incurred.

Our contracts frequently provide customers with rights to use or access our products or technology, along with other promises or performance obligations. Under ASC 606, we must first determine whether the license is distinct from other promises, such as our promise to perform research and development services. If we determine that the customer cannot benefit from the license without our services, the license will be accounted for as combined with the other performance obligations. If we determine that a license is distinct, we would recognize an allocable portion of the transaction price when the license is transferred to the customer, and the customer can use and benefit from it. We estimate the SSP for license rights by using historical information if licenses have been previously sold to customers and for new licenses, we consider multiple methods, a discounted cash flow method which includes the following key assumptions: the development timelines, revenue forecasts, commercialization expenses, discount rate, and the probability of technical and regulatory success. For licenses that have been previously sold to other customers, we use historical information to determine SSP.

At the inception of each arrangement that includes variable consideration such as development milestone payments, we evaluate whether the milestones are considered probable of being reached and estimate the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within our control or the licensee, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. The transaction price is then allocated to each performance obligation on a relative stand-alone selling price basis, for which we recognize revenue as or when the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, we re-evaluate the probability of achievement of such development milestones and any related constraint, and if necessary, adjust our estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect license, collaboration and other revenues and earnings in the period of adjustment.

Our CodeEvolver® platform technology transfer collaboration agreements typically include license fees, upfront fees, and variable consideration in the form of milestone payments, and sales or usage-based royalties. We have recognized revenues from our platform technology transfer agreements over time.

We also have an agreement under which we have granted a functional license to some elements of our biocatalyst technology. We will recognize revenues for the functional license at a point in time when the control of the license transfers to the customer.

For license agreements that include sales or usage-based royalty payments to us for which the license is the predominant item to which the royalty relates, we do not recognize revenue until the underlying sales of the product or usage has occurred. At the end of each reporting period, we estimate the royalty amount. We recognize revenue at the later of (i) when the related sale of the product occurs, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied, or partially satisfied.

Stock-Based Compensation

We use the Black-Scholes-Merton option pricing model to estimate the fair value of options granted under our equity incentive plans. The Black-Scholes-Merton option pricing model requires the use of assumptions, including the expected term of the award and the expected stock price volatility. The expected term is based on historical exercise behavior on similar awards, giving consideration to the contractual terms, vesting schedules and expectations of future employee behavior. We use historical volatility to estimate expected stock price volatility. The risk-free rate assumption is based on United States Treasury instruments whose terms are consistent with the expected term of the stock options. The expected dividend assumption is based on our history and expectation of dividend payouts.

Restricted Stock Units ("RSUs"), Restricted Stock Awards ("RSAs") and performance-contingent restricted stock units ("PSUs") are measured based on the fair market values of the underlying stock on the dates of grant. Performance based options ("PBOs") are measured using Black-Scholes-Merton option pricing model. The vesting of PBOs and PSUs awarded is conditioned upon the attainment of one or more performance objectives over a specified period and upon continued employment through the applicable vesting date. At the end of the performance period, shares of stock subject to the PBOs and PSUs vest based upon both the level of achievement of performance objectives within the performance period and continued employment through the applicable vesting date.

Stock-based compensation expense is calculated based on awards ultimately expected to vest and is reduced for estimated forfeitures at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates. The estimated annual forfeiture rates for stock options, RSUs, PSUs, PBOs, and RSAs are based on historical forfeiture experience.

The estimated fair value of stock options, RSUs and RSAs are expensed on a straight-line basis over the vesting term of the grant and the estimated fair value of PSUs and PBOs are expensed using an accelerated method over the term of the award once management has determined that it is probable that the performance objective will be achieved. Compensation expense is recorded over the requisite service period based on management's best estimate as to whether it is probable that the shares awarded are expected to vest. Management assesses the probability of the performance milestones being met on a continuous basis.

Lease Accounting

We determine if an arrangement is a lease at inception. Where an arrangement is a lease we determine if it is an operating lease or a finance lease. At lease commencement, we record a lease liability and corresponding ROU asset. Lease liabilities represent the present value of our future lease payments over the expected lease term which includes options to extend or terminate the lease when it is reasonably certain those options will be exercised. The present value of our lease liability is determined using our incremental collateralized borrowing rate at lease inception. ROU assets represent our right to control the use of the leased asset during the lease and are recognized in an amount equal to the lease liability for leases with an initial term greater than 12 months. Over the lease term we use the effective interest rate method to account for the lease liability as lease payments are made and the ROU asset is amortized to consolidated statement of operations in a manner that results in straight-line expense recognition.

We elected to apply the practical expedient for short-term leases and accordingly do not apply lease recognition requirements for short-term leases. Instead, we recognize payments related to these arrangements in the consolidated statement of operations as lease costs on a straight-line basis over the lease term.

Income Taxes

We use the liability method of accounting for income taxes, whereby deferred tax asset or liability account balances are calculated at the balance sheet date using current tax laws and rates in effect for the year in which the differences are expected to affect taxable income. Valuation allowances are provided when necessary to reduce deferred tax assets to the amount that will more likely than not be realized.

We make certain estimates and judgments in determining income tax expense for financial statement purposes. These estimates and judgments occur in the calculation of tax credits, benefits and deductions and in the calculation of certain tax assets and liabilities, which arise from differences in the timing of recognition of revenues and expenses for tax and financial statement purposes. Significant changes to these estimates may result in an increase or decrease to our tax provision in a subsequent period.

In assessing the realizability of deferred tax assets, we consider whether it is more likely than not that some portion or all of the deferred tax assets will be realized on a jurisdiction by jurisdiction basis. The ultimate realization of deferred tax assets is dependent upon the generation of taxable income in the future. We have recorded a valuation allowance against these deferred tax assets in jurisdictions where ultimate realization of deferred tax assets is more likely than not to occur. As of December 31, 2020, we maintain a full valuation allowance in all jurisdictions against the net deferred tax assets as we believe that it is more likely than not that the majority of deferred tax assets will not be realized.

We make estimates and judgments about our future taxable income that are based on assumptions that are consistent with our plans and estimates. Should the actual amounts differ from our estimates, the amount of our valuation allowance may be materially impacted. Any adjustment to the deferred tax asset valuation allowance would be recorded in the statements of operations for the periods in which the adjustment is determined to be required.

We account for uncertainty in income taxes as required by the provisions of ASC Topic 740 (“ASC 740”), which clarifies the accounting for uncertainty in income taxes recognized in an enterprise’s financial statements. The first step is to evaluate the tax position for recognition by determining if the weight of available evidence indicates that it is more likely than not that the position will be sustained on audit, including resolution of related appeals or litigation processes, if any. The second step is to estimate and measure the tax benefit as the largest amount that is more than 50% likely of being realized upon ultimate settlement. It is inherently difficult and subjective to estimate such amounts, as this requires us to determine the probability of various possible outcomes. We consider many factors when evaluating and estimating our tax positions and tax benefits, which may require periodic adjustments and may not accurately anticipate actual outcomes.

The Tax Reform Act of 1986 and similar state provisions limit the use of net operating loss (“NOL”) carryforwards in certain situations where equity transactions result in a change of ownership as defined by Internal Revenue Code Section 382. In the event we should experience such a change of ownership, utilization of our federal and state NOL carryforwards could be limited. We performed an analysis in 2020 and determined that there was not a limitation that would result in the expiration of carryforwards before they are utilized.

We maintain a full valuation allowance against net deferred tax assets as we believe that it is more likely than not that the majority of deferred tax assets will not be realized.

Changes to Tax Law

On March 27, 2020, the Coronavirus Aid, Relief, and Economic Security Act (“CARES Act”), P.L. 116-136 was passed into law, amending portions of certain relevant US tax laws. The CARES Act included a number of federal income tax law changes, including, but not limited to: (i) permitting net operating loss carrybacks to offset 100% of taxable income for taxable years beginning before 2021, (ii) accelerating alternative minimum tax credit refunds, (iii) temporarily increasing the allowable business interest deduction from 30% to 50% of adjusted taxable income, and (iv) providing a technical correction for depreciation related to qualified improvement property. The CARES Act had no impact on our consolidated financial statements.

Beginning in 2018, the global intangible low-taxed income (“GILTI”) provisions in the Federal Tax Cuts and Jobs Act ("Tax Act") required us to include, in our U.S. income tax return, foreign subsidiary earnings in excess of an allowable return on the foreign subsidiary’s tangible assets. Per guidance issued by the FASB, companies can either account for deferred taxes related to GILTI or treat tax arising from GILTI as a period cost. Both are acceptable methods subject to an accounting policy election. At December 31, 2018, we finalized our policy and elected to use the period cost method for GILTI. In 2020, we did not incur any GILTI inclusion as our foreign subsidiaries generated losses. Due to losses incurred in the U.S., we will not be eligible for an Internal Revenue Code Section 250 deduction for foreign derived intangible income.

The Base Erosion and Anti-Abuse Tax ("BEAT") provisions in the Tax Act eliminated the deduction of certain base-erosion payments made to related foreign corporations and imposed a minimum base erosion anti-abuse tax if greater than regular tax. In 2020, our company was not subject to BEAT as it did not meet the requirements to be subject to BEAT.

Financial Assets and Allowances

We currently sell enzymes primarily to pharmaceutical and fine chemicals companies throughout the world by the extension of trade credit terms based on an assessment of each customer's financial condition. Trade credit terms are generally offered without collateral and may include an insignificant discount for prompt payment for specific customers. To manage our credit exposure, we perform ongoing evaluations of our customers' financial conditions. In addition, accounts receivable include amounts owed to us under our collaborative research and development agreements and we recognize accounts receivables at invoiced amounts. Our significant financial assets are comprised of accounts receivable, contract assets, and unbilled receivables. We maintain a valuation allowance on our significant financial assets as follows:

Policy from January 1, 2019

Effective January 1, 2019, we adopted ASU 2016-13,*Financial Instruments - Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments*, which amends guidance for impairment of financial instruments. The standard adds a new impairment model (known as the “current expected credit loss model” or “CECL”) based on estimates and forecasts of future conditions requiring recognition of a lifetime of expected credit losses at inception on our financial assets measured at amortized costs. Our significant financial assets measured at amortized costs are comprised of accounts receivable, contract assets, and unbilled receivables. We have determined that our financial assets share similar risk characteristics including: (i) customer origination in the pharmaceutical and fine chemicals industry, (ii) similar historical credit loss pattern of customers (iii) no meaningful trade receivable differences in terms, (iv) similar historical credit loss experience and (v) our belief that the composition of certain assets are comparable to our historical portfolio used to develop loss history. As a result, we measured the allowance for credit loss (“ACL”) on a collective basis. Our ACL methodology considers how long the asset has been past due, the financial condition of the customers, which includes ongoing quarterly evaluations and assessments of changes in customer credit ratings, and other market data that we believe are relevant to the collectability of the assets. Nearly all financial assets are due from customers that are highly rated by major rating agencies and have a long history of no credit loss. We derive our ACL by establishing an impairment rate attributable to assets not yet identified as impaired.

We derive our ACL by initially relying on our historical financial asset loss rate which contemplates the full contractual life of the assets sharing similar risk characteristics, adjusted to reflect (i) the extent to which we have determined current conditions differ from the conditions that existed for the period over which historical loss information was evaluated and (ii) by taking into consideration the changes in certain macroeconomic historical and forecasted information. We apply the ACL to past due financial assets and record charges to the ACL as a provision to credit loss expense in the Statement of Operations. Financial assets we identify as uncollectible are also charged against the ACL. We adjust the impairment rate to reflect the extent to which we have determined current conditions differ from the conditions that existed for the period over which historical loss information was evaluated. Adjustments to historical loss information may be qualitative or quantitative in nature and reflect changes related to relevant data.

Policy before January 1, 2019

For periods prior to the adoption of ASU 2016-13, the allowances for doubtful accounts reflects our best estimates of probable losses inherent in our accounts receivable and contract asset balances. The allowance determination is based on known troubled accounts, historical experience, and other currently available evidence. Uncollectible accounts receivable are written off against the allowance for doubtful accounts when all efforts to collect them have been exhausted. Recoveries are recognized when they were received. Actual collection losses may differ from our estimates and could be material to our consolidated financial position, results of operations, and cash flows.

Investment in Non-Marketable Securities

Investment in Non-Marketable Equity Securities

Our non-marketable equity securities are accounted for under the measurement alternative. Under the measurement alternative, the carrying value of our non-marketable equity investments is adjusted to fair value for observable transactions for identical or similar investments of the same issuer or impairment. Adjustments are determined primarily based on a market approach as of the transaction date and are recorded as a component of other income (expense), net. We measure investments in non-marketable equity securities without a readily determinable fair value using a measurement alternative that measures these securities at the cost method minus impairment, if any, plus or minus changes resulting from observable price changes on a non-recurring basis. Gains and losses on these securities are recognized in other income and expenses.

Investment in Non-Marketable Debt Securities

We measure available for sale investments in non-marketable debt at fair value. Unrealized gains and losses on these securities are recognized in other comprehensive income until realized. Non-marketable debt securities are classified as available-for-sale securities.

We classify non-marketable debt securities as Level 3 in the fair value hierarchy because we estimate the fair value based on a qualitative analysis using the most recent observable transaction price and other significant unobservable inputs including volatility, rights, and obligations of the securities we hold. Significant changes to the unobservable inputs may result in a significantly higher or lower fair value estimate. We may value these securities based on significant recent arms-length transactions with sophisticated non-strategic unrelated new investors, providing the terms of these transactions are substantially similar to the terms between the company and us. The impact of the difference in transaction terms on the market value of the investment may be difficult or impossible to quantify. See Note 7, "*Fair Value Measurements"* for additional details.

We evaluate both equity and debt securities for impairment when circumstances indicate that we may not be able to recover the carrying value. We may impair these securities and establish an allowance for a credit loss when we determine that there has been an "other-than-temporary" decline in estimated fair value of the debt or equity security compared to its carrying value. We calculate the estimated fair value of these securities using information from the investee, which may include:

- Audited and unaudited financial statements;
- Projected technological developments of the company;
- Projected ability of the company to service its debt obligations;
- If a deemed liquidation event were to occur;
- Current fundraising transactions;
- Current ability of the company to raise additional financing if needed;
- Changes in the economic environment which may have a material impact on the operating results of the company;
- Contractual rights, obligations or restrictions associated with the investment; and
- Other factors deemed relevant by our management to assess valuation.
- The valuation may be reduced if the company's potential has deteriorated significantly. If the factors that led to a reduction in valuation are overcome, the valuation may be readjusted.

Recent Accounting Pronouncements

See Note 2, "*Basis of Presentation and Summary of Significant Accounting Policies*" in the Notes to the Consolidated Financial Statements set forth in Item 8 of this Annual Report on Form 10-K for a full description of recent accounting standards, including the respective dates of adoption and effects on our consolidated financial position, results of operations and cash flows.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Interest Rate Sensitivity

Our unrestricted cash and cash equivalents total $149.1 million at December 31, 2020. We primarily invest these amounts in money market funds which are held for working capital purposes. We do not enter into investments for trading or speculative purposes. As of December 31, 2020, the effect of a hypothetical 10% decrease in market interest rates would have an immaterial impact on a potential loss in future interest income and cash flows.

In June 2017, we entered into a Credit Facility with Western Alliance Bank consisting of term loans up to $10.0 million, and advances under a revolving line of credit up to $5.0 million. Term loans made under the Term Debt bear interest at variable rate through maturity at the greater of (i) 3.75% or (ii) the sum of (A) Index Rate (prime rate published in the Money Rates section of the Western Edition of The Wall Street Journal plus (B) 0.50%. Advances made under the Revolving Line of Credit bear interest at a variable annual rate equal to the greater of (i) 4.25% or (ii) the sum of (A) the prime rate plus (B) 1.00%. Increases in these variable interest rates will increase our future interest expense and decrease our results of operations and cash flows. No amounts were drawn under the Credit Facility as of December 31, 2020. Our exposure to interest rates risk relates to our 2017 Credit Facility with variable interest rates, where an increase in interest rates may result in higher borrowing costs. Since we have no outstanding borrowings under our 2017 Credit Facility as of December 31, 2020, the effect of a hypothetical 10% change in interest rates would not have any impact on our interest expense.

Foreign Currency Risk

Our results of operations and cash flows are subject to fluctuations due to changes in foreign currency exchange rates. In periods when the USD declines in value as compared to the foreign currencies in which we incur expenses, our foreign-currency based expenses increase when translated into United States dollars. Although substantially all of our sales are denominated in United States dollars, future fluctuations in the value of the USD may affect the price competitiveness of our products outside the United States. Our most significant foreign currency exposure is due to non-functional currency denominated monetary assets, primarily currencies denominated in other than their functional currency. These non-functional currency denominated monetary assets are subject to re-measurement which may create fluctuations in other expense, net, a component in our consolidated statement of operations and in the fair value of the assets in the consolidated balance sheets. As of December 31, 2020, the effect of a hypothetical 10% unfavorable change in exchange rates on currencies denominated in other than their functional currency would result in a potential loss in future earnings in our consolidated statement of operations and a reduction in the fair value of the assets of approximately $0.1 million. We did not engage in hedging transactions in 2020, 2019 and 2018.

Investment in Non-Marketable Debt and Equity Securities

We own investments in non-marketable available-for-sale debt security and non-marketable equity securities without readily determinable fair values. To analyze the fair value measurement of these debt securities, we perform a qualitative analysis using significant unobservable inputs. Significant changes to the unobservable inputs may result in a significantly higher or lower fair value estimate.

We may value these equity securities based on significant recent arms-length equity transactions with sophisticated non-strategic unrelated investors, providing the terms of these security transactions are substantially similar to the security transactions terms between the investors and us. The impact of the difference in transaction terms on the market value of the portfolio company may be difficult or impossible to quantify.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

Codexis, Inc.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

Shareholders and Board of Directors
Codexis, Inc.
Redwood City, California

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of Codexis, Inc. (the "Company") as of December 31, 2020 and 2019, the related consolidated statements of operations, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2020, and the related Notes (collectively referred to as the "Consolidated Financial Statements"). In our opinion, the Consolidated Financial Statements present fairly, in all material respects, the financial position of the Company at December 31, 2020 and 2019, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2020, in conformity with accounting principles generally accepted in the United States of America.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) ("PCAOB"), the Company's internal control over financial reporting as of December 31, 2020, based on criteria established in Internal Control - Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission ("COSO") and our report dated March 1, 2021 expressed an unqualified opinion thereon.

Change in Accounting Principle

As discussed in Note 13 to the consolidated financial statements, the Company has changed its accounting method for accounting for leases in fiscal year 2019 due to the adoption of Topic 842: *Leases* using a modified retrospective approach.

Basis for Opinion

These Consolidated Financial Statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's Consolidated Financial Statements based on our audits. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the Consolidated Financial Statements are free of material misstatement, whether due to error or fraud.

Our audits included performing procedures to assess the risks of material misstatement of the Consolidated Financial Statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the Consolidated Financial Statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the Consolidated Financial Statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current period audit of the consolidated financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the consolidated financial statements and (2) involved especially challenging, subjective, or complex judgments. The communication of critical audit matters does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing separate opinions on the critical audit matter or on the accounts or disclosures to which it relates.

Revenue Recognition

As described in Note 2 to the consolidated financial statements, the Company recognizes revenue in a manner that best depicts the transfer of promised goods or services to the customer, when control of the product or service is transferred to a customer. The Company's contracts with customers include enzyme supply, licensing, and collaborative research and development agreements. Contracts with customers may contain multiple performance obligations and may contain up-front or annual

license fees, fees for full time employee research and development services, contingent milestone payments upon achievement of contractual criteria, and royalty fees based on the licensees' product revenue or usage. The Company makes significant judgments in determining revenue recognition for customer contracts.

We identified management's significant judgments and estimates related to revenue recognition for contracts with customers as a critical audit matter. Auditing the evaluation of distinct performance obligations, determination and estimation of material rights, determination of standalone selling prices, determination of the pattern of transfer of control for each distinct performance obligation and estimation of variable consideration required significant audit effort and auditor subjectivity in evaluating management's judgments and estimates.

The primary procedures we performed to address this critical audit matter included:

- Testing the design and operating effectiveness of internal controls relating to the identification of distinct performance obligations and material rights, the determination of the timing of revenue recognition, the estimation of standalone selling prices, and the estimation of variable consideration.
- Examining a sample of revenue contracts and other source documents to test management's identification of significant terms for completeness, including the identification of distinct performance obligations, material rights and variable consideration including sending confirmations to a sample of customers to confirm our understanding of the parties' rights and obligations.
- Assessing the reasonableness of management's estimates and assumptions used in determining stand-alone selling prices for new products and services and those products and services that are not sold separately.
- Evaluating the reasonableness of management's judgments and estimates used to assess the stand-alone selling prices for new functional licenses when granted to customers as part of contracts containing multiple performance obligations.
- Evaluating the reasonableness and accuracy of management's judgments and estimates used in accounting for identified material rights, including transactions accounted for under the alternative approach to estimating the standalone selling price of a material right. This includes testing management's estimates of the expected consideration from the customer's exercise of options.
- Assessing the reasonableness of management's judgments and estimates to calculate variable consideration, and the timing of recognizing the related revenue subject to any constraints.
- Evaluating the appropriateness of management's determination of whether identified performance obligations meet the criteria for over-time revenue recognition, including whether certain products and services have alternative use.

/s/ BDO USA, LLP

We have served as the Company's auditor since 2013.

San Jose, California

March 1, 2021

Report of Independent Registered Public Accounting Firm

Shareholders and Board of Directors
Codexis, Inc.
Redwood City, California

Opinion on Internal Control over Financial Reporting

We have audited Codexis, Inc.'s (the "Company's") internal control over financial reporting as of December 31, 2020, based on criteria established in Internal Control - Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (the "COSO criteria"). In our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2020, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) ("PCAOB"), the consolidated balance sheets of the Company as of December 31, 2020 and 2019, the related consolidated statements of operations, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2020 and the related Notes, and our report dated March 1, 2021 expressed an unqualified opinion thereon.

Basis for Opinion

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying "Item 9A, Management's Report on Internal Control over Financial Reporting". Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit of internal control over financial reporting in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audit also included performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ BDO USA, LLP

San Jose, California

March 1, 2021

Codexis, Inc.
Consolidated Balance Sheets
(In Thousands, Except Per Share Amounts)

	December 31,	
	2020	**2019**
Assets		
Current assets:		
Cash and cash equivalents	$ 149,117	$ 90,498
Restricted cash, current	638	661
Investment in non-marketable debt security	1,000	—
Financial assets:		
Accounts receivable	13,894	9,063
Contract assets	4,526	1,027
Unbilled receivables	10,942	10,099
Total financial assets	29,362	20,189
Less: allowances	(74)	(34)
Total financial assets, net	29,288	20,155
Inventories	964	371
Prepaid expenses and other current assets	3,416	2,520
Total current assets	184,423	114,205
Restricted cash	1,062	1,062
Investment in non-marketable equity securities	1,450	—
Right-of-use assets - Operating leases, net	21,382	23,837
Right-of-use assets - Finance leases, net	119	268
Property and equipment, net	9,675	6,282
Goodwill	3,241	3,241
Other non-current assets	294	178
Total assets	$ 221,646	$ 149,073
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 2,970	$ 2,621
Accrued compensation	7,288	5,003
Other accrued liabilities	10,272	6,540
Current portion of lease obligations - Operating leases	2,627	1,107
Current portion of lease obligations - Finance leases	—	60
Deferred revenue	1,824	57
Total current liabilities	24,981	15,388
Deferred revenue, net of current portion	2,967	1,987
Long-term lease obligations, Operating leases	22,324	24,951
Other long-term liabilities	1,271	1,230
Total liabilities	51,543	43,556
Commitments and contingencies (Note 13)	—	—
Stockholders' equity:		
Preferred stock, $0.0001 par value per share; 5,000 shares authorized, none issued and outstanding	—	—
Common stock, $0.0001 par value per share; 100,000 shares authorized; 64,283 and 58,877 shares issued and outstanding at December 31, 2020 and December 31, 2019, respectively	6	6
Additional paid-in capital	536,516	447,920
Accumulated deficit	(366,419)	(342,409)
Total stockholders' equity	170,103	105,517
Total liabilities and stockholders' equity	$ 221,646	$ 149,073

See Accompanying Notes to Consolidated Financial Statements

Codexis, Inc.

Consolidated Statements of Operations
(In Thousands, Except Per Share Amounts)

	Year Ended December 31,		
	2020	2019	2018
Revenues:			
Product revenue	$ 30,220	$ 29,465	$ 25,590
Research and development revenue	38,836	38,993	35,004
Total revenues	69,056	68,458	60,594
Costs and operating expenses:			
Cost of product revenue	13,742	15,632	12,620
Research and development	44,185	33,873	29,978
Selling, general and administrative	35,049	31,502	29,291
Total costs and operating expenses	92,976	81,007	71,889
Loss from operations	(23,920)	(12,549)	(11,295)
Interest income	405	1,287	671
Other expenses, net	(156)	(656)	(291)
Loss before income taxes	(23,671)	(11,918)	(10,915)
Provision for (benefit from) income taxes	339	17	(37)
Net loss	$ (24,010)	$ (11,935)	$ (10,878)
Net loss per share, basic and diluted	$ (0.40)	$ (0.21)	$ (0.21)
Weighted average common stock shares used in computing net loss per share, basic and diluted	59,360	56,525	52,205

See Accompanying Notes to Consolidated Financial Statements

Codexis, Inc.

Consolidated Statements of Stockholders' Equity
(In Thousands)

	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
December 31, 2017	48,365	$ 5	$ 340,079	$ (472)	$ (315,065)	$ 24,547
Exercise of stock options	856	—	4,680	—	—	4,680
Release of stock awards	832	—	—	—	—	—
Employee stock-based compensation	—	—	7,865	—	—	7,865
Non-employee stock-based compensation	—	—	24	—	—	24
Taxes paid related to net share settlement of equity awards	(301)	—	(3,190)	—	—	(3,190)
Issuance of common stock, net of issuance costs	4,313	—	37,317	—	—	37,317
Cumulative effect of change in accounting principles [1]	—	—	—	472	(4,531)	(4,059)
Net Loss	—	—	—	—	(10,878)	(10,878)
December 31, 2018	54,065	5	386,775	—	(330,474)	56,306
Exercise of stock options	1,466	—	7,099	—	—	7,099
Release of stock awards	449	—	—	—	—	—
Employee stock-based compensation	—	—	6,943	—	—	6,943
Taxes paid related to net share settlement of equity awards	(152)	—	(2,850)	—	—	(2,850)
Issuance of common stock, net of issuance costs of $123	3,049	1	49,876	—	—	49,877
Short swing profit settlement	—	—	77	—	—	77
Net Loss	—	—	—	—	(11,935)	(11,935)
December 31, 2019	58,877	6	447,920	—	(342,409)	105,517
Exercise of stock options	210	—	1,323	—	—	1,323
Release of stock awards	370	—	—	—	—	—
Employee stock-based compensation	—	—	7,622	—	—	7,622
Non-employee stock-based compensation	—	—	106	—	—	106
Taxes paid related to net share settlement of equity awards	(103)	—	(1,257)	—	—	(1,257)
Issuance of common stock, net of issuance costs of $5,448	4,929	—	80,802	—	—	80,802
Net Loss	—	—	—	—	(24,010)	(24,010)
December 31, 2020	64,283	$ 6	$ 536,516	$ —	$ (366,419)	$ 170,103

[1] Cumulative effect of change in accounting principles included: Accounting Standards Update 2014-9 (Topic 606), of $4.1 million and Accounting Standards Update 2016-01 (Subtopic 825-10), of $0.5 million.

See Accompanying Notes to Consolidated Financial Statements

Codexis, Inc.
Consolidated Statements of Cash Flows
(In Thousands)

	Year Ended December 31,		
	2020	**2019**	**2018**
Operating activities:			
Net loss	$ (24,010)	$ (11,935)	$ (10,878)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation	1,950	1,570	1,147
Amortization expense - right-of-use assets - operating and finance leases	2,604	2,987	—
Stock-based compensation	7,728	6,943	7,889
Equity securities earned from research and development activities	(900)	—	—
Other non-cash items	55	525	91
Changes in operating assets and liabilities:			
Financial assets, net	(8,723)	(5,867)	(1,424)
Inventories	(593)	217	447
Prepaid expenses and other assets	(1,012)	(1,324)	191
Accounts payable	101	(428)	(524)
Accrued compensation and other accrued liabilities	6,175	2,205	502
Other long-term liabilities	(2,586)	(1,210)	(904)
Deferred revenue	2,747	(6,243)	(10,631)
Net cash used in operating activities	(16,464)	(12,560)	(14,094)
Investing activities:			
Purchase of property and equipment	(3,748)	(3,730)	(2,768)
Proceeds from disposal of property and equipment	—	3	2
Proceeds from sale of investment securities	—	62	—
Investment in non-marketable securities	(2,000)	—	—
Net cash used in investing activities	(5,748)	(3,665)	(2,766)
Financing activities:			
Proceeds from exercises of stock options	1,323	7,099	4,680
Proceeds from issuance of common stock in connection with public offering, net of underwriting discounts and commission	86,250	—	37,497
Costs incurred in connection with public offering	(5,448)	—	(180)
Proceeds from issuance of common stock in connection with private offering	—	50,000	—
Costs incurred in connection with private placement	—	(123)	—
Payments of lease obligations - Finance leases	(60)	(242)	(238)
Recovery of short swing profit	—	77	—
Taxes paid related to net share settlement of equity awards	(1,257)	(2,850)	(3,190)
Net cash provided by financing activities	80,808	53,961	38,569
Net increase in cash, cash equivalents and restricted cash	58,596	37,736	21,709
Cash, cash equivalents and restricted cash at the beginning of the year	92,221	54,485	32,776
Cash, cash equivalents and restricted cash at the end of the year	$ 150,817	$ 92,221	$ 54,485
Supplemental disclosure of cash flow information:			
Interest paid	$ 52	$ 49	$ 84
Income taxes	$ 312	$ 5	$ 5
Supplemental non-cash investing and financing activities:			
Capital expenditures incurred but not yet paid	$ 1,750	$ 140	$ 300
Assets received for research & development revenue earned	$ 900	$ —	$ —

The following table provides a reconciliation of cash, cash equivalents and restricted cash reported within the consolidated balance sheets to the total of the same such amounts shown above (in thousands):

	Year Ended December 31,		
	2020	**2019**	**2018**
Cash and cash equivalents	$ 149,117	$ 90,498	$ 53,039
Restricted cash, current and non-current	1,700	1,723	1,446
Total cash, cash equivalents and restricted cash at the end of the period	$ 150,817	$ 92,221	$ 54,485

See Accompanying Notes to Consolidated Financial Statements

Note 1. Description of Business

In these Notes to the Consolidated Financial Statements, the "Company," "we," "us," and "our" refers to Codexis, Inc. and its subsidiaries on a consolidated basis.

We discover, develop and sell enzymes and other proteins that deliver value to our clients in a growing set of industries. We view proteins as a vast, largely untapped source of value-creating products, and we are using our proven technologies, which we have been continuously improving since our inception in 2002, to commercialize an increasing number of novel enzymes, both as proprietary Codexis products and in partnership with our customers.

We are a pioneer in harnessing computational technologies to drive biology advancements. Since 2002, we have made substantial investments in the development of our CodeEvolver® protein engineering technology platform, the primary source of our competitive advantage. Our technology platform is powered by proprietary, artificial intelligence-based, computational algorithms that rapidly mine the structural and performance attributes of our large and continuously growing library of protein variants. These computational outputs enable increasingly reliable predictions for next generation protein variants to be engineered, enabling time- and cost-efficient delivery of the targeted performance enhancements. In addition to its computational prowess, our CodeEvolver® protein engineering technology platform integrates additional modular competencies, including robotic high-throughput screening and genomic sequencing, organic chemistry and bioprocess development which are all coordinated to rapidly innovate novel, fit-for-purpose products.

The core historical application of the technology has been in developing commercially viable biocatalytic manufacturing processes for more sustainable production of complex chemicals. It begins by conceptually designing the most cost-effective and practical process for a targeted product. We then develop optimized biocatalysts to enable the designed process, using our CodeEvolver® platform. Engineered biocatalyst candidates, numbering many thousands for each project, are then rapidly screened and validated using high throughput methods under process-relevant operating conditions. This approach results in an optimized biocatalyst that enables cost-efficient processes that are relatively simple to run in conventional manufacturing equipment. This also allows for efficient technical transfer of our processes to our manufacturing partners.

The successful embodiment of our CodeEvolver® protein engineering technology platform in commercial manufacturing processes requires well-integrated expertise in a number of technical disciplines. In addition to those competences directly integrated in our CodeEvolver® protein engineering platform, such as molecular biology, enzymology, microbiology, cellular engineering, metabolic engineering, bioinformatics, biochemistry and high throughput analytical chemistry, our process development projects also involve integrated expertise in organic chemistry, chemical process development, chemical engineering, bioprocess development and fermentation engineering. Our integrated, multi-disciplinary approach to product and process development is a critical success factor for the Company.

We initially commercialized our CodeEvolver® protein engineering technology platform and products in the manufacture of small molecule pharmaceuticals, which remains a primary business focus. Our customers, which include many large, global pharmaceutical companies, use our technology, products and services in their process development and in manufacturing. Additionally, we have licensed our proprietary CodeEvolver® protein engineering technology platform to global pharmaceutical companies enabling them to use this technology, in house, to engineer enzymes for their own businesses. Most recently, in May 2019, we entered into a Platform Technology Transfer and License Agreement (the "Novartis CodeEvolver® Agreement") with Novartis. The Novartis CodeEvolver® Agreement (Codexis' third such agreement with large pharma companies) allows Novartis to use our proprietary CodeEvolver® protein engineering platform technology in the field of human healthcare.

As evidence of our strategy to extend our technology beyond pharmaceutical manufacturing, we have also used the technology to develop biocatalysts and enzyme products for use in a broader set of industrial markets, including several large verticals, such as food, feed, consumer care and fine chemicals. In addition, we are using our technology to develop enzymes for various life science related applications, such as next generation sequencing ("NGS") and polymerase chain reaction ("PCR/qPCR") for in vitro molecular diagnostic and genomic research applications. In December 2019, we entered into a license agreement to provide Roche Sequencing Solutions, Inc. with our first enzyme for this target market: the Company's EvoT4™ DNA ligase. In June 2020, we also entered into a Master Collaboration and Research Agreement with MAI (the "MAI Agreement") pursuant to which we are leveraging our CodeEvolver® platform technology to improve the DNA polymerase enzymes that are critical for enzymatic DNA synthesis. Concurrently with the MAI Agreement, we entered into a Stock Purchase Agreement with Molecular Assemblies, Inc ("MAI") pursuant to which we purchased 1,587,050 shares of MAI's Series A preferred stock for

$1.0 million and, in connection with the transaction, John Nicols, our President and Chief Operating Officer, also joined MAI's board of directors.

Approximately five years ago, we began using the CodeEvolver® protein engineering technology platform to develop early stage, novel biotherapeutic product candidates, both in partnership with customers and for our own proprietary Codexis drug candidates. Our first program was for the potential treatment of phenylketonuria ("PKU") in humans. PKU is an inherited metabolic disorder in which the enzyme that converts the essential amino acid phenylalanine into tyrosine is deficient. In October 2017, we entered into a Global Development, Option and License Agreement (the "Nestlé License Agreement") with Societé des Produits Nestlé S.A., formerly known as Nestec Ltd. ("Nestlé Health Science") to advance CDX-6114, our enzyme biotherapeutic product candidate for the potential treatment of PKU. In February 2019, Nestlé Health Science exercised its option to obtain an exclusive license to develop and commercialize CDX-6114. Also in October 2017, we entered into the Nestlé SCA pursuant to which we and Nestlé Health Science are collaborating to leverage the CodeEvolver® platform technology to develop other novel enzymes for Nestlé Health Science's established Consumer Care and Medical Nutrition business areas. In January 2020, we entered into a development agreement with Nestlé Health Science to advance a new lead candidate discovered under the Nestlé SCA, CDX-7108, into preclinical development and early clinical studies as a potential treatment for a gastro-intestinal disorder. In parallel, the Nestlé SCA was extended through December 2021 to support the discovery of therapeutic candidates for additional disorders. In March 2020, we entered into a Strategic Collaboration and License Agreement ("Takeda Agreement") with Shire Human Genetic Therapies, Inc., a wholly-owned subsidiary of Takeda Pharmaceutical Company Limited ("Takeda"), for the research and development of novel gene therapies for certain disease indications, including the treatment of lysosomal storage disorders and a blood factor deficiency.

Below are brief descriptions of our business segments:

Performance Enzymes

We initially commercialized our CodeEvolver® protein engineering technology platform and products in the manufacture of small molecule pharmaceuticals and, to date, this continues to be our largest market served. Our customers, which include many large global pharmaceutical companies, use our technology, products and services in their manufacturing processes and process development. We have also used the technology to develop customized enzymes for use in other industrial markets. These markets consist of several large industrial verticals, including food, feed, consumer care, and fine chemicals. We also use our technology in the life sciences markets to develop enzymes for customers using NGS and PCR/qPCR for in vitro molecular diagnostic and molecular biology research applications, as well DNA/RNA synthesis and health monitoring applications.

Novel Biotherapeutics

We are also targeting new opportunities in the pharmaceutical industry to discover, improve, and/or develop biotherapeutic drug candidates. We believe that our CodeEvolver® protein engineering platform technology can be used to discover novel biotherapeutic drug candidates that will target human diseases that are in need of improved therapeutic interventions. Similarly, we believe that we can deploy our platform technology to improve specific characteristics of a customer's pre-existing biotherapeutic drug candidate, such as its activity, stability or immunogenicity.

Our first lead program was for the potential treatment of hyperphenylalaninemia ("HPA") (also referred to as PKU) in humans. PKU is an inherited metabolic disorder in which the enzyme that converts the essential amino acid phenylalanine into tyrosine is deficient. In October 2017, we announced a global development, option and license agreement with Nestlé Health Science to advance CDX-6114, our own novel orally administrable enzyme therapeutic candidate for the potential treatment of PKU. In July 2018, we announced that we had dosed the first subjects in a first-in-human Phase 1a dose-escalation trial with CDX-6114, which was conducted in Australia. The initiation of the trial triggered a $4.0 million milestone payment from Nestlé Health Science. The $1.0 million milestone payment that was triggered by the achievement of a formulation relating to CDX-6114 was received in February 2019. In January 2019, we received notice from the U.S. Food and Drug Administration that it had completed its review of our investigational drug application for CDX-6114 and concluded that we may proceed with the proposed Phase 1b multiple ascending dose study in healthy volunteers in the United States.

In February 2019, Nestlé Health Science exercised its option to obtain an exclusive, worldwide, royalty-bearing, sub-licensable license for the global development and commercialization of CDX-6114 for the management of PKU. As a result of the option exercise, we earned a milestone and recognized $3.0 million in revenues in the first quarter of 2019. Upon exercising its option, Nestlé Health Science assumed all responsibilities for future clinical development and commercialization of CDX-6114.

In October 2017, we entered into the Nestlé SCA pursuant to which we and Nestlé Health Science are collaborating to leverage the CodeEvolver® platform technology to develop other novel enzymes for Nestlé Health Science's established Consumer Care and Medical Nutrition business areas. In January 2020, we and Nestlé Health Science entered into a development agreement pursuant to which we and Nestlé Health Science are collaborating to advance into pre-clinical and early clinical studies a lead

candidate targeting a gastro-intestinal disorder, CDX-7108, discovered through the Nestlé SCA. The Nestlé SCA was extended through December 2021. During 2020, we, together with Nestlé Health Science, continued to advance CDX-7108 towards initiation of a Phase 1 clinical trial which we anticipate will begin in 2021. Additionally, the parties initiated two new programs under the Nestlé SCA targeting a gastro-intestinal disorder.

Our most recent achievement in novel biotherapeutics came in March 2020, when we announced a strategic collaboration and license agreement with Takeda in which we will collaborate with Takeda to research and develop protein sequences for use in gene therapy products for certain disease indications. Under the terms of the Takeda Agreement, we have agreed to generate novel gene sequences encoding protein variants designed to enhance efficacy as a result of increased activity, stability, and cellular uptake using our CodeEvolver® protein engineering platform. Takeda will combine these improved transgenes with its gene therapy capabilities to generate novel candidates for the treatment of rare genetic disorders. We are currently collaborating on three initial programs for the treatment of Fabry disease, Pompe disease, and an undisclosed blood factor deficiency. The Company is responsible for the creation of novel enzyme sequences for advancement as gene therapies into pre-clinical development. Takeda is responsible for the pre-clinical and clinical development and commercialization of gene therapy products resulting from the collaboration programs. Under the terms of the agreement, in addition to the three initial programs, Takeda may initiate up tofour additional programs for separate target indications. In March 2020, we began research and development activities under the program plans and received a $8.5 million one-time, non-refundable cash payment.

We expect to continue to make additional investments in our pipeline with the aim of advancing additional product candidates targeting other therapeutic areas.

For additional discussion of our business segments, see Note 15, “Segment, Geographical and Other Revenue Information.”

Business Update Regarding COVID-19

We are subject to risks and uncertainties as a result of the current COVID-19 pandemic. The COVID-19 pandemic has presented a substantial public health and economic challenge around the world and is affecting our employees, communities and business operations, as well as the U.S. economy and other economies worldwide. The full extent to which the COVID-19 pandemic will directly or indirectly impact our business, results of operations and financial condition will depend on future developments that are highly uncertain and may not be accurately predicted, including the duration and severity of the pandemic and the extent and severity of the impact on our customers, new information that may emerge concerning COVID-19, the actions taken to contain it or treat its impact and the economic impact on local, regional, national and international markets.

To date, we and our collaboration partners have been able to continue to supply our enzymes to our customers worldwide. However, we are dependent on our manufacturing and logistics partners and consequently, disruptions in operations of our partners and customers may affect our ability to supply enzymes to our customers. Furthermore, our ability to provide future research and development (“R&D”) services will continue to be impacted as a result of governmental orders and any disruptions in operations of our customers with whom we collaborate. We believe that these disruptions have had a negative impact on revenue for the year ended December 31, 2020, although we are unable to fully determine and quantify the extent to which this pandemic has affected the amount and timing of our total revenues. The extent to which the pandemic may impact our business operations and operating results will continue to remain highly dependent on future developments, which are uncertain and cannot be predicted with confidence.

In the U.S., the impact of COVID-19, including governmental orders (“Orders”) governing the operation of businesses during the pandemic, caused the temporary closure of our Redwood City, California facilities and has disrupted our R&D operations. R&D operations for several projects were temporarily suspended from mid-March 2020 through the end of April in accordance with these Orders. In May 2020, we re-initiated limited R&D operations and have ramped up operations such that we are currently utilizing the majority of our normal R&D capacity while following county, state and federal COVID-19 guidance for the protection of our employees. Additionally, we resumed small scale manufacturing at our Redwood City pilot plant in May 2020.

Our future results of operations and liquidity could be adversely impacted by delays in payments of outstanding receivable amounts beyond normal payment terms, supply chain disruptions and uncertain demand, and the impact of any initiatives or programs that we may undertake to address financial and operations challenges faced by our customers. As of the date of issuance of our Consolidated Financial Statements, the extent to which the COVID-19 pandemic may materially impact our financial condition, liquidity, or results of operations in the future is uncertain.

Note 2. Basis of Presentation and Summary of Significant Accounting Policies

Basis of Presentation and Principles of Consolidation

The accompanying consolidated financial statements have been prepared in accordance with generally accepted accounting principles in the United States of America ("GAAP") and the applicable rules and regulations of the Securities and Exchange Commission ("SEC") and include the accounts of Codexis, Inc. and its wholly-owned subsidiaries.

Certain prior year amounts have been reclassified to conform to 2020 presentation. In June 2016, the Financial Accounting Standards Board ("FASB") issued guidance requiring implementation of a new impairment model applicable to financial assets measured at amortized cost which, among other things required that accounts receivable, contract assets, unbilled receivables and related allowances be reclassified as financial assets. The results of the year ended December 31, 2020 reflect the adoption of the accounting standards including Accounting Standard Update ("ASU") 2016-13, *Financial Instruments - Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments* which added a new impairment model applicable to our financial assets measured at amortized cost. See "Recently adopted accounting pronouncements" for details regarding the adoption of these standards. The consolidated financial statements include the accounts of Codexis, Inc. and its wholly owned subsidiaries. All significant intercompany balances and transactions have been eliminated in consolidation.

Financial Statement Exclusion

The total net loss in the consolidated statements of operations for the years ended December 31, 2020, 2019 and 2018 is not different from our consolidated comprehensive loss. The consolidated financial statements exclude the consolidated statements of comprehensive loss for the years ended December 31, 2020, 2019 and 2018.

Use of Estimates

The preparation of our consolidated financial statements in conformity with GAAP requires us to make estimates, judgments and assumptions that may affect the reported amounts of assets, liabilities, equity, revenues and expenses and related disclosure of contingent assets and liabilities. We regularly assess these estimates which primarily affect revenue recognition, inventories, goodwill arising out of business acquisitions, accrued liabilities, stock awards, and the valuation allowances associated with deferred tax assets. Actual results could differ from those estimates and such differences may be material to the consolidated financial statements. The full extent to which the COVID-19 pandemic will directly or indirectly impact our business, results of operations and financial condition, including sales, expenses, reserves and allowances, manufacturing, research and development costs and employee-related amounts, will depend on future developments that are highly uncertain, and may not be accurately predicted, including as a result of new information that may emerge concerning COVID-19 and the actions taken to contain or treat COVID-19, as well as the economic impact on local, regional, national and international customers, markets and economies.

Segment Reporting

We report two business segments, Performance Enzymes and Novel Biotherapeutics, which are based on our operating segments. Operating segments are defined as components of an enterprise about which separate financial information is available that is evaluated regularly by the chief operating decision maker or decision making group ("CODM"), in deciding how to allocate resources, and in assessing performance. Our CODM is our Chief Executive Officer. Our business segments are primarily based on our organizational structure and our operating results as used by our CODM in assessing performance and allocating resources for the Company. We do not allocate or evaluate assets by segment.

The Novel Biotherapeutics segment focuses on new opportunities in the pharmaceutical industry to discover or improve novel biotherapeutic drug candidates that will target human diseases that are in need of improved therapeutic interventions. Similarly, we believe that we can deploy our platform technology to improve specific characteristics of a customer's pre-existing biotherapeutic drug candidate, such as its activity, stability, or immunogenicity. The Performance Enzymes segment consists of biocatalyst products and services with focus on pharmaceutical, food, molecular diagnostics, and other industrial markets.

Foreign Currency Translation

The USD is the functional currency for our operations outside the United States. Accordingly, nonmonetary assets and liabilities originally acquired or assumed in other currencies are recorded in USD at the exchange rates in effect at the date they were acquired or assumed. Monetary assets and liabilities denominated in other currencies are translated into United States dollars at the exchange rates in effect at the balance sheet date. Translation adjustments are recorded in other expense in the consolidated statements of operations. Gains and losses realized from non-USD transactions, including intercompany balances not considered as permanent investments, denominated in currencies other than an entity's functional currency are included in other expense in the accompanying consolidated statements of operations.

Revenue Recognition

Our revenues are derived primarily from product revenue and collaborative research and development agreements. The majority of our contracts with customers typically contain multiple products and services. We account for individual products and services separately if they are distinct-that is, if a product or service is separately identifiable from other items in the contract and if a customer can benefit from it on its own or with other resources that are readily available to the customer.

In determining the appropriate amount of revenue to be recognized as we fulfill our obligations under our product revenue and collaborative research and development agreements, we perform the following steps: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations, including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations based on estimated selling prices; and (v) recognition of revenue when (or as) we satisfy each performance obligation.

The majority of our collaborative contracts contain multiple revenue streams such as upfront and/or annual license fees, fees for research and development services, contingent milestone payments upon achievement of contractual criteria, and royalty fees based on the licensees' product revenue or usage, among others. We determine the stand-alone selling price ("SSP") and allocate consideration to distinct performance obligations. Typically, we base our SSPs on our historical sales. If an SSP is not directly observable, then we estimate the SSP taking into consideration market conditions, forecasted sales, entity-specific factors and available information about the customer. We estimate the SSP for license rights by using historical information if licenses have been previously sold to customers and for new licenses, we consider multiple methods, including a discounted cash flow method which includes the following key assumptions: the development timelines, revenue forecasts, commercialization expenses, discount rate, and the probability of technical and regulatory success.

We account for a contract with a customer when there is approval and commitment from both parties, the rights of the parties are identified, payment terms are identified, the contract has commercial substance and collectability of consideration is probable. Non-cancellable purchase orders received from customers to deliver a specific quantity of product, when combined with our order confirmation, in exchange for future consideration, create enforceable rights and obligations on both parties and constitute a contract with a customer.

We measure revenue based on the consideration specified in the contract with each customer, net of any sales incentives and taxes collected on behalf of government authorities. We recognize revenue in a manner that best depicts the transfer of promised goods or services to the customer, when control of the product or service is transferred to a customer. We make significant judgments when determining the appropriate timing of revenue recognition.

The following is a description of principal activities from which we generate revenue:

Product Revenue

Product revenue consist of sales of biocatalysts, pharmaceutical intermediates and Codex® biocatalyst panels and kits. A majority of our product revenue is made pursuant to purchase orders or supply agreements and is recognized at a point in time when the control of the product has been transferred to the customer typically upon shipment. For some of the products that we develop, we recognize revenue over time as the product is manufactured because we have a right to payment from the customer under a binding, non-cancellable purchase order, and there is no alternate use of the product for us as it is specifically made for the customer's use.

Certain of our agreements provide options to customers which they can exercise at a future date, such as the option to purchase our product during the contract duration at discounted prices and an option to extend their contract, among others. In accounting for customer options, we determine whether an option is a material right and this requires us to exercise significant judgment. If a contract provides the customer an option to acquire additional goods or services at a discount that exceeds the range of discounts that we typically give for that product or service for the same class of customer, or if the option provides the customer certain additional goods or services for free, the option may be considered a material right. If the contract gives the customer the option to acquire additional goods or services at their normal SSPs, we would likely determine that the option is not a material right and, therefore, account for it as a separate performance obligation when the customer exercises the option. We primarily account for options which provide material rights using the alternative approach available pursuant to the applicable accounting guidance, as we concluded we meet the criteria for using the alternative approach. Therefore, the transaction price is calculated as the expected consideration to be received for all the goods and services we expect to provide under the contract. We update the transaction price for expected consideration, subject to constraint, each reporting period if our estimate of future goods to be ordered by customers change.

Research and Development Revenues

We perform research and development activities as specified in each respective customer agreement. We identify each performance obligation in our research and development agreements at contract inception. We allocate the consideration to each distinct performance obligation based on the estimated SSP of each performance obligation. Performance obligations included in our research and services agreements typically include research and development services for a specified term, periodic reports and small samples of enzyme produced.

The majority of our research and development agreements are based on a contractual rate per dedicated project team working on the project. The underlying product that we develop for customers does not create an asset with an alternative use to us and the customer receives benefits as we perform the work towards completion. Thus, our performance obligations are generally satisfied over time as the service is performed. We utilize an appropriate method of measuring progress towards the completion of our performance obligations to determine the timing of revenue recognition. For each performance obligation that is satisfied over time, we recognize revenue using a single measure of progress, typically based on hours incurred.

Our contracts frequently provide customers with rights to use or access our products or technology, along with other promises or performance obligations. We must first determine whether the license is distinct from other promises, such as our promise to manufacture a product. If we determine that the customer cannot benefit from the license without our manufacturing capability, the license will be accounted for as combined with the other performance obligations. If we determine that a license is distinct and has significant standalone functionality, we would recognize revenues from a functional license at a point in time when the license is transferred to the customer, and the customer can use and benefit from it. We estimate the SSP for license rights by using historical information if licenses have been previously sold to customers and for new licenses, we consider multiple methods, including a discounted cash flow method which includes the following key assumptions: the development timelines, revenue forecasts, commercialization expenses, discount rate, and the probability of technical and regulatory success. For licenses that have been previously sold to other customers, we use historical information to determine SSP.

At the inception of each arrangement that includes variable consideration such as development milestone payments, we evaluate whether the milestones are considered probable of being reached and estimate the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within our control or the licensee, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. The transaction price is then allocated to each performance obligation on a relative stand-alone selling price basis, for which we recognize revenue as or when the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, we re-evaluate the probability of achievement of such development milestones and any related constraint, and if necessary, adjust our estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect license, collaboration and other revenues and earnings in the period of adjustment.

Our CodeEvolver® platform technology transfer collaboration agreements typically include license fees, upfront fees, and variable consideration in the form of milestone payments, and sales or usage-based royalties. We have recognized revenues from our platform technology transfer agreements over time as our customer learns to use our technology.

We also have an agreement under which we have granted a functional license to some elements of our biocatalyst technology. We recognize revenues for the functional license at a point in time when the control of the license and technology transfers to the customer.

For license agreements that include sales or usage-based royalty payments to us, we do not recognize revenue until the underlying sales of the product or usage has occurred. At the end of each reporting period, we estimate the royalty amount. We recognize revenue at the later of (i) when the related sale of the product occurs, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied, or partially satisfied.

Practical Expedients, Elections, and Exemptions

We apply certain practical expedients available which permit us not to adjust the amount of consideration for the effects of a significant financing component if, at contract inception, the expected period between the transfer of promised goods or services and customer payment is one year or less.

We perform monthly services under our research and development agreements and we use a practical expedient permitting us to recognize revenue at the same time that we have the right to invoice our customer for monthly services completed to date.

We have elected to treat shipping and handling activities as fulfillment costs.

We have elected to record revenue net of sales and other similar taxes.

Contract Assets

Contract assets include amounts related to our contractual right to consideration for completed performance obligations not yet invoiced. Contract assets are reclassified to receivables when the rights become unconditional.

Contract Liabilities

Contract liabilities are recorded as deferred revenues and include payments received in advance of performance under the contract. Contract liabilities are realized when the development services are provided to the customer or control of the products has been transferred to the customer. A portion of our contract liabilities relate to supply arrangements that contain material rights that are recognized using the alternative method, under which the aggregate amount invoiced to the customer for shipped products, including contractual fees, is higher than the amount of revenue recognized based on the transaction price allocated to the shipped products.

Contract Costs

We recognize a non-current asset for the incremental costs of obtaining a contract with a customer if the entity expects to recover such costs. Incremental costs are costs that would not have been incurred if the contract had not been obtained. Examples of contract costs are commissions paid to sales personnel. We do not typically incur significant incremental costs because the compensation of our salespeople are not based on contracts closed but on a mixture of company goals, individual goals, and sales goals. If a commission paid is directly related to obtaining a specific contract, our policy is to capitalize and amortize such costs on a systematic basis, consistent with the pattern of transfer of the good or service to which the asset relates. Contract costs are reported in other non-current assets.

Cost of Product Revenue

Cost of product revenue comprises both internal and third party fixed and variable costs including materials and supplies, labor, facilities, and other overhead costs associated with our product sales. Shipping costs are included in our cost of product revenue. Such charges were not significant in any of the periods presented.

Fulfillment costs, such as shipping and handling, are recognized at a point in time and are included in cost of product sales.

Cost of Research and Development Services

Cost of research and development services related to services under research and development agreements approximate the research funding over the term of the respective agreements and is included in research and development expense. Costs of services provided under license and platform technology transfer agreements are included in research and development expenses and are expensed in the periods in which such costs are incurred.

Research and Development Expenses

Research and development expenses consist of costs incurred for internal projects and partner-funded collaborative research and development activities, as well as license and platform technology transfer agreements, as mentioned above. These costs include our direct and research-related overhead expenses, which include salaries and other personnel-related expenses (including stock-based compensation), occupancy-related costs, supplies, and depreciation of facilities and laboratory equipment, as well as external costs, and are expensed as incurred. Costs to acquire technologies that are utilized in research and development and that have no alternative future use are expensed when incurred.

Advertising

Advertising costs are expensed as incurred and included in selling, general and administrative expenses in the consolidated statements of operations.Advertising costs were $0.3 million, $0.5 million and $0.5 million in the years ended December 31, 2020, 2019 and 2018, respectively.

Stock-Based Compensation

We use the Black-Scholes-Merton option pricing model to estimate the fair value of options granted under our equity incentive plans. The Black-Scholes-Merton option pricing model requires the use of assumptions, including the expected term of the award and the expected stock price volatility. The expected term is based on historical exercise behavior on similar awards, giving consideration to the contractual terms, vesting schedules and expectations of future employee behavior. We use historical volatility to estimate expected stock price volatility. The risk-free rate assumption is based on United States Treasury instruments whose terms are consistent with the expected term of the stock options. The expected dividend assumption is based on our history and expectation of dividend payouts.

Restricted Stock Units (“RSUs"), Restricted Stock Awards (“RSAs”) and performance-contingent restricted stock units (“PSUs”) are measured based on the fair market values of the underlying stock on the dates of grant. Performance based options (“PBOs”) are measured using Black-Scholes-Merton option pricing model. The vesting of PBOs and PSUs awarded is conditioned upon the attainment of one or more performance objectives over a specified period and upon continued employment through the applicable vesting date. At the end of the performance period, shares of stock subject to the PBOs and PSUs vest based upon both the level of achievement of performance objectives within the performance period and continued employment through the applicable vesting date.

Stock-based compensation expense is calculated based on awards ultimately expected to vest and is reduced for estimated forfeitures at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates. The estimated annual forfeiture rates for stock options, RSUs, PSUs, PBOs, and RSAs are based on historical forfeiture experience.

The estimated fair value of stock options, RSUs and RSAs are expensed on a straight-line basis over the vesting term of the grant and the estimated fair value of PSUs and PBOs are expensed using an accelerated method over the term of the award once management has determined that it is probable that the performance objective will be achieved. Compensation expense is recorded over the requisite service period based on management's best estimate as to whether it is probable that the shares awarded are expected to vest. Management assesses the probability of the performance milestones being met on a continuous basis.

Cash and Cash Equivalents

We consider all highly liquid investments with maturity dates of three months or less at the date of purchase to be cash equivalents. Cash and cash equivalents consist of cash on deposit with banks and money market funds. The majority of cash and cash equivalents is maintained with major financial institutions in the United States. Deposits with these financial institutions may exceed the amount of insurance provided on such deposits. Cash and cash equivalents totaled $149.1 million and were comprised of cash of $21.5 million and money market funds of $127.6 million at December 31, 2020. Cash and cash equivalents totaled $90.5 million, comprised of cash of $19.3 million and money market funds of $71.2 million at December 31, 2019.

Restricted Cash

In 2016, we began the process of liquidating our Indian subsidiary. The local legal requirements for liquidation required us to maintain our subsidiary's cash balance in an account managed by a legal trustee to satisfy our financial obligations. This balance is recorded as current restricted cash on the consolidated balance sheets of $0.6 million as of December 31, 2020 and $0.7 million as of December 31, 2019.

Pursuant to the terms of a lease agreement for our Redwood City, CA facilities, we obtained a letter of credit collateralized by cash deposit balances of $1.1 million as of December 31, 2020 and 2019. These cash deposit balances are recorded as non-current restricted cash on the consolidated balance sheets. See Note 13, “Commitments and Contingencies” in the Notes to the Consolidated Financial Statements set forth in Item 8 of this Annual Report on Form 10-K.

Fair Value Measurements

Fair value is defined as the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. In determining fair value, we utilize valuation techniques that maximize the use of observable inputs and minimize the use of unobservable inputs to the extent possible and we consider counterparty credit risk in our assessment of fair value. Carrying amounts of financial instruments, including cash equivalents, accounts receivable, accounts payable, and accrued liabilities, approximate their fair values as of the balance sheet dates because of their short maturities.

The fair value hierarchy distinguishes between (1) market participant assumptions developed based on market data obtained from independent sources (observable inputs) and (2) an entity’s own assumptions about market participant assumptions developed based on the best information available in the circumstances (unobservable inputs). The fair value hierarchy consists of three broad levels, giving the highest priority to unadjusted quoted prices in active markets for identical assets or liabilities (Level 1) and the lowest priority to unobservable inputs (Level 3). The three levels of the fair value hierarchy are described below:

- Level 1: Inputs that are unadjusted, quoted prices in active markets for identical assets or liabilities at the measurement date.

- Level 2: Inputs that are either directly or indirectly observable for the asset or liability through correlation with market data at the measurement date and for the duration of the instrument's anticipated life.
- Level 3: Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities and which reflect management's best estimate of what market participants would use in pricing the asset or liability at the measurement date.

See Note 7, "*Fair Value Measurements"* for additional details.

Concentrations of Credit Risk

Financial instruments that potentially subject us to significant concentrations of credit risk consist primarily of cash and cash equivalents, accounts receivable, contract assets, non-marketable securities, and restricted cash. Cash that is not required for immediate operating needs is invested principally in money market funds. Cash and cash equivalents are invested through banks and other financial institutions in the United States, India, and the Netherlands. Such deposits in those countries may be in excess of insured limits.

Financial Assets and Allowances

We currently sell enzymes primarily to pharmaceutical and fine chemicals companies throughout the world by the extension of trade credit terms based on an assessment of each customer's financial condition. Trade credit terms are generally offered without collateral and may include an insignificant discount for prompt payment for specific customers. To manage our credit exposure, we perform ongoing evaluations of our customers' financial conditions. In addition, accounts receivable include amounts owed to us under our collaborative research and development agreements. We recognize accounts receivable at invoiced amounts and we maintain a valuation allowance as follows:

Allowance for credit losses from January 1, 2020

On and subsequent to January 1, 2020, our financial results reflect an impairment model (known as the "current expected credit loss model" or "CECL") based on estimates and forecasts of future conditions requiring recognition of a lifetime of expected credit losses at inception on our financing receivables measured at amortized costs which is comprised of accounts receivable, contract assets, and unbilled receivables. We have determined that our financing receivables share similar risk characteristics including: (i) customer origination in the pharmaceutical and fine chemicals industry, (ii) similar historical credit loss pattern of customers (iii) no meaningful trade receivable differences in terms, (iv) similar historical credit loss experience and (v) our belief that the composition of certain assets are comparable to our historical portfolio used to develop loss history. As a result, we measured the allowance for credit loss ("ACL") on a collective basis. Our ACL methodology considers how long the asset has been past due, the financial condition of the customers, which includes ongoing quarterly evaluations and assessments of changes in customer credit ratings, and other market data that we believe are relevant to the collectability of the assets. Nearly all financing receivables are due from customers that are highly rated by major rating agencies and have a long history of no credit loss. We derive our ACL by establishing an impairment rate attributable to assets not yet identified as impaired.

We derive our ACL by initially relying on our historical financing receivable loss rate which contemplates the full contractual life of the assets sharing similar risk characteristics, adjusted to reflect (i) the extent to which we have determined current conditions differ from the conditions that existed for the period over which historical loss information was evaluated and (ii) by taking into consideration the changes in certain macroeconomic historical and forecasted information. We apply the ACL to past due financing receivables and record charges to the ACL as a provision to credit loss expense in the Statement of Operations. Financing receivables we identify as uncollectible are also charged against the ACL. We adjust the impairment rate to reflect the extent to which we have determined current conditions differ from the conditions that existed for the period over which historical loss information was evaluated. Adjustments to historical loss information may be qualitative or quantitative in nature and reflect changes related to relevant data.

In the year ended December 31, 2020, inputs to our CECL forecast incorporated forward-looking adjustments associated with the COVID-19 pandemic which we believe are appropriate to incorporate due to the uncertainty of the economic impact on cash flows from our financial assets.

Allowance for credit losses before January 1, 2020

Prior to January 1, 2020, the allowances for doubtful accounts reflected our best estimates of probable losses inherent in our accounts receivable and contract assets balances. The allowance determination was based on known troubled accounts, historical experience, and other currently available evidence. Uncollectible accounts receivable were written off against the allowance for doubtful accounts when all efforts to collect them have been exhausted. Recoveries were recognized when they were received.

Accounts Receivable

Trade credit terms are generally offered without collateral and may include an insignificant discount for prompt payment for specific customers. To manage our credit exposure, we perform ongoing evaluations of our customers' financial conditions. In addition, accounts receivable include amounts owed to us under our collaborative research and development agreements and we recognize accounts receivables at invoiced amounts.

Unbilled Receivable

The timing of revenue recognition may differ from the timing of invoicing to our customers. When we satisfy (or partially satisfy) a performance obligation, prior to being able to invoice the customer, we recognize an unbilled receivable when the right to consideration is unconditional. As of December 31, 2020 and 2019, unbilled receivables of $10.9 million and $10.1 million, respectively, were included in our consolidated balance sheets.

Inventories

Inventories are stated at the lower of cost or net realizable value. Cost is determined using a weighted-average approach, assuming full absorption of direct and indirect manufacturing costs, or based on cost of purchasing from our vendors. If inventory costs exceed expected net realizable value due to obsolescence or lack of demand, valuation adjustments are recorded for the difference between the cost and the expected net realizable value.

Concentrations of Supply Risk

We rely on a limited number of suppliers for our products. We believe that other vendors would be able to provide similar products; however, the qualification of such vendors may require substantial start-up time. In order to mitigate any adverse impacts from a disruption of supply, we attempt to maintain an adequate supply of critical single-sourced materials. For certain materials, our vendors maintain a supply for us. We outsource the large scale manufacturing of our products to contract manufacturers with facilities in Austria and Italy.

Property and Equipment

Property, equipment and leasehold improvements are stated at cost less accumulated depreciation and amortization and depreciated using the straight-line method over their estimated useful lives as follows:

Asset classification	Estimated useful life
Laboratory equipment	5 years
Computer equipment and software	3 to 5 years
Office equipment and furniture	5 years
Leasehold improvements	Lesser of useful life or lease term

Property and equipment classified as construction in process includes equipment that has been received but not yet placed in service. Normal repairs and maintenance costs are expensed as incurred.

Impairment of Long-Lived Assets

We have not identified property and equipment by segment since these assets are shared or commingled. We evaluate the carrying values of long-lived assets, which include property and equipment and right-of-use assets, whenever events, changes in business circumstances or our planned use of long-lived assets indicate that their carrying amounts may not be fully recoverable or that their useful lives are no longer appropriate. If these facts and circumstances exist, we assess for recovery by comparing the carrying values of long-lived assets with their future net undiscounted cash flows. If the comparison indicates that impairment exists, long-lived assets are written down to their respective fair values based on discounted cash flows. Significant management judgment is required in the forecast of future operating results that are used in the preparation of unexpected undiscounted cash flows.

As of December 31, 2020 and 2019, there were no events or changes in circumstances which indicated that the carrying amount of our Asset Group might not be recoverable. No impairment charges for long-lived assets were recorded during the years ended December 31, 2020, 2019 and 2018.

Investment in Non-Marketable Securities

Investment in Non-Marketable Equity Securities

Our non-marketable equity securities are accounted for under the measurement alternative. Under the measurement alternative, the carrying value of our non-marketable equity investments is adjusted to fair value for observable transactions for identical or similar investments of the same issuer or impairment. Adjustments are determined primarily based on a market approach as of the transaction date and are recorded as a component of other income (expense), net. We measure investments in non-marketable equity securities without a readily determinable fair value using a measurement alternative that measures these securities at the cost method minus impairment, if any, plus or minus changes resulting from observable price changes on a non-recurring basis. Gains and losses on these securities are recognized in other income and expenses.

Investment in Non-Marketable Debt Securities

We measure available-for-sale investments in non-marketable debt at fair value. Unrealized gains and losses on these securities are recognized in other comprehensive income until realized. Non-marketable debt securities are classified as available-for-sale securities.

We classify non-marketable debt securities as Level 3 in the fair value hierarchy because we estimate the fair value based on a qualitative analysis using the most recent observable transaction price and other significant unobservable inputs including volatility, rights, and obligations of the securities we hold. Significant changes to the unobservable inputs may result in a significantly higher or lower fair value estimate. We may value these securities based on significant recent arms-length transactions with sophisticated non-strategic unrelated new investors, providing the terms of these transactions are substantially similar to the terms between the company and us. The impact of the difference in transaction terms on the market value of the investment may be difficult or impossible to quantify. See Note 7, "*Fair Value Measurements"* for additional details.

We evaluate both equity and debt securities for impairment when circumstances indicate that we may not be able to recover the carrying value. We may impair these securities and establish an allowance for a credit loss when we determine that there has been an "other-than-temporary" decline in estimated fair value of the debt or equity security compared to its carrying value. We calculate the estimated fair value of these securities using information from the investee, which may include:

- Audited and unaudited financial statements;
- Projected technological developments of the company;
- Projected ability of the company to service its debt obligations;
- If a deemed liquidation event were to occur;
- Current fundraising transactions;
- Current ability of the company to raise additional financing if needed;
- Changes in the economic environment which may have a material impact on the operating results of the company;
- Contractual rights, obligations or restrictions associated with the investment; and
- Other factors deemed relevant by our management to assess valuation.
- The valuation may be reduced if the company's potential has deteriorated significantly. If the factors that led to a reduction in valuation are overcome, the valuation may be readjusted.

Goodwill

Goodwill represents the excess of the consideration transferred over the fair value of net assets of businesses acquired and is assigned to reporting units. We test goodwill for impairment considering amongst other things, whether there have been sustained declines in our share price. If we conclude it is more likely than not that the fair value of a reporting unit is less than its carrying amount, a quantitative fair value test is performed. We manage our business as two reporting units and we test goodwill for impairment at the reporting unit level. We allocated goodwill to the two reporting units using a relative fair value allocation methodology that primarily relied on our estimates of revenue and future earnings for each reporting unit. Using the relative fair value allocation methodology, we have determined that approximately $2.4 million, or 76%, of the goodwill allocated to the Performance Enzymes segment and $0.8 million, or 24%, is assigned to the Novel Biotherapeutics segment. We test goodwill for impairment for each reporting unit on an annual basis on the last day of the fourth fiscal quarter and, when

specific circumstances dictate, between annual tests by first assessing qualitative factors to determine whether it is more likely than not that the fair value of a reporting unit is less than its carrying amount. During 2020, 2019 and 2018, we did not record impairment charges related to goodwill. We test for goodwill impairment as follows:

Goodwill impairment testing from January 1, 2020

We test for impairment annually on a reporting unit basis, on the last day of the fourth fiscal quarter, and between annual tests if events and circumstances indicate it is more likely than not that the fair value of a reporting unit is less than its carrying amount. The annual impairment test is completed using either: a qualitative "Step 0" assessment based on reviewing relevant events and circumstances; or a quantitative "Step 1" assessment, which determines the fair value of the reporting unit. To the extent the carrying amount of a reporting unit is less than its estimated fair value, an impairment charge is recorded. Using the relative fair value allocation methodology for assets and liabilities used in both of our reporting units, we compare the allocated carrying amount of each reporting unit's net assets and the assigned goodwill to its fair value. If the fair value of the reporting unit exceeds its carrying amount, goodwill of the reporting unit is considered not impaired. Any excess of the reporting unit's carrying amount of goodwill over its fair value is recognized as an impairment.

Since late 2019, the COVID-19 pandemic has spread worldwide. The COVID-19 pandemic has caused a decline in global and domestic macroeconomic conditions, the general deterioration of the U.S. economy and other economies worldwide, all of which may negatively impact our overall financial performance, driving a reduction in our cash flows. We believe that the impact of the COVID-19 pandemic was a triggering event that gave rise to a qualitative goodwill impairment test in the second quarter ended June 30, 2020. We also conducted a qualitative impairment assessment as of December 31, 2020, which included an evaluation of our cash flow projections to reflect the current economic environment, including the uncertainty surrounding the nature, timing, and extent of the impact of the pandemic in operating our business. We determined that it was more likely than not that the fair value of each of the reporting units exceeded its respective carrying amount as of December 31, 2020. Therefore, a quantitative impairment test of our goodwill at the reporting unit level was not required to be performed.

Goodwill impairment testing before January 1, 2020

Prior to January 1, 2020, the goodwill impairment test consisted of a two-step process. The first step of the goodwill impairment test, used to identify potential impairment, compared the fair value of each reporting unit to its carrying value. Using the relative fair value allocation methodology for assets and liabilities used in both of our reporting units, we compared the allocated carrying amount of each reporting unit's net assets and the assigned goodwill to its fair value. If the fair value of the reporting unit exceeded its carrying amount, goodwill of the reporting unit was considered not impaired, and the second step of the impairment test was not required. The second step, if required, compared the implied fair value of the reporting unit's goodwill with the carrying amount of that goodwill. Implied fair value was the excess of the fair value of the reporting unit over the fair value of all identified or allocated assets and liabilities. Any excess of the reporting unit's carrying amount goodwill over the respective implied fair value was recognized as an impairment.

Lease Accounting

We determine if an arrangement is a lease at inception. Where an arrangement is a lease we determine if it is an operating lease or a finance lease. At lease commencement, we record a lease liability and ROU asset. Lease liabilities represent the present value of our future lease payments over the expected lease term which includes options to extend or terminate the lease when it is reasonably certain those options will be exercised. The present value of our lease liability is determined using our incremental collateralized borrowing rate at lease inception. ROU assets represent our right to control the use of the leased asset during the lease and are recognized in an amount equal to the lease liability for leases with an initial term greater than 12 months. Over the lease term, we use the effective interest rate method to account for the lease liability as lease payments are made and the ROU asset is amortized to the consolidated statement of operations in a manner that results in straight-line expense recognition. We do not apply lease recognition requirements for short-term leases. Instead, we recognize payments related to these arrangements in the consolidated statement of operations as lease costs on a straight-line basis over the lease term.

Income Taxes

We use the liability method of accounting for income taxes, whereby deferred tax asset or liability account balances are calculated at the balance sheet date using current tax laws and rates in effect for the year in which the differences are expected to affect taxable income. Valuation allowances are provided when necessary to reduce deferred tax assets to the amount that will more likely than not be realized.

We make certain estimates and judgments in determining income tax expense for financial statement purposes. These estimates and judgments occur in the calculation of tax credits, benefits and deductions and in the calculation of certain tax assets and liabilities, which arise from differences in the timing of recognition of revenues and expenses for tax and financial statement

purposes. Significant changes to these estimates may result in an increase or decrease to our tax provision in a subsequent period.

In assessing the realizability of deferred tax assets, we consider whether it is more likely than not that some portion or all of the deferred tax assets will be realized on a jurisdiction by jurisdiction basis. The ultimate realization of deferred tax assets is dependent upon the generation of taxable income in the future. We have recorded a valuation allowance against these deferred tax assets in jurisdictions where ultimate realization of deferred tax assets is more likely than not to occur. As of December 31, 2020, we maintain a full valuation allowance in all jurisdictions against the net deferred tax assets as we believe that it is more likely than not that the majority of deferred tax assets will not be realized.

We make estimates and judgments about our future taxable income that are based on assumptions that are consistent with our plans and estimates. Should the actual amounts differ from our estimates, the amount of our valuation allowance may be materially impacted. Any adjustment to the deferred tax asset valuation allowance would be recorded in the statements of operations for the periods in which the adjustment is determined to be required.

We account for uncertainty in income taxes as required by the provisions of ASU 2009-06,*Income Taxes (Topic 740) Implementation Guidance on Accounting for Uncertainty in Income Taxes and Disclosure Amendments for Nonpublic Entities*, which clarifies the accounting for uncertainty in income taxes recognized in an enterprise's financial statements. The first step is to evaluate the tax position for recognition by determining if the weight of available evidence indicates that it is more likely than not that the position will be sustained on audit, including resolution of related appeals or litigation processes, if any. The second step is to estimate and measure the tax benefit as the largest amount that is more than 50% likely of being realized upon ultimate settlement. It is inherently difficult and subjective to estimate such amounts, as this requires us to determine the probability of various possible outcomes. We consider many factors when evaluating and estimating our tax positions and tax benefits, which may require periodic adjustments and may not accurately anticipate actual outcomes.

The Tax Reform Act of 1986 and similar state provisions limit the use of net operating loss ("NOL") carryforwards in certain situations where equity transactions result in a change of ownership as defined by Internal Revenue Code Section 382. In the event we should experience such a change of ownership, utilization of our federal and state NOL carryforwards could be limited.

We recognized income tax provision of $0.3 million, income tax provision of $17 thousand and income tax benefit of $37 thousand for the years ended December 31, 2020, 2019 and 2018, respectively. The provision for income taxes for 2020 was primarily due to foreign withholding taxes on certain sales to a non-U.S. customer. The provision for income taxes in 2019 was primarily due to the accrual of interest and penalties on historic uncertain tax positions. The benefit from income taxes in 2018 was primarily related to a net loss from our foreign operations and a reduction in the deferred tax liability for accrued future withholding taxes on dividends. We continue to maintain a full valuation allowance against our net deferred tax assets as we believe that it is more likely than not that the majority of our deferred tax assets will not be realized.

Changes to Tax Law

On March 27, 2020, the Coronavirus Aid, Relief, and Economic Security Act ("CARES Act"), P.L. 116-136, was passed into law, amending portions of certain relevant US tax laws. The CARES Act included a number of federal income tax law changes, including, but not limited to: (i) permitting net operating loss carrybacks to offset 100% of taxable income for taxable years beginning before 2021, (ii) accelerating alternative minimum tax credit refunds, (iii) temporarily increasing the allowable business interest deduction from 30% to 50% of adjusted taxable income, and (iv) providing a technical correction for depreciation related to qualified improvement property. The CARES Act had no impact on our consolidated financial statements.

Beginning in 2018, the global intangible low-taxed income ("GILTI") provisions in the Tax Act required us to include, in our U.S. income tax return, foreign subsidiary earnings in excess of an allowable return on the foreign subsidiary's tangible assets. Per guidance issued by the FASB, companies can either account for deferred taxes related to GILTI or treat tax arising from GILTI as a period cost. Both are acceptable methods subject to an accounting policy election. At December 31, 2018, we finalized our policy and elected to use the period cost method for GILTI. In 2020, we did not incur any GILTI inclusion as our foreign subsidiaries generated losses. Due to losses incurred in the U.S. we will not be eligible for an Internal Revenue Code Section 250 deduction for foreign derived intangible income.

The BEAT provisions in the Tax Act eliminated the deduction of certain base-erosion payments made to related foreign corporations and imposed a minimum base erosion anti-abuse tax if greater than regular tax. In 2020, our company was not subject to BEAT as it did not meet the requirements to be subject to BEAT.

Accounting Pronouncements

Recently adopted accounting pronouncements

In June 2016, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") 2016-13,*Financial Instruments - Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments*, which amends the FASB's guidance on the impairment of financial instruments. The standard adds a new impairment model, known as CECL, which replaces the probable loss model. The CECL impairment model is based on estimates and forecasts of future conditions which requires recognition of a lifetime of expected credit losses at inception on financial assets measured at amortized costs. Our financial assets consist of non-marketable debt and equity securities and financing receivable assets measured at amortized cost, comprised of accounts receivable, contract assets, and unbilled receivables . We adopted the new standard in the first quarter of 2020 using a modified retrospective approach requiring a cumulative-effect adjustment to the opening accumulated deficit as of the date of adoption. The ASU establishes a new valuation account "allowance for credit losses" replacing the "allowance for doubtful accounts" in the consolidated balance sheets, which is used to adjust the amortized cost basis of assets in presentation of the net amount expected to be collected. The adoption required certain additional disclosures but had no other impact on our consolidated financial statements.

In January 2017, the FASB issued ASU No. 2017-04,*Intangibles - Goodwill and Other (Topic 350): Simplifying the Test for Goodwill Impairment.*The amendment eliminates Step 2 from the goodwill impairment test. The annual, or interim, goodwill impairment test is performed by comparing the fair value of a reporting unit to its carrying amount. An impairment charge should be recognized for the amount by which the carrying amount exceeds the reporting unit's fair value; however, the loss recognized should not exceed the total amount of goodwill allocated to that reporting unit. In addition, income tax effects from any tax-deductible goodwill on the carrying amount of the reporting unit should be considered when measuring the goodwill impairment loss, if applicable. The ASU eliminates the requirements for any reporting unit with a zero or negative carrying amount to perform a qualitative assessment, and if it fails that qualitative test, to perform Step 2 of the goodwill impairment test. An entity still has the option to perform the qualitative assessment for a reporting unit to determine if the quantitative impairment test is necessary. We adopted the ASU in the first quarter of 2020 using a prospective approach. The adoption required certain additional disclosures but had no impact on our consolidated financial statements.

In August 2018, the FASB issued ASU 2018-13,*Fair Value Measurement (Topic 820): Disclosure Framework—Changes to the Disclosure Requirements for Fair Value Measurement.* The primary focus of the standard is to improve the effectiveness of the disclosure requirements for fair value measurements. The changes affect all companies that are required to include fair value measurement disclosures. The standard requires the use of the prospective method of transition for disclosures related to changes in unrealized gains and losses, the range and weighted average of significant unobservable inputs used to develop fair value measurements categorized within Level 3 of the fair value hierarchy, and narrative description of measurement uncertainty. All other amendments in the standard are required to be adopted retrospectively. We adopted the ASU in the first quarter of 2020 and the adoption had no impact on our consolidated financial statements nor on our related disclosures.

In November 2018, the FASB issued ASU 2018-18,*Collaborative Arrangements (Topic 808): Clarifying the Interaction Between Topic 808 and Topic 606.* ASU 2018-18 provides guidance on how to assess whether certain transactions between collaborative arrangement participants should be accounted for within the revenue recognition standard. The standard also provides more comparability in the presentation of revenue for certain transactions between collaborative arrangement participants. The ASU is to be applied retrospectively to the date of the initial application of Topic 606 which also requires recognition of the cumulative effect of applying the amendments as an adjustment to the opening balance of retained earnings of the later or the earliest annual period presented and the annual period inclusive of the initial application of Topic 606. We adopted the ASU in the first quarter of 2020 and the adoption had no impact on our consolidated financial statements nor on our related disclosures.

Recently issued accounting pronouncements not yet adopted

From time to time, new accounting pronouncements are issued by the FASB or other standards setting bodies that are adopted by us as of the specified effective date. Unless otherwise discussed, we believe that the impact of recently issued standards that are not yet effective will not have a material impact on our consolidated financial statements upon adoption.

In December 2019, the FASB issued ASU 2019-12,*Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes which is intended to simplify various aspects related to accounting for income taxes*. The standard is effective for fiscal years, and interim periods within those years, beginning after December 15, 2020, with early adoption permitted. The standard will be adopted upon the effective date for us beginning January 1, 2021 on a retrospective basis. We believe that the adoption of ASU 2019-12 will have minimal impact on our consolidated financial Statements and related disclosures.

In March 2020, the FASB issued ASU 2020-04, Reference Rate Reform (Topic 848) *Facilitation of the Effects of Reference Rate Reform on Financial Reporting* The standard provides optional expedients and exceptions for applying GAAP to contracts, hedging relationships, and other transactions in which the reference LIBOR or another reference rate are expected to be discontinued as a result of the Reference Rate Reform. The standard is effective for all entities. The standard may be adopted as of any date from the beginning of an interim period that includes or is subsequent to March 12, 2020 through December 31, 2022, on a prospective basis. We will evaluate transactions or contract modifications occurring as a result of reference rate reform and determine whether to elect the optional expedients for contract modification; however, we believe that the adoption of ASU 2020-04 will have minimal impact on our consolidated financial statements and related disclosures.

In August 2020, FASB issued ASU No 2020-06*Debt—Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging— Contracts in Entity's Own Equity (Subtopic 815-40) No. 2020-06 August 2020 Accounting for Convertible Instruments and Contracts in an Entity's Own Equity*, to reduce the complexity and to simplify the accounting for convertible debt instruments and convertible preferred stock, and the derivatives scope exception for contracts in an entity's own equity. In addition, the guidance on calculating diluted earnings per share has been simplified and made more internally consistent. The standard is effective the for fiscal years beginning after December 15, 2021, and interim periods within those fiscal years, with early adoption permitted for fiscal periods beginning after December 15, 2020. The standard will be adopted by us beginning January 1, 2021. Entities are allowed to adopt the standard using a either a modified retrospective method of transition or a fully retrospective method of transition. We are currently evaluating the effects of the standard on our consolidated financial statements and related disclosures; however, we believe that the adoption of ASU 2020-06 will have minimal impact on our consolidated financial statements and related disclosures.

In October 2020, the FASB issued ASU No. 2020-10,*Codification Improvements*. ASU 2020-10 provides amendments to a wide variety of topics in the FASB's Accounting Standards Codification, which applies to all reporting entities within the scope of the affected accounting guidance. The standard is effective for annual periods beginning after December 15, 2020 with early adoption permitted. The standard will be adopted upon the effective date for us beginning January 1, 2021 on a retrospective basis. We are currently evaluating the effects of the standard on our consolidated financial statements and related disclosures, however we believe that the adoption of ASU 2020-10 will have no impact the our consolidated financial statements and related disclosures.

Note 3. Revenue Recognition

Disaggregation of Revenue

The following table provides information about disaggregated revenue from contracts with customers into the nature of the products and services, and geographic regions, and includes a reconciliation of the disaggregated revenue with reportable segments. The geographic regions that are tracked are the Americas (United States, Canada, and Latin America), EMEA (Europe, Middle East, and Africa), and APAC (Australia, New Zealand, Southeast Asia, and China).

Segment information for fiscal year 2020 is as follows (in thousands):

	Year Ended December 31, 2020		
	Performance Enzymes	**Novel Biotherapeutics**	**Total**
Major products and service:			
Product Revenue	$ 30,220	$ —	$ 30,220
Research and development revenue	17,886	20,950	38,836
Total revenues	$ 48,106	$ 20,950	$ 69,056
Primary geographical markets:			
Americas	$ 11,111	$ 13,241	$ 24,352
EMEA	11,548	7,709	19,257
APAC	25,447	—	25,447
Total revenues	$ 48,106	$ 20,950	$ 69,056

Segment information for fiscal year 2019 is as follows (in thousands):

	Year Ended December 31, 2019		
	Performance Enzymes	Novel Biotherapeutics	Total
Major products and service:			
Product Revenue	$ 29,465	$ —	$ 29,465
Research and development revenue	28,691	10,302	38,993
Total revenues	$ 58,156	$ 10,302	$ 68,458
Primary geographical markets:			
Americas	$ 13,039	$ —	$ 13,039
EMEA	26,831	10,302	37,133
APAC	18,286	—	18,286
Total revenues	$ 58,156	$ 10,302	$ 68,458

Segment information for fiscal year 2018 is as follows (in thousands):

	Year Ended December 31, 2018		
	Performance Enzymes	Novel Biotherapeutics	Total
Major products and service:			
Product Revenue	$ 25,590	$ —	$ 25,590
Research and development revenue	21,483	13,521	35,004
Total revenues	$ 47,073	$ 13,521	$ 60,594
Primary geographical markets:			
Americas	$ 15,332	$ 38	$ 15,370
EMEA	8,878	13,483	22,361
APAC	22,863	—	22,863
Total revenues	$ 47,073	$ 13,521	$ 60,594

Contract Balances

The following table presents balances of contract assets, unbilled receivables, contract costs, and contract liabilities (in thousands):

	December 31, 2020	December 31, 2019
Contract assets	$ 4,526	$ 1,027
Unbilled receivables	$ 10,942	$ 10,099
Contract costs	$ 90	$ —
Contract liabilities: deferred revenue	$ 4,791	$ 2,044

We recognize accounts receivable when we have an unconditional right to recognize revenue and have issued an invoice to the customer. Our payment terms are generally between 30 and 90 days. We recognize unbilled receivables when we have an unconditional right to recognize revenue and have not issued an invoice to our customer. Unbilled receivables, current are transferred to accounts receivable on issuance of an invoice. Unbilled receivables, non-current are transferred to accounts receivable on issuance of an invoice; payment is expected from the customer thereon. Unbilled receivables are classified separately on the consolidated balance sheets as assets. We maintain a valuation allowance on accounts receivables and unbilled receivables.

Contract assets represent our right to recognize revenue for custom products with no alternate use and under binding non-cancellable purchase orders and are largely related to our procurement of product. We recognize contract assets when we have a conditional right to recognize revenue. The delivery pattern of certain of products occurs in advance of the invoicing process, which generates contract assets. In addition, we recognize a contract asset related to milestones not eligible for royalty accounting when we assess it is probable of being achieved and there will be no significant reversal of cumulative revenues. Contract assets are classified separately on the consolidated balance sheets as an asset and transferred to accounts receivable when our rights to payment become unconditional. We maintain a valuation allowance on contract assets.

Contract liabilities, or deferred revenue, represent our obligation to transfer a product or service to the customer, and for which we have received consideration from the customer. We recognize a contract liability when we receive advance customer payments under development agreements for research and development services, upfront license payments, and from upfront customer payments received under product supply agreements. Contract liabilities are classified as a liability on the consolidated balance sheet.

Contract costs relate to incremental costs of obtaining a contract with a customer. Contract costs are amortized along with the associated revenue over the term of the contract.

During the years ended December 31, 2020 and 2019, we had no asset impairment charges related to contract assets.

We recognized the following revenues (in thousands):

	Year Ended December 31,	
Revenue recognized in the period for:	**2020**	**2019**
Amounts included in contract liabilities at the beginning of the period:		
Performance obligations satisfied	$ 57	$ 4,567
Changes in the period:		
Changes in the estimated transaction price allocated to performance obligations satisfied in prior periods	774	1,442
Performance obligations satisfied from new activities in the period - contract revenue	68,225	62,449
Total revenues	$ 69,056	$ 68,458

Performance Obligations

The following table includes estimated revenue expected to be recognized in the future related to performance obligations that are unsatisfied or partially unsatisfied at the end of the reporting periods. The estimated revenue does not include contracts with original durations of one year or less, amounts of variable consideration attributable to royalties, or contract renewals that are unexercised as of December 31, 2020.

The balances in the table below are partially based on judgments involved in estimating future orders from customers subject to the exercise of material rights pursuant to respective contracts (in thousands):

	2021	**2022**	**2023**	**2024 and Thereafter**	**Total**
Product Revenue	$ 67	$ 67	$ 431	$ 1,923	$ 2,488
Research and development revenue	1,757	—	546	—	2,303
Total revenues	$ 1,824	$ 67	$ 977	$ 1,923	$ 4,791

Note 4. Net Loss per Share

Basic net loss per share is computed by dividing the net loss by the weighted-average number of shares of common stock outstanding, less restricted stock awards ("RSAs") subject to forfeiture. Diluted net loss per share is computed by dividing net loss by the weighted-average number of shares of common stock shares outstanding, less RSAs subject to forfeiture, plus all additional common shares that would have been outstanding, assuming dilutive potential common stock shares had been issued for other dilutive securities. For periods presented, diluted and basic net loss per share are identical since potential common stock shares are excluded from the calculation, as their effect was anti-dilutive.

Anti-Dilutive Securities

In periods of net loss, the weighted average number of shares outstanding, prior to the application of the treasury stock method, excludes potentially dilutive securities from the computation of diluted net loss per common share because including such shares would have an anti-dilutive effect.

The following shares were not considered in the computation of diluted net loss per share because their effect was anti-dilutive (in thousands):

	Year Ended December 31,		
	2020	2019	2018
Shares issuable under the Equity Incentive Plan	5,348	4,763	6,339

Note 5. Collaborative Arrangements

GSK Platform Technology Transfer, Collaboration and License Agreement

In July 2014, we entered into a CodeEvolver® protein engineering platform technology transfer collaboration and license agreement (the "GSK CodeEvolver® Agreement") with GSK. Pursuant to the terms of the agreement, we granted GSK a non-exclusive license to use the CodeEvolver® protein engineering platform technology to develop novel enzymes for use in the manufacture of GSK's pharmaceutical and health care products.

We received an upfront fee upon the execution of the agreement in July 2014 and milestone payments in each of the years from 2014 through April 2016. We completed the transfer of the CodeEvolver® protein engineering platform technology to GSK in April 2016 and all revenues relating to the technology transfer have been recognized as of April 2016. We have the potential to receive additional cumulative contingent payments that range from $5.75 million to $38.5 million per project based on GSK's successful application of the licensed technology. We are also eligible to receive royalties, based on net sales of GSK's sales of licensed enzyme products, that are currently not being recognized.

In 2019, we received a $2.0 million milestone payment relating to the advancement of an enzyme developed by GSK using our CodeEvolver® protein engineering platform technology. We recognized research and development revenue of nil, $2.0 million, and nil in the year ended December 31, 2020, 2019, and 2018, respectively.

Merck Platform Technology Transfer and License Agreement

In August 2015, we entered into a CodeEvolver® platform technology transfer collaboration and license agreement (the "Merck CodeEvolver® Agreement") with Merck, Sharp & Dohme ("Merck") which allows Merck to use the CodeEvolver® protein engineering technology platform in the field of human and animal healthcare.

We received an upfront license fee upon execution of the Merck CodeEvolver® Agreement and milestone payments in September 2015 and in September 2016, when we completed the transfer of the engineering platform technology. We recognized research and development revenues of $3.1 million, $4.0 million, and $4.1 million in the years ended December 31, 2020, 2019 and 2018, respectively, for various research projects under our collaborative arrangement.

We have the potential to receive payments of up to a maximum of $15.0 million for each commercial active pharmaceutical ingredient ("API") that is manufactured by Merck using one or more novel enzymes developed by Merck using the CodeEvolver® protein engineering technology platform. The API payments, which are currently not recognized in revenue, are based on the quantity of API developed and manufactured by Merck and will be recognized as usage-based royalties.

In October 2018, we entered into an amendment to the Merck CodeEvolver® Agreement which amended certain licensing provisions and one exhibit. In January 2019, we entered into an amendment to the Merck CodeEvolver® Agreement to install certain CodeEvolver® protein engineering technology upgrades into Merck's platform license installation and maintain those upgrades for a multi-year term expiring in January 2022. The license installation was completed in 2019 and we recognized $0.9 million as license fee revenue accordingly under the amendment. Pursuant to the agreement, Merck has options to future technology enhancements for a specified fee. As of December 31, 2020, Merck has not exercised its option for technology enhancements. We recognized $0.1 million and $0.9 million in research and development revenues under the terms of the amendment in 2020 and 2019, respectively.

Merck Sitagliptin Catalyst Supply Agreement

In February 2012, we entered into a five-year Sitagliptin Catalyst Supply Agreement ("Sitagliptin Catalyst Supply Agreement") with Merck whereby Merck may obtain commercial scale enzyme for use in the manufacture of Januvia®, its product based on the active ingredient sitagliptin. In December 2015, Merck exercised its option under the terms of the Sitagliptin Catalyst Supply Agreement to extend the agreement for an additional five years through February 2022.

Effective as of January 2016, we and Merck amended the Sitagliptin Catalyst Supply Agreement to prospectively provide for variable pricing based on the cumulative volume of sitagliptin catalyst purchased by Merck and to allow Merck to purchase a percentage of its requirements for sitagliptin catalyst from a specified third-party supplier. Merck received a distinct, functional license to manufacture a portion of its demand beginning January 1, 2018, which we recognized as research and development revenue. We recognized no research and development revenues in the years ended December 31, 2020 and 2019 and $1.3 million of research and development revenues in the year ended December 31, 2018.

We have determined that the variable pricing, which provides a discount based on the cumulative volume of sitagliptin catalyst purchased by Merck, provides Merck material rights and we are recognizing product revenues using the alternative method. Under the alternative approach, we estimate the total expected consideration and allocate it proportionately with the expected sales.

The Sitagliptin Catalyst Supply Agreement requires Merck to pay an annual fee for the rights to the sitagliptin technology each year for the term of the Sitagliptin Catalyst Supply Agreement. Amounts of annual license fees are based on contractually agreed prices and are on a declining scale over the term of the contract.

Pursuant to the terms of the Sitagliptin Catalyst Supply Agreement, Merck may purchase supply from us for a fee based on contractually stated prices. We recognized $13.4 million, $15.1 million and $12.3 million in product revenues for the years ended December 31, 2020, 2019 and 2018, respectively. Revenues recognized by us under the Sitagliptin Catalyst Supply Agreement comprised 19%, 22%, and 22% of our total revenues for the years ended December 31, 2020, 2019 and 2018, respectively.

The Sitagliptin Catalyst Supply Agreement will terminate in February 2022 unless extended and we have not received an amendment to extend the agreement.

Enzyme Supply Agreement

In November 2016, we entered into a supply agreement whereby our customer may purchase quantities of one of our proprietary enzymes for use in its commercial manufacture of a product. Pursuant to the supply agreement, we received an upfront payment in December 2016 which was recorded as deferred revenues. Such upfront payment will be recognized over the period of the supply agreement as the customer purchases our proprietary enzyme. We additionally have determined that the volume discounts under the supply agreement provides the customer material rights and we are recognizing revenues using the alternative method. As of December 31, 2020 and 2019, we had deferred revenue balances from the supply agreement of $2.0 million.

Research and Development Agreement

In March 2017, we entered into a multi-year research and development services agreement with Tate & Lyle Ingredients Americas LLC ("Tate & Lyle") to develop enzymes for use in the manufacture of Tate & Lyle's zero-calorie TASTEVA® M Stevia sweetener. Under the agreement, we received an upfront payment of $3.0 million, which was recognized ratably over the maximum term of the services period of 21 months . Beginning January 1, 2018, we are recognizing revenue using a single measure of progress that depicts our performance in transferring the services. During the second quarter of 2018, Tate & Lyle opted to obtain additional development services that we completed by June 30, 2018 and we earned milestone payments upon completion of the services. We recognized nil, $0.1 million and $7.1 million in revenue in the years ended December 31, 2020, 2019 and 2018, respectively, in research and development services under the research and development services agreement.

Commercial Agreement

In April 2019, we entered intoa multi-year commercial agreement with Tate & Lyle under which Tate & Lyle has received an exclusive license to use a suite of Codexis novel performance enzymes in the manufacture of Tate & Lyle's zero-calorie stevia sweetener, TASTEVA® M, and other stevia products. Under the agreement, we will supply Tate & Lyle with its requirements for these enzymes over a multiple year period and receive royalties on stevia products. In November 2020, we amended the commercial agreement based on Tate & Lyle's intent to use a specific Codexis novel performance enzyme in its production of TASTEVA® M Stevia Sweetener and became eligible to receive milestone payments of up to $1.1 million. In the fourth quarter of 2020, we became eligible to receive a milestone payment of $0.4 million, which we subsequently received in the fourth

quarter of 2020. We recognized $0.2 million in revenue in the year ended December 31, 2020. As of December 31, 2020, we had a deferred revenue balance of $0.2 million.

Global Development, Option and License Agreement and Strategic Collaboration Agreement

In October 2017, we entered into a Global Development, Option and License Agreement (the "Nestlé License Agreement") with Société des Produits Nestlé (formerly known as Nestec Ltd.) ("Nestlé Health Science") and, solely for the purpose of the integration and the dispute resolution clauses of the Nestlé License Agreement, Nestlé Health Science S.A., to advance CDX-6114, our enzyme biotherapeutic product candidate for the potential treatment of PKU.

We received an upfront cash payment of $14.0 million in 2017 upon the execution of the Nestlé License Agreement, a $4.0 million milestone payment after dosing the first subjects in a first-in-human Phase 1a dose-escalation trial with CDX-6114, and a $1.0 million milestone payment upon achievement of a milestone relating to formulation of CDX-6114. The $4.0 million milestone payment that was triggered by the initiation of the trial was received in 2018 and the $1.0 million milestone payment that was triggered by the achievement of a formulation relating to CDX-6114 was received in February 2019. The upfront payment and the variable consideration relating to the progress payment of $4.0 million and a milestone payment of $1.0 million were recognized over time as the development work was performed. Revenue was recognized using a single measure of progress that depicted our performance in transferring control of the services, which was based on the ratio of level of effort incurred to date compared to the total estimated level of effort required to complete all performance obligations under the agreement. We recognized $13 thousand, $1.9 million and $9.9 million in research and development revenue in 2020, 2019 and 2018, respectively.

In January 2019, we received notice from the FDA that it had completed its review of our IND for CDX-6114 and concluded that we may proceed with the proposed Phase 1b multiple ascending dose study in healthy volunteers in the United States. In February 2019, Nestlé Health Science exercised its option to obtain an exclusive, worldwide, royalty-bearing, sub-licensable license for the global development and commercialization of CDX-6114 for the management of PKU and paid us $3.0 million which we recognized as research and development revenue in 2019. Upon exercising its option, Nestlé Health Science assumed all responsibilities for future clinical development and commercialization of CDX-6114. Other potential payments from Nestlé Health Science to us under the Nestlé License Agreement include (i) development and approval milestones of up to $85.0 million, (ii) sales-based milestones of up to $250.0 million in the aggregate, which aggregate amount is achievable if net sales exceed $1.0 billion in a single year, and (iii) tiered royalties, at percentages ranging from the middle single digits to low double-digits, of net sales of product.

In October 2017, we entered into the "Nestlé SCA pursuant to which we and Nestlé Health Science are collaborating to leverage the CodeEvolver® protein engineering technology platform to develop novel enzymes for Nestlé Health Science's established Consumer Care and Medical Nutrition business areas. Under the Strategic Collaboration Agreement, we received an upfront payment of $1.2 million in 2017 and an incremental payment of $0.6 million in September 2018 for additional services. The Nestlé SCA has been extended through December 2021.

In January 2020, we entered into a development agreement with Nestlé Health Science pursuant to which we and Nestlé Health Science are collaborating to advance a lead candidate targeting a gastro-intestinal disorder discovered through our Nestlé SCA into pre-clinical and early clinical studies.

Under the Nestlé SCA and the development agreement, we recognized $7.9 million, $5.4 million and $3.6 million in research and development revenue in years ended December 31, 2020, 2019, and 2018, respectively.

Strategic Collaboration Agreement

In April 2018, we entered into the Porton Agreement with Porton to license key elements of our biocatalyst technology for use in Porton's global custom intermediate and API development and manufacturing business. Under the Porton Agreement, we are eligible to receive annual collaboration fees and research and development revenues. We received initial collaboration payments of $0.5 million and $0.5 million within 30 days of the effective date and on the first anniversary of the effective date of the Porton Agreement, respectively. We also received annual collaboration payments of $1.0 million for each on the first and second anniversaries of the effective date of the Porton Agreement, respectively. We are eligible to receive $1.0 million each annual collaboration payment on the third and fourth anniversaries of the effective date of the Porton Agreement, respectively. We completed the technical transfer in the fourth quarter of 2018 and recognized $2.8 million in research and development revenue. We recognized revenue related to the functional license provided to Porton at a point in time when control of the license was transferred to the customer. We recognized research and development revenue related to the Porton Agreement of $1.1 million, nil and $2.8 million in the years ended December 31, 2020, 2019 and 2018, respectively. As of December 31, 2020 and 2019, we had deferred revenue balances of $0.1 million and nil, respectively.

Platform Technology Transfer and License Agreement

In May 2019, we entered into a Platform Technology Transfer and License Agreement (the "Novartis CodeEvolver® Agreement") with Novartis. The Agreement allows Novartis to use our proprietary CodeEvolver® protein engineering platform technology in the field of human healthcare. Under the Novartis CodeEvolver® Agreement, we are transferring our proprietary CodeEvolver® protein engineering platform technology to Novartis over approximately 25 months, starting with the date on which we commenced the technology transfer (the "Technology Transfer Period"). As a part of this technology transfer, the Company provided to Novartis our proprietary enzymes, proprietary protein engineering protocols and methods, and proprietary software algorithms. In addition, teams of the Company and Novartis scientists participated in technology training sessions and collaborative research projects at our laboratories in Redwood City, California and at a designated Novartis laboratory in Basel, Switzerland. Upon completion of technology transfer, Novartis will have the CodeEvolver® protein engineering platform technology installed at its designated laboratory.

Pursuant to the agreement, we received an upfront payment of $5.0 million shortly after the effective date of the Novartis CodeEvolver® Agreement. In the second quarter of 2020 we completed the second technology milestone transfer under the agreement and became eligible to receive a milestone payment of $4.0 million, which we subsequently received in July 2020. We have also recognized $3.4 million for partial completion of the third technology milestone and we expect to receive payment in the first quarter of 2021. Additionally, we are eligible to receive an additional $1.6 million upon satisfactory completion of the third technology transfer milestone. In consideration for the continued disclosure and license of improvements to our technology and materials during a multi-year period that begins on the conclusion of the Technology Transfer Period ("Improvements Term"), Novartis will pay Codexis annual payments which amount to an additional $8.0 million. The Company also has the potential to receive quantity-dependent, usage payments for each API that is manufactured by Novartis using one or more enzymes that have been developed or are in development using the CodeEvolver® protein engineering platform technology during the period that begins on the conclusion of the Technology Transfer Period and ends on the expiration date of the last to expire licensed patent. These product-related usage payments, if any, will be paid by Novartis to the Company for each quarter that Novartis manufactures API using a CodeEvolver®-developed enzyme. The usage payments will be based on the total volume of API produced using the CodeEvolver®-developed enzyme. These usage payments can begin in the clinical stage and will extend throughout the commercial life of each API. Revenue for the combined initial license and technology transfer performance obligation, which is expected to occur over twenty-three months, is being recognized using a single measure of progress that depicts our performance in transferring control of the services, which is based on the ratio of level of effort incurred to date compared to the total estimated level of effort required to complete the performance obligation relating to the combined initial license and technology transfer. Revenue allocated to future improvements will be recognized during the Improvement Term.

We recognized $6.2 million and $11.3 million in research and development revenue in the year ended December 31, 2020 and 2019, respectively, from the Novartis CodeEvolver® Agreement.

License Agreement

In December 2019, we entered a license agreement with Roche Sequencing Solutions, Inc. ("Roche") to provide Roche with our EvoT4 DNA™ ligase high-performance molecular diagnostic enzyme. The royalty bearing license grants Roche worldwide rights to include the EvoT4 DNA™ ligase in its nucleic acid sequencing products and workflows. Under the license agreement, we received an initial collaboration fee payment of $0.8 million within 45 days of the effective date of the agreement, and we received an additional $0.9 million milestone after the completion of technology transfer in October 2020. The agreement also contemplates milestone payments to Codexis upon the achievement of various development and commercialization events and royalty payments from commercial sales of the enzyme. We recognized research and development fees of $1.1 million and nil in the years ended December 31, 2020 and 2019.

Strategic Collaboration and License Agreement

In March 2020, we entered into a Strategic Collaboration and License Agreement (the "Takeda Agreement") with Shire Human Genetic Therapies, Inc., a wholly-owned subsidiary of Takeda Pharmaceutical Co. Ltd. ("Takeda") under which we are collaborating to research and develop protein sequences for use in gene therapy products for certain diseases (each, a "Field") in accordance with each applicable program plan (each, a "Program Plan").

In March 2020, we received an upfront nonrefundable cash payment of $8.5 million and we initiated activities under three Program Plans for Fabry Disease, Pompe Disease, and an undisclosed blood factor deficiency respectively (the "Initial Programs"). We are primarily responsible for the research and development of protein sequences under the Program Plans (the "Protein Sequences") and we are eligible to earn $15.4 million of research and development fees and pre-clinical milestone payments for the Initial Programs. Takeda has the right, but not the obligation, to develop, manufacture and commercialize gene

therapy products that include nucleic acid sequences that encode the Protein Sequences (“Products”) at their expense. Takeda has the right to a certain number of additional disease indications (“Reserved Target Indications”) for a limited period in which Takeda may initiate a Program Plan for one or more Reserved Target Indications (“Additional/Option Program,” with Initial Programs, the “Programs”), provided, (a) if Takeda elects to initiate an Additional/Option Program while the parties are collaborating on three other Programs at the time of such election, or (b) if Takeda elects to initiate an Additional/Option Program using the last remaining Reserved Target Indication, then Takeda must pay us an option exercise fee to initiate such Additional/Option Program. We will own all rights to the Protein Sequences and corresponding nucleic acid sequences and related intellectual property rights and Takeda will own all rights to Products and related intellectual property rights.

We granted to Takeda an exclusive, worldwide, royalty-bearing, sublicensable license to use the Protein Sequences and their corresponding nucleic acid sequences to develop, manufacture and commercialize the applicable Products in the applicable Field. We also granted to Takeda a limited non-exclusive, worldwide, sublicensable license (a) to research the Protein Sequences within or outside the applicable Fields and (b) to research the Products outside of the applicable Fields, which such rights exclude Takeda's right to perform any Investigational New Drug-enabling activities. The licenses to research the Protein Sequences expire after a pre-determined period of time.

The term of the Takeda Agreement begins on the Effective Date and continues on a Product-by-Product and country-by-country basis, until the expiration of Takeda’s obligation to pay royalties to the Company with respect to that Product in that country. The Takeda Agreement expires in its entirety upon the expiration of Takeda’s obligation to pay royalties to the Company with respect to the Products in all countries worldwide. Subject to the terms of the Takeda Agreement, and after the first anniversary of the Effective Date with respect to the Initial Programs or after the first anniversary of confirmation of the applicable Program Plan by the parties with respect to the Additional/Option Programs, Takeda may terminate a Program upon specified prior written notice to the Company. Subject to the terms of the Takeda Agreement, Takeda may terminate the Takeda Agreement, at will, on a Product-by-Product basis upon specified prior written notice to the Company and the Takeda Agreement in its entirety upon specified prior written notice to the Company. Subject to the terms of the Takeda Agreement, Takeda may terminate the Takeda Agreement on a Product-by-Product basis for safety reasons upon specified prior written notice to the Company. Either party may terminate the Takeda Agreement for an uncured material breach by the other party, or the other party’s insolvency or bankruptcy.

We are eligible to receive certain development and commercialization milestone payments up to $100.0 million per target gene, the modulation of which would lead to the treatment of the disease indications by the applicable Product. We are also eligible to receive tiered royalties based on net sales of Products at percentages ranging from the middle-single digits to low single-digits. We recognized research and development revenue related to the Takeda Agreement of $13.2 million in the year ended December 31, 2020. As of December 31, 2020, we had a deferred revenue balance of $1.5 million from Takeda.

Master Collaboration and Research Agreement and Stock Purchase Agreement

In June 2020, we entered into a Stock Purchase Agreement with Molecular Assemblies, Inc. (“MAI”) pursuant to which we purchased1,587,050 shares of MAI's Series A preferred stock for $1.0 million. In connection with the transaction, John Nicols, our President and Chief Operating Officer, also joined MAI’s board of directors. Concurrently with our initial equity investment, we entered into a Master Collaboration and Research Agreement with MAI (the “MAI Agreement”), pursuant to which we are performing services utilizing our CodeEvolver® protein engineering platform technology to improve DNA polymerase enzymes in exchange for compensation in the form of additional shares of MAI's Series A preferred stock. Based on these services, the Company is eligible to earn additional shares of MAI's Series A preferred stock. MAI will combine its advanced chemistries with our enzymes to drive the process to commercialization. We are eligible to earn such non-monetary payments over ten to thirteen months, and any such shares would be issued thirty days in arrears after each calendar quarter-end. We are also eligible to receive amounts for bonuses, targets and milestones on achievement of timeline and project goals specified in the statement of work ("SOW"). Payments for bonuses, targets and milestones on achievement of timeline and project goals are to be issued thirty days after the Company provides notification of completion. Under the MAI Agreement, we will have the right to use and sell the engineered enzymes to third parties for any purpose other than for the synthesis of native DNA. Under the MAI Agreement, we would make a $0.5 million payment to MAI upon our achievement of a milestone of $5.0 million in aggregate commercial sales to third parties of the engineered enzymes or any product incorporating or derived from the engineered enzymes for any purpose other than the synthesis of native DNA. The MAI Agreement contemplates that we and MAI will enter into a Commercialization and Enzyme Supply Agreement (the “CESA”) within six months following the completion of certain timelines specified in the SOW. In addition, we and MAI have agreed pursuant to the MAI Agreement to certain terms to be contained within the CESA in the event that the CESA becomes executed in the future. Those include: (a) that MAI would receive an exclusive license to use the DNA polymerase enzymes engineering by us under the MAI Agreement in the synthesis of native DNA and a non-exclusive license to use these enzymes for research and development on the synthesis of non-native DNA, and (b) we would become the exclusive manufacturer of these enzymes for MAI, its affiliates and licensees.

We received 714,171 shares of MAI's Series A preferred stock from research and development services in the year ended December 31, 2020, and recognized $0.9 million from these services with MAI in the year ended December 31, 2020. At December 31, 2020, we had $0.5 million in contract asset due from MAI for services rendered. Payment for the services rendered was subsequently received in form of additional MAI Series A preferred stock in the first quarter of 2021.

Note 6. Investments in Non-Marketable Securities

Non-Marketable Debt Securities

We classify non-marketable debt securities, which are accounted for as available-for-sale, within Level 3 in the fair value hierarchy because we estimate the fair value based on a qualitative analysis using the most recent observable transaction price and other significant unobservable inputs including volatility, rights, and obligations of the securities we hold.

We determine gains or losses on the sale or extinguishment of non-marketable debt securities using a specific identification method. Unrealized gains and losses on non-marketable debt securities are recorded as a component of other comprehensive loss until realized. Realized gains or losses are recorded as a component of other expenses, net. We recognized no unrealized or realized gains or losses during the year ended December 31, 2020. As of December 31, 2020 and 2019, the fair value of non-marketable debt securities was $1.0 million and nil, respectively.

As of December 31, 2020, the adjusted cost, carrying value and fair value of non-marketable debt securities is the following (in thousands):

	December 31, 2020	
By contractual maturity:	Adjusted Cost and Carrying value	Fair Value
Non-marketable debt securities due in 1 year or less	$ 1,000	$ 1,000

There were no investments in non-marketable debt securities at December 31, 2019.

Non-Marketable Equity Securities

Non-marketable equity securities are investments in privately held companies without readily determinable market values. We measure investments in non-marketable equity securities without a readily determinable fair value using a measurement alternative that measures these securities at the cost method minus impairment, if any, plus or minus changes resulting from observable price changes on a non-recurring basis. The fair value of non-marketable equity securities that have been remeasured due to impairment are classified within Level 3. We adjust the carrying value of non-marketable equity securities which have been remeasured during the period and recognize resulting gains or losses as a component of other expenses, net. We recognized no unrealized or realized gain or losses during the year ended December 31, 2020.

At December 31, 2020 and 2019, the carrying value of non-marketable equity securities is the following (in thousands):

	December 31,	
	2020	2019
Non-marketable equity securities	$ 1,450	$ —

Note 7. Fair Value Measurements

The following tables present the financial instruments that were measured at fair value on a recurring basis at December 31, 2020 and 2019 by level within the fair value hierarchy (in thousands):

	December 31, 2020			
	Level 1	Level 2	Level 3	Total
Money market funds	$ 127,567	$ —	$ —	$ 127,567
Non-marketable debt securities	$ —	$ —	$ 1,000	$ 1,000
Total	$ 127,567	$ —	$ 1,000	$ 128,567

	December 31, 2019			
	Level 1	Level 2	Level 3	Total
Money market funds	$ 71,248	$ —	$ —	$ 71,248

There were no investments in non-marketable debt and equity securities at December 31, 2019.

The fair value of non-marketable securities remeasured due to impairment would be classified within level 3.

During the year ended December 31, 2020, we didnot recognize any significant other-than-temporary impairment losses. After the adoption of ASU 2016-13, we didnot recognize any significant credit losses.

Note 8. Balance Sheets Details

Cash Equivalents

Cash equivalents at December 31, 2020 and 2019 consisted of the following (in thousands):

	December 31, 2020		December 31, 2019	
	Adjusted Cost	Estimated Fair Value	Adjusted Cost	Estimated Fair Value
Money market funds [1] [2]	$ 127,567	$ 127,567	$ 71,248	$ 71,248

[1] Money market funds are classified in cash and cash equivalents on our consolidated balance sheets.
[2] Average Contractual Maturities (in days) is not applicable.

As of December 31, 2020, the total cash and cash equivalents balance of $149.1 million was comprised of money market funds of $127.6 million and cash of $21.5 million held with major financial institutions worldwide. As of December 31, 2019, the total cash and cash equivalents balance of $90.5 million was comprised of money market funds of $71.2 million and cash of $19.3 million held with major financial institutions worldwide.

Inventories

Inventories consisted of the following (in thousands):

	December 31,	
	2020	2019
Raw materials	$ 77	$ 7
Work in process	82	26
Finished goods	805	338
Inventories	$ 964	$ 371

Property and Equipment, net

Property and equipment, net consisted of the following (in thousands):

	December 31,	
	2020	2019
Laboratory equipment [1]	$ 25,468	$ 23,561
Leasehold improvements	10,785	10,804
Computer equipment and software	3,192	3,016
Office equipment and furniture	1,246	1,461
Construction in progress [2]	2,357	691
Property and equipment	43,048	39,533
Less: accumulated depreciation and amortization	(33,373)	(33,251)
Property and equipment, net	$ 9,675	$ 6,282

[1] Fully depreciated property and equipment with a cost of $1.8 million and $1.0 million were retired during the years ended December 31, 2020 and 2019, respectively.
[2] Construction in progress includes equipment received but not yet placed into service pending installation.

Depreciation expense included in the consolidated statements of operations as follows (in thousands):

	Year Ended December 31,		
	2020	2019	2018
Depreciation expense	$ 1,950	$ 1,570	$ 1,147

Goodwill

Goodwill had a carrying value of approximately of $3.2 million as of December 31, 2020 and 2019.

Other Accrued Liabilities

Other accrued liabilities consisted of the following (in thousands):

	December 31,	
	2020	2019
Accrued purchases	$ 7,170	$ 4,386
Accrued professional and outside service fees	2,589	1,802
Other	513	352
Total	$ 10,272	$ 6,540

Note 9. Stock-based Compensation

Equity Incentive Plans

In 2019, our board of directors (the "Board") and stockholders approved the 2019 Incentive Award Plan (the "2019 Plan"). The 2019 Plan superseded and replaced in its entirety our 2010 Equity Incentive Plan (the "2010 Plan") which was effective in March 2010, and no further awards will be granted under the 2010 Plan; however, the terms and conditions of the 2010 Plan will continue to govern any outstanding awards thereunder. The 2010 Plan provided for the grant of incentive stock options, non-statutory stock options, restricted stock units ("RSUs"), restricted stock awards ("RSAs"), performance-contingent

restricted stock units (“PSUs”), performance based options (“PBOs”), stock appreciation rights, and stock purchase rights to our employees, non-employee directors and consultants.

The number of shares of our common stock available for issuance under the 2019 Plan is equal to the sum of (i) 7,897,144 shares and (ii) any shares subject to awards granted under the 2010 Plan that were outstanding as of April 22, 2019 and thereafter terminate, expire, lapse or are forfeited; provided that no more than 14,000,000 shares may be issued upon the exercise of incentive stock options (“ISOs”). In June 2019, 8.1 million shares authorized for issuance under the 2019 Plan were registered under the Securities Act of 1933, as amended (the “Securities Act”).

The 2019 Plan provides for the grant of stock options, including incentive stock options and non-qualified stock options, stock appreciation rights, restricted stock, restricted stock units, other stock or cash based awards and dividend equivalents to eligible employees and consultants of the Company or any parent or subsidiary, as well as members of the Board.

As of December 31, 2020, total shares remaining available for issuance under the 2019 Plan were approximately 6.8 million shares.

Stock Options

The option exercise price for incentive stock options must be at least 100% of the fair value of our common stock on the date of grant and the option exercise price for non-statutory stock options is 85% of the fair value of our common stock on the date of grant, as determined by the Board. If, at the time of a grant, the optionee directly or by attribution owns stock possessing more than 10% of the total combined voting power of all of our outstanding capital stock, the exercise price for these options must be at least 110% of the fair value of the underlying common stock. Stock options granted to employees generally have a maximum term of ten years and vest over four years from the date of grant, of which 25% vest at the end of one year, and 75% vest monthly over the remaining three years. We may grant options with different vesting terms from time to time. Unless an employee's termination of service is due to disability or death, upon termination of service, any unexercised vested options will be forfeited at the end of three months or the expiration of the option, whichever is earlier.

Restricted Stock Units (RSUs)

We also grant employees RSUs, which generally vest over either a three year period with one-third of the shares subject to the RSUs vesting on each yearly anniversary of the vesting commencement date or over a four year period with 25% of the shares subject to the RSU vesting on each yearly anniversary of the vesting commencement date, in each case contingent upon such employee’s continued service on such vesting date. RSUs are generally subject to forfeiture if employment terminates prior to the release of vesting restrictions. We may grant RSUs with different vesting terms from time to time.

Performance-contingent Restricted Stock Units (PSUs) and Performance Based Options (PBOs)

The compensation committee of the Board approved, solely in respect of non-executive employees, delegated to our Chief Executive Officer the authority to approve grants of PSUs. The compensation committee of the Board also approved grants of PBOs and PSUs to our executives. The PSUs and PBOs vest based upon both the successful achievement of certain corporate operating milestones in specified timelines and continued employment through the applicable vesting date. When the performance goals are deemed to be probable of achievement for these types of awards, recognition of stock-based compensation expense commences. Once the number of shares eligible to vest is determined, those shares vest in two equal installments with 50% vesting upon achievement and the remaining 50% vesting on the first anniversary of achievement, in each case, subject to the recipient’s continued service through the applicable vesting date. If the performance goals are achieved at the threshold level, the number of shares eligible to vest in respect of the PSUs and PBOs would be equal to half the number of PSUs granted and one-quarter the number of shares underlying the PBOs granted. If the performance goals are achieved at the target level, the number of shares eligible to vest in respect of the PSUs and PBOs would be equal to the number of PSUs granted and half of the shares underlying the PBOs granted. If the performance goals are achieved at the superior level, the number of shares eligible to vest in respect of the PSUs would be equal to two times the number of PSUs granted and equal to the number of PBOs granted. The number of shares issuable upon achievement of the performance goals at the levels between the threshold and target levels for the PSUs and PBOs or between the target level and superior levels for the PSUs would be determined using linear interpolation. Achievement below the threshold level would result in no shares being eligible to vest in respect of the PSUs and PBOs.

In 2020, we awarded PSUs (“2020 PSUs”) and PBOs (“2020 PBOs”), each of which commence vesting based upon the achievement of various weighted performance goals, including corporate revenue, performance enzyme segment gross margin, major new biotherapeutics publicity events, strategic performance enzyme and biotherapeutics deliverables, and strategic plan development. As of December 31, 2020, we estimated that the 2020 PSUs and 2020 PBOs performance goals would be achieved at 88% of the target level, and recognized expenses accordingly.

In 2019, we awarded PSUs ("2019 PSUs") and PBOs ("2019 PBOs"), each of which commenced vesting based upon the achievement of various weighted performance goals, including sustained revenue and performance enzyme growth, strategic advancement of biotherapeutics, cash balance and strategic plan development. In the first quarter of 2020, we determined that the 2019 PSUs and 2019 PBOs performance goals had been achieved at 84% of the target level, and recognized expenses accordingly. Accordingly, 50% of the shares underlying the 2019 PSUs and PBOs vested in the first quarter of 2020 and50% of the shares underlying the 2019 PSUs and PBOs will vest in the first quarter of 2021, in each case subject to the recipient's continued service on each vesting date.

In 2018, we awarded PSUs ("2018 PSUs") and PBOs ("2018 PBOs"), each of which commenced vesting based upon the achievement of various weighted performance goals, including core business revenue growth, cash balance, new licensing collaborations, new research and development service revenue arrangements, technology advancement and novel therapeutic enzymes advancement. In the first quarter of 2019, we determined that the 2018 PSUs and 2018 PBOs performance goals had been achieved at 118% of the target level, and recognized expenses accordingly. Accordingly, 50% of the shares underlying the 2018 PSUs and PBOs vested in the first quarter of 2019 and in the first quarter of 2020, respectively, in each case subject to the recipient's continued service on each vesting date.

Stock-Based Compensation Expense:

Stock-based compensation expense is included in the consolidated statements of operations as follows (in thousands):

	Year Ended December 31,		
	2020	2019	2018
Research and development	$ 1,620	$ 1,562	$ 2,055
Selling, general and administrative	6,108	5,381	5,834
Total	$ 7,728	$ 6,943	$ 7,889

The following table presents total stock-based compensation expense by security type included in the consolidated statements of operations (in thousands):

	Year Ended December 31,		
	2020	2019	2018
Stock options	$ 2,381	$ 2,149	$ 1,975
RSUs and RSAs	2,231	1,805	1,770
PSUs	1,160	1,087	1,511
PBOs	1,956	1,902	2,633
Total	$ 7,728	$ 6,943	$ 7,889

Grant Award Activities:

Stock Option Awards

We estimated the fair value of stock options using the Black-Scholes-Merton option-pricing model based on the date of grant.The following summarizes the weighted-average assumptions used to estimate the fair value of employee and non-employee stock options granted:

	Year Ended December 31,		
	2020	2019	2018
Expected life (years)	5.3	5.6	5.6
Volatility	50.4 %	55.3 %	60.0 %
Risk-free interest rate	1.0 %	2.4 %	2.7 %
Expected dividend yield	0.0 %	0.0 %	0.0 %

The following summarizes the weighted-average assumptions used to estimate the fair value of76,000 shares of stock options granted to non-employees during the year ended December 31, 2020 for services valued at $0.4 million:

Expected life (years)	5.4
Volatility	51.6 %
Risk-free interest rate	0.4 %
Expected dividend yield	0.0 %

The weighted average grant date fair value per share of non-employee stock options granted in 2020 was $5.04. The Company did not grant shares of stock options to non-employees during the years ended December 31, 2019 and 2018.

The following tables summarizes stock option activities:

	Number of Shares	Weighted Average Exercise Price Per Share
	(In Thousands)	
Outstanding at December 31, 2017	4,579	$ 4.40
Granted	645	$ 9.56
Exercised	(772)	$ 5.56
Forfeited/Expired	(340)	$ 6.66
Outstanding at December 31, 2018	4,112	$ 4.81
Granted	406	$ 20.68
Exercised	(1,045)	$ 4.50
Forfeited/Expired	(326)	$ 11.01
Outstanding at December 31, 2019	3,147	$ 6.31
Granted	496	$ 13.30
Exercised	(210)	$ 6.30
Forfeited/Expired	(48)	$ 16.71
Outstanding at December 31, 2020	3,385	$ 7.19

	Number of Shares	Weighted Average Exercise Price Per Share	Weighted Average Remaining Contractual Term	Aggregate Intrinsic Value
	(In Thousands)		(In Years)	(In Thousands)
Outstanding at December 31, 2020	3,385	$ 7.19	5.4	$ 49,542
Exercisable at December 31, 2020	2,569	$ 5.09	4.3	$ 42,998
Vested and expected to vest at December 31, 2020	3,279	$ 6.96	5.3	$ 48,786

The weighted average grant date fair value per share of employee stock options granted in 2020, 2019 and 2018 were $6.03, $10.77 and $5.34, respectively. The total intrinsic value of options exercised in 2020, 2019 and 2018 were $1.8 million, $13.6 million and $7.6 million, respectively.

As of December 31, 2020, there was $4.1 million of unrecognized stock-based compensation, net of expected forfeitures, related to unvested stock options, which we expect to recognize over a weighted average period of 2.4 years.

Restricted Stock Awards (RSAs)

The following table summarizes RSA activities:

	Number of Shares	Weighted Average Grant Date Fair Value Per Share
Non-vested balance at December 31, 2017	159	$ 4.68
Granted	47	$ 14.35
Vested	(151)	$ 4.71
Non-vested balance at December 31, 2018	55	$ 12.83
Granted	40	$ 17.18
Vested	(56)	$ 12.83
Forfeited/Expired	(4)	$ 17.18
Non-vested balance at December 31, 2019	35	$ 17.18
Granted	96	$ 11.44
Vested	(35)	$ 17.18
Non-vested balance at December 31, 2020	96	$ 11.44

The total fair value, as of the vesting date, of RSAs vested in fiscal 2020, 2019 and 2018 were $0.4 million, $1.0 million and $2.1 million respectively.

As of December 31, 2020, there was $0.6 million of unrecognized stock-based compensation cost related to non-vested RSAs, which we expect to recognize over a weighted average period of 1.6 years.

Restricted Stock Units (RSUs)

The following table summarizes RSU activities:

	Number of Shares	Weighted Average Grant Date Fair Value Per Share
	(In Thousands)	
Non-vested balance at December 31, 2017	560	$ 4.08
Granted	86	$ 10.56
Vested	(290)	$ 4.09
Forfeited/Expired	(8)	$ 4.73
Non-vested balance at December 31, 2018	348	$ 5.66
Granted	72	$ 19.19
Vested	(210)	$ 5.03
Forfeited/Expired	(9)	$ 13.60
Non-vested balance at December 31, 2019	201	$ 10.76
Granted	156	$ 14.22
Vested	(168)	$ 10.05
Forfeited/Expired	(13)	$ 15.16
Non-vested balance at December 31, 2020	176	$ 14.17

The total fair value, as of the vesting date, of RSUs vested in fiscal 2020, 2019 and 2018 were $2.1 million, $4.1 million and $2.9 million respectively.

As of December 31, 2020, there was $1.4 million of unrecognized stock-based compensation cost related to non-vested RSUs, which we expect to recognize over a weighted average period of 1.9 years.

Performance-Contingent Restricted Stock Units (PSUs)

The following table summarizes PSU activities:

	Number of Shares	Weighted Average Grant Date Fair Value Per Share
	(In Thousands)	
Non-vested balance at December 31, 2017	429	$ 4.20
Granted	306	$ 6.71
Vested	(495)	$ 7.16
Non-vested balance at December 31, 2018	240	$ 7.48
Granted	95	$ 14.98
Vested	(200)	$ 6.58
Forfeited/Expired	(15)	$ 15.58
Non-vested balance at December 31, 2019	120	$ 13.88
Granted	124	$ 13.59
Vested	(107)	$ 11.28
Forfeited/Expired	(6)	$ 21.80
Non-vested balance at December 31, 2020	131	$ 15.34

The total fair value, as of the vesting date, of PSUs vested in the years ended December 31, 2020, 2019, and 2018 were $.3 million, $3.8 million, and $5.4 million, respectively.

As of December 31, 2020, there was $0.5 million of unrecognized stock-based compensation cost related to non-vested PSUs, which we expect to recognize over a weighted average period of 0.6 years.

Performance Based Options (PBOs)

We estimated the fair value of PBO using the Black-Scholes-Merton option-pricing model based on the date of grant.The following summarize the ranges of weighted-average assumptions used to estimate the fair value of employee stock options granted:

	Year Ended December 31,		
	2020	2019	2018
Expected life (years)	5.3	5.6	5.6
Volatility	49.9 %	55.8 %	60.3 %
Risk-free interest rate	1.3 %	2.5 %	2.7 %
Expected dividend yield	0.0 %	0.0 %	0.0 %

The following tables summarizes PBO activities:

	Number of Shares	Weighted Average Grant Date Fair Value Per Share
	(in thousands)	
Outstanding at December 31, 2017	1,720	$ 2.54
Granted	1,200	$ 5.02
Exercised	(84)	$ 2.54
Forfeited	(1,254)	$ 3.73
Outstanding at December 31, 2018	1,582	$ 3.47
Granted	718	$ 11.44
Exercised	(422)	$ 3.17
Forfeited	(618)	$ 10.34
Outstanding at December 31, 2019	1,260	$ 4.75
Granted	689	$ 6.37
Forfeited	(389)	$ 6.42
Outstanding at December 31, 2020	1,560	$ 5.05

	Number of Shares	Weighted Average Exercise Price Per Share	Weighted Average Remaining Contractual Term	Aggregate Intrinsic Value
	(In Thousands)		(In Years)	(In Thousands)
Exercisable at December 31, 2020	1,156	$ 7.55	6.6	$ 16,504
Vested and expected to vest at December 31, 2020	1,510	$ 9.54	7.2	$ 18,567

The total fair value of exercised PBOs were nil for 2020, $1.3 million for 2019 and $0.2 million for 2018. As of December 31, 2020, there was $1.1 million of unrecognized stock-based compensation cost related to non-vested PBOs, which we expect to recognize over a weighted average period of 0.5 years.

Note 10. Capital Stock

Public Offerings

In December 2020, we completed an underwritten public offering in which we issued and sold 4,928,572 shares of our common stock, par value $0.0001 per share, at a public offering price of $17.50 per share. We received gross proceeds of $86.3 million, net of underwriting discounts and commissions of $5.2 million and direct offering expenses of $0.3 million for net proceeds of $80.8 million.

In April 2018, we completed an underwritten public offering of 4,312,500 shares of our common stock, par value $0.0001 per share, at a public offering price of $9.25 per share. We received net proceeds after deducting the underwriting discounts and commissions and estimated offering expenses of approximately $37.3 million.

Private Placement

In June 2019, we entered into a Securities Purchase Agreement with an affiliate of Casdin Capital, LLC (Casdin) pursuant to which we issued and sold to Casdin 3,048,780 shares of our common stock at a purchase price of $16.40 per share. After deducting issuance costs of $0.1 million from the Private Offering, our net proceeds were $49.9 million. The Private Offering was exempt from registration pursuant to the exemption for transactions by an issuer not involving any public offering under Section 4(a)(2) the Securities Act, and Regulation D under the Securities Act.

Note 11. 401(k) Plan

In January 2005, we implemented a 401(k) Plan covering certain employees. Currently, all of our United States based employees over the age of 18 are eligible to participate in the 401(k) Plan. Under the 401(k) Plan, eligible employees may elect

to reduce their current compensation up to a certain annual limit and contribute these amounts to the 401(k) Plan. We may make matching or other contributions to the 401(k) Plan on behalf of eligible employees. We recorded employer matching contributions expense of $0.8 million, $0.7 million, and $0.6 million in the years ended December 31, 2020, 2019, and 2018, respectively.

Note 12. Income Taxes

Our loss before provision for (benefit from) income taxes was as follows (in thousands):

	Year Ended December 31,		
	2020	2019	2018
United States	$ (23,452)	$ (11,751)	$ (10,653)
Foreign	(219)	(167)	(262)
Loss before provision for income taxes	$ (23,671)	$ (11,918)	$ (10,915)

The tax provision (benefit from) for the years ended December 31, 2020, 2019 and 2018 consists primarily of taxes attributable to foreign operations. The components of the provision for income taxes are as follows (in thousands):

	Year Ended December 31,		
	2020	2019	2018
Current provision (benefit):			
State	$ 5	$ 5	$ 5
Foreign	342	18	(13)
Total current provision (benefit)	347	23	(8)
Deferred provision (benefit):			
Foreign	(8)	(6)	(29)
Total deferred provision (benefit)	(8)	(6)	(29)
Provision for (benefit from) income taxes	$ 339	$ 17	$ (37)

Reconciliation of the provision for (benefit from) income taxes calculated at the statutory rate to our provision for (benefit from) income taxes is as follows (in thousands):

	Year Ended December 31,		
	2020	2019	2018
Tax benefit at federal statutory rate	$ (4,971)	$ (2,503)	$ (2,292)
State taxes	(465)	(1,120)	222
Research and development credits	(811)	(693)	(499)
Foreign operations taxed at different rates	2	1	(17)
Stock-based compensation	132	(3,606)	(2,587)
Other nondeductible items	69	505	(3)
Executive compensation	24	872	838
Change in valuation allowance	6,359	6,561	4,301
Provision for (benefit from) income taxes	$ 339	$ 17	$ (37)

Deferred income taxes reflect the net tax effects of (a) temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes, and (b) operating losses and tax credit carryforwards.

Significant components of our deferred tax assets and liabilities are as follows (in thousands):

	December 31,	
	2020	2019
Deferred tax assets:		
Net operating losses	$ 72,530	$ 68,422
Credits	9,914	8,494
Deferred revenues	1,080	468
Stock-based compensation	2,576	2,338
Reserves and accruals	1,914	1,545
Depreciation	1,115	1,358
Intangible assets	1,714	2,159
Capital losses	25	26
Unrealized gain/loss	400	406
Lease liability	5,626	5,974
Other assets	100	92
Total deferred tax assets:	96,994	91,282
Valuation allowance	(92,126)	(85,768)
Deferred tax liabilities:		
Right-of-use assets	(4,848)	(5,514)
Other	(52)	(40)
Total deferred tax liabilities:	(4,900)	(5,554)
Net deferred tax liabilities	$ (32)	$ (40)

ASC 740 requires that the tax benefit of NOLs, temporary differences and credit carryforwards be recorded as an asset to the extent that management assesses that realization is "more likely than not." Realization of the future tax benefits is dependent on our ability to generate sufficient taxable income within the carryforward period. Because of our history of operating losses, management believes that recognition of the deferred tax assets arising from the above-mentioned future tax benefits is currently not more likely than not to be realized and, accordingly, has provided a valuation allowance against our deferred tax assets. Accordingly, the net deferred tax assets in all our jurisdictions have been fully reserved by a valuation allowance. The net valuation allowance increased by $6.4 million during the year ended December 31, 2020, increased by $6.5 million during the year ended December 31, 2019, and increased by $5.2 million during the year ended December 31, 2018. At such time as it is determined that it is more likely than not that the deferred tax assets are realizable, the valuation allowance will be reduced.

The following table sets forth our federal, state and foreign NOL carryforwards and federal research and development tax credits as of December 31, 2020 (in thousands):

	December 31, 2020	
	Amount	Expiration Years
Net operating losses, federal	$ 224,475	2022-2037
Net operating losses, federal	$ 82,931	Do not expire
Net operating losses, state	$ 127,317	2028-2040
Tax credits, federal	$ 10,654	2022-2040
Tax credits, state	$ 11,977	Do not expire
Net operating losses, foreign	$ 778	Various

Current U.S. federal and California tax laws include substantial restrictions on the utilization of NOLs and tax credit carryforwards in the event of an ownership change of a corporation. Accordingly, the Company's ability to utilize NOLs and tax credit carryforwards may be limited as a result of such ownership changes. We performed an analysis in 2020 and determined that there was not a limitation that would result in the expiration of carryforwards before they are utilized.

Income tax expense or benefit from continuing operations is generally determined without regard to other categories of earnings, such as discontinued operations and other comprehensive income. An exception is provided in ASC 740 when there is aggregate income from categories other than continuing operations and a loss from continuing operations in the current year. In this case, the tax benefit allocated to continuing operations is the amount by which the loss from continuing operations reduces the tax expenses recorded with respect to the other categories of earnings, even when a valuation allowance has been established against the deferred tax assets. In instances where a valuation allowance is established against current year losses, income from other sources is considered when determining whether sufficient future taxable income exists to realize the deferred tax assets.

In 2014, we determined that the undistributed earnings of our India subsidiary will be repatriated to the United States, and accordingly, we have provided a deferred tax liability totaling $0.1 million as of December 31, 2020, for local taxes that would be incurred upon repatriation. We have not provided for U.S. federal and state income taxes on all of the remaining non-U.S. subsidiaries' undistributed earnings as of December 31, 2020 as the remaining foreign jurisdictions are in an accumulative loss position.

We apply the provisions of ASC 740 to account for uncertain income taxes.A reconciliation of the beginning and ending amount of unrecognized tax benefits is as follows (in thousands):

	December 31,		
	2020	2019	2018
Balance at beginning of year	$ 11,330	$ 9,980	$ 9,422
Additions based on tax positions related to current year	1,357	1,362	1,087
Reductions to tax provision of prior years	(4)	(12)	(529)
Balance at end of year	$ 12,683	$ 11,330	$ 9,980

We recognize interest and penalties as a component of our income tax expense. Total interest and penalties recognized in the consolidated statement of operations was $9 thousand, $32 thousand and $37 thousand, respectively, in 2020, 2019 and 2018. Total penalties and interest recognized in the balance sheet was $0.4 million in 2020 and 2019. The total unrecognized tax benefits that, if recognized currently, would impact our company's effective tax rate were $0.3 million as of December 31, 2020 and 2019. We do not expect any material changes to our uncertain tax positions within the next 12 months. We are not subject to examination by United States federal or state tax authorities for years prior to 2002 and foreign tax authorities for years prior to 2013.

In December 2017, the Securities and Exchange Commission issued Staff Accounting Bulletin No. 118 ("SAB 118"), which provided a measurement period of up to one year from the enactment date of the Tax Cuts and Jobs Act of 2017 (the "Act") for companies to complete the accounting for the Tax Act and its related impacts. In 2018, the Company completed its accounting for the Tax Act. The income tax effects of the Tax Act for which the accounting was completed in 2018 include: the impact of the Transition Tax, the revaluation of deferred tax assets and liabilities to reflect the 21% corporate tax rate, the impact to the aforementioned items on state income taxes. We completed our accounting for the income tax effects under the Tax Cuts and Jobs Act (the "Act") that are relevant to the Company and required to be recorded and disclosed pursuant to ASC 740. Accordingly, any and all provisional amounts previously recorded in accordance with SAB 118 were adjusted to reflect their final amounts.

Beginning in 2018, the global intangible low-taxed income ("GILTI") provisions in the Tax Act required us to include, in our U.S. income tax return, foreign subsidiary earnings in excess of an allowable return on the foreign subsidiary's tangible assets. Per guidance issued by the FASB, companies can either account for deferred taxes related to GILTI or treat tax arising from GILTI as a period cost. Both are acceptable methods subject to an accounting policy election. At December 31, 2018, we finalized our policy and elected to use the period cost method for GILTI. In 2020, we did not incur any GILTI inclusion as our foreign subsidiaries generated losses.

The BEAT provisions in the Tax Act eliminated the deduction of certain base-erosion payments made to related foreign corporations and impose a minimum base erosion anti-abuse tax if greater than regular tax. In 2020, our company was not subject to BEAT as it did not meet the requirements to be subject to BEAT.

Note 13. Commitments and Contingencies

Operating Leases

Our headquarters are located in Redwood City, California, where we occupy approximately 77,300 square feet of office and laboratory space in four buildings within the same business park of Metropolitan Life Insurance Company ("MetLife"). Our Lease agreement with MetLife ("RWC Lease") includes approximately 28,200 square feet of space located at 200 and 220 Penobscot Drive, Redwood City, California (the "200/220 Penobscot Space") and approximately 37,900 square feet of space located at 400 Penobscot Drive, Redwood City, California (the "400 Penobscot Space") (the 200/220 Penobscot Space and the 400 Penobscot Space are collectively referred to as the "Penobscot Space"), and approximately 11,200 square feet of space located at 501 Chesapeake Drive, Redwood City, California (the "501 Chesapeake Space").

Until the end of January 2020, we also leased approximately 29,900 square feet of space located at 101 Saginaw Drive, Redwood City, California (the "Saginaw Space"). During the period January 1, 2020 through January 31, 2020, we subleased approximately 26,500 square feet of the Saginaw Space to Minerva Surgical, Inc. The lease and sublease for the Saginaw Space both expired at the end of January 2020. During the period from February 1, 2020 through April 30, 2020, we subleased approximately 3,400 square feet at 101 Saginaw Drive from Minerva Surgical, Inc. The sublease expired at the end of April 2020.

We entered into the initial lease with MetLife for our facilities in Redwood City in 2004 and the RWC lease has been amended multiple times since then to adjust the leased space and terms of the Lease. In February 2019, we entered into an Eighth Amendment to the Lease (the "Eighth Amendment") with MetLife with respect to the Penobscot Space and the 501 Chesapeake Space to extend the term of the Lease for additional periods. Pursuant to the Eighth Amendment, the term of the lease of the Penobscot Space has been extended through May 2027. The lease term for the 501 Chesapeake Space has been extended to May 2029. We have one (1) option to extend the term of the lease for the Penobscot Space for five (5) years, and one (1) separate option to extend the term of the lease for the 501 Chesapeake Space for five (5) years.

We incurred $3.6 million of capital improvement costs related to the facilities leased from MetLife through December 31, 2012. During 2011 and 2012, we requested and received $3.1 million of reimbursements from the landlord for the tenant improvement and HVAC allowances for the completed construction. The reimbursements were recorded once cash was received. In those fiscal periods prior to January 1, 2019, we recorded reimbursements from the landlord for tenant improvements as liabilities in the consolidated balance sheets and we amortized the reimbursements on a straight line basis over the term of the RWC Lease as a reduction to rent expense. On January 1, 2019 we adopted ASU 2016-02 and related amendments, *Leases (Topic 842)* ("ASC 842"), which provided a new basis of accounting for leases. Under the provisions of ASC 842, we reclassified lease incentive obligations as operating lease right-of-use assets in the consolidated balance sheets. Rent expense for the Redwood City properties is recognized on a straight-line basis over the term of the RWC Lease.

We are required to restore certain areas of the Redwood City facilities that we are renting to their original form. We are expensing the asset retirement obligation over the terms of the respective leases. We review the estimated obligation each reporting period and make adjustments if our estimates change. We recorded asset retirement obligations of $0.2 million as of December 31, 2020 and 2019, which are included in other liabilities on the consolidated balance sheets. Accretion expense related to our asset retirement obligations was nominal in 2020 and 2019.

Pursuant to the terms of the RWC Lease, we exercised our right to deliver a letter of credit in lieu of a security deposit. The letter of credit is collateralized by deposit balances held by the bank in the amount of $1.1 million as of December 31, 2020 and 2019, and are recorded as non-current restricted cash on the consolidated balance sheets.

Finance Leases

In December 2016, we entered into a three-year financing lease agreement with a third party supplier for the purchase of laboratory equipment that was partially financed through a finance lease of approximately $0.4 million. The lease became effective upon delivery of the equipment, in February 2017 and term of the three-year lease was from February 2017 and expired in February 2020. This financing agreement was accounted for as a finance lease due to bargain purchase options at the end of the lease. In April 2017, we entered into a three-year financing lease agreement with a third party supplier for the purchase of information technology equipment for approximately $0.3 million. The effective term the three-year lease was from May 2017 and expired in April 2020.

Lease costs, amounts included in measurement of lease obligations and other information related to non-cancellable operating leases and finance leases for the year ended December 31, 2020 and 2019 were as follows (in thousands):

	Year Ended December 31,	
	2020	2019
Amortization of right-of-use assets	$ 152	$ 217
Interest on lease obligations	1	10
Finance lease costs	153	227
Operating lease cost	3,879	4,556
Short-term lease costs [1]	47	—
Sublease income	(55)	(957)
Total lease cost [2]	$ 4,024	$ 3,826

[1] Short-term lease costs on leases with terms of over one month and less than one year.

[2] The Company had no variable lease costs.

Lease costs for the years ended December 31, 2020 and 2019 as compared to year ended December 31, 2018 reflected the effects of adopting the provisions of ASC 842 which provided a new basis of accounting for leases in 2019. Operating lease costs were $3.2 million for the year ended December 31, 2018, partially offset by sublease income of $1.1 million. Finance lease payments were $0.3 million for the year ended December 31, 2018.

Amounts included in measurement of lease obligations:

	Year Ended December 31,	
	2020	2019
Cash paid:		
Operating cash flows from operating leases	$ 2,816	$ 3,279
Operating cash flow from finance leases	$ 1	$ 10
Financing cash flows from finance leases	$ 60	$ 242
Non-cash activity:		
Operating Lease - Right-of-use assets obtained in exchange for lease liabilities	$ —	$ 26,617
Finance Lease - Right-of-use assets obtained in exchange for lease liabilities	$ —	$ 493

	Operating Lease	Finance Lease
Other information:		
Weighted-average remaining lease term (in years)	5.5 years	—
Weighted-average discount rate	6.6 %	5.0 %

As of December 31, 2020, our maturity analyses of annual undiscounted cash flows of the non-cancellable operating leases are as follows (in thousands):

Years ending December 31,	Operating Leases
2021	$ 4,197
2022	4,285
2023	4,589
2024	4,726
2025	4,868
Thereafter	8,626
Total minimum lease payments	31,291
Less: imputed interest	6,340
Lease obligations	$ 24,951

Subsequent Event

In the first quarter of 2021, we entered into a lease agreement with ARE-San Francisco No. 63, LLC ("ARE") to lease a portion of a facility comprising approximately 36,593 rentable square feet in San Carlos, California to serve as additional office and research and development laboratory space (the "San Carlos Space"). We expect to commence occupancy of the San Carlos Space in November 2021 once tenant improvements are substantially completed by ARE in accordance with the construction plan. For additional information and a maturity analyses of the estimated annual undiscounted cash flows of the operating lease, see Note 17, *"Subsequent Events"*

Other Commitments

We enter into supply and service arrangements in the normal course of business. Supply arrangements are primarily for fixed-price manufacture and supply. Service agreements are primarily for the development of manufacturing processes and certain studies. Commitments under service agreements are subject to cancellation at our discretion which may require payment of certain cancellation fees. The timing of completion of service arrangements is subject to variability in estimates of the time required to complete the work.

The following table provides quantitative data regarding our other commitments. Future minimum payments reflect amounts that we expect to pay including potential obligations under services agreements subject to risk of cancellation by us (in thousands):

Other Commitment Agreement Type	Agreement Date	Future Minimum Payment
Manufacture and supply agreement with expected future payment date of December 2022	April 2016	$ 320
Development and manufacturing services agreements	September 2019	2,341
Total other commitments		$ 2,661

Credit Facility

In June 30, 2017, we entered into a credit facility (the "Credit Facility") with Western Alliance Bank consisting of term loans ("Term Debt") up to $10.0 million, and advances ("Advances") under a revolving line of credit ("Revolving Line of Credit") up to $5.0 million with an accounts receivable borrowing base of 80% of eligible accounts receivable. At December 31, 2020 and 2019, we have not drawn from the Credit Facility. We may draw on the Term Debt and the Revolving Line of Credit at any time prior to October 1, 2021 and October 1, 2024, respectively. On October 1, 2024 loans drawn under the Term Debt mature and the Revolving Line of Credit terminate. Loans made under the Term Debt bear interest through maturity equal to the greater of (i) 3.75% or (ii) the sum of (A) Index Rate (prime rate published in the Money Rates section of the Western Edition of The Wall Street Journal plus (B) 0.50%. Advances made under the Revolving Line of Credit bear interest at a variable annual rate equal to the equal to the greater of (i) 4.25% or (ii) the sum of (A) the prime rate plus (B) 1.0%.

Our obligations under the Credit Facility are secured by a lien on substantially all of our personal property other than our intellectual property. The Credit Facility includes a number of customary covenants and restrictive financial covenants including meeting minimum product revenue levels and maintaining certain minimum cash levels with the lender. The Credit Facility's financial covenants restrict the ability of the Company to transfer collateral, incur additional indebtedness, engage in mergers or acquisitions, pay dividends or make other distributions, make investments, create liens, sell assets, or sell certain assets held at foreign subsidiaries. A failure to comply with these covenants could permit the lender to exercise remedies against us and the collateral securing the Credit Facility, including foreclosure of our properties securing the Credit Facilities and our cash. At December 31, 2020, we were in compliance with the covenants for the Credit Facility.

The Credit Facility allows for interest-only payments on the Term Debt through November 1, 2022. Monthly payments of principal and interest on the Term Debt are required following the applicable amortization date. We may elect to prepay in full the Term Debt and Advances under the Revolving Line of Credit at any time.

Legal Proceedings

We are not currently a party to any material pending litigation or other material legal proceedings.

Indemnifications

We are required to recognize a liability for the fair value of any obligations we assume upon the issuance of a guarantee. We have certain agreements with licensors, licensees and collaborators that contain indemnification provisions. In such provisions, we typically agree to indemnify the licensor, licensee and collaborator against certain types of third party claims. The maximum amount of the indemnifications is not limited. We accrue for known indemnification issues when a loss is probable and can be reasonably estimated. There were no accruals for expenses related to indemnification issues for any periods presented.

Impact of COVID-19

We are subject to risks and uncertainties as a result of the current COVID-19 pandemic. The COVID-19 pandemic has presented a substantial public health and economic challenge around the world and is affecting our employees, communities and business operations, as well as the U.S. economy and other economies worldwide. The full extent to which the COVID-19 pandemic will directly or indirectly impact our business, results of operations and financial condition will depend on future developments that are highly uncertain and may not be accurately predicted, including the duration and severity of the pandemic and the extent and severity of the impact on our customers, new information that may emerge concerning COVID-19, the actions taken to contain it or treat its impact and the economic impact on local, regional, national and international markets.

To date, we and our collaboration partners have been able to continue to supply our enzymes to our customers worldwide. However, we are dependent on our manufacturing and logistics partners and consequently, disruptions in operations of our partners and customers may affect our ability to supply enzymes to our customers. Furthermore, our ability to provide future research and development ("R&D") services will continue to be impacted as a result of governmental orders and any disruptions in operations of our customers with whom we collaborate. We believe that these disruptions have had a negative impact on revenue for the year ended December 31, 2020, although we are unable to fully determine and quantify the extent to which this pandemic has affected the amount and timing of our total revenues. The extent to which the pandemic may impact our business operations and operating results will continue to remain highly dependent on future developments, which are uncertain and cannot be predicted with confidence.

In the U.S., the impact of COVID-19, including governmental orders ("Orders") governing the operation of businesses during the pandemic, caused the temporary closure of our Redwood City, California facilities and has disrupted our R&D operations. R&D operations for several projects were temporarily suspended from mid-March 2020 through the end of April in accordance with these Orders. In May 2020, we initiated limited R&D operations and have gradually ramped up operations such that we are currently utilizing the majority of our normal R&D capacity. Additionally, we resumed small scale manufacturing at our Redwood City pilot plant in May 2020.

Our future results of operations and liquidity could be adversely impacted by delays in payments of outstanding receivable amounts beyond normal payment terms, supply chain disruptions and uncertain demand, and the impact of any initiatives or programs that we may undertake to address financial and operations challenges faced by our customers. As of the date of issuance of these consolidated financial statements, the extent to which the COVID-19 pandemic may materially impact our financial condition, liquidity, or results of operations in the future is uncertain.

Note 14. Related Party Transactions

Molecular Assemblies, Inc.

In June 2020, we entered into a Stock Purchase Agreement with Molecular Assemblies, Inc. ("MAI") pursuant to which we purchased1,587,050 shares of MAI's Series A preferred stock for $1.0 million. In connection with the transaction,

John Nicols, our President and Chief Executive Officer, also joined MAI's board of directors. Concurrently with our initial equity investment, we entered into a Master Collaboration and Research Agreement with MAI (the "MAI Agreement"), pursuant to which we are performing services utilizing our CodeEvolver® protein engineering platform technology to improve DNA polymerase enzymes in exchange for compensation in the form of additional shares of MAI's Series A preferred stock.

We received 714,171 shares of MAI's Series A preferred stock from research and development services with MAI and we recognized $0.9 million in research and development revenue from these services with MAI in the year ended December 31, 2020. Our investment in MAI Series A preferred stock was $1.5 million at December 31, 2020. At December 31, 2020, we had $0.5 million in contract asset due from MAI for services rendered. Payment for the services rendered was subsequently received in the form of additional MAI Series A preferred stock in the first quarter of 2021. For addition information, see Note 5, "Collaborative Arrangements."

Arzeda Corp.

In November 2020, we entered into the SynBio Innovation Accelerator ("Accelerator") collaboration with Casdin Capital, LLC ("Casdin"). The Accelerator is an informal collaboration with no commitment, designed to invest in the bio-production space to stimulate innovation which may deliver products leveraging the engineering technology and operational capability of Codexis and the resources, network and investment processes of Casdin, a shareholder with greater than a 5% ownership in Codexis' publicly traded common stock. The first Accelerator investment was in an available-for-sale non-marketable interest-bearing debt securities which are convertible subordinated notes issued by Arzeda Corp., an early-stage computational protein design company. The cost to acquire and the carrying value of the investment as of December 31, 2020 was $1.0 million. For additional information, see Note 7, "Fair Value Measurements."

AstraZeneca PLC

Pam P. Cheng, who served as a member of our board of directors until June 2020, joined AstraZeneca PLC as Executive Vice President, Operations and Information Technology in June 2015. We sold biocatalyst products to AstraZeneca PLC and its controlled purchasing agents and contract manufacturers. We recognized $0.1 million of revenue in 2020 through the date of Ms. Cheng's departure from our board of directors. We recognized $1.0 million and $0.6 million of revenue from transactions with AstraZeneca in the years ended December 30, 2019 and 2018, respectively. At December 31, 2020 and 2019, we had nil

and $0.3 million of related party receivables from AstraZeneca PLC and its controlled purchasing agents and contract manufacturers, respectively.

Settlement of Short Swing Profit Claim

In August 2019, we recorded approximately $77 thousand related to the short swing profit settlement remitted by a shareholder of our company under Section 16(b) of the Securities Exchange Act of 1934, as amended. We recognized the proceeds as an increase to additional paid-in capital in the consolidated balance sheets as of December 31, 2019 and consolidated statements of stockholders' equity as well as in cash provided by financing activities in the consolidated statements of cash flows for the year ended December 31, 2019.

Note 15. Segment, Geographical and Other Revenue Information

Segment Information

We manage our business as two business segments: Performance Enzymes and Novel Biotherapeutics.

We report corporate-related expenses such as legal, accounting, information technology, and other costs that are not otherwise included in our reportable business segments as "Corporate costs." All items not included in income (loss) from operations are excluded from the business segments.

We manage our assets on a total company basis, not by business segment, as the majority of our operating assets are shared or commingled. Our CODM does not review asset information by business segment in assessing performance or allocating resources, and accordingly, we do not report asset information by business segment.

Performance Enzymes

We initially commercialized our CodeEvolver® protein engineering technology platform and products in the pharmaceuticals market, and to date this continues to be our largest market served. Our customers, which include many large global pharmaceutical companies, use our technology, products and services in their manufacturing processes and process development. We have also used the technology to develop customized enzymes for use in other industrial markets. These markets consist of several large industrial verticals, including food and food ingredients, animal feed, flavors, fragrances, and agricultural chemicals. We also use our technology to develop enzymes for customers using NGS and PCR/qPCR for *in vitro* molecular diagnostic and molecular biology research applications.

Novel Biotherapeutics

We are also targeting new opportunities in the pharmaceutical industry to discover, improve, and/or develop biotherapeutic drug candidates. We believe that our CodeEvolver® protein engineering platform technology can be used to discover novel biotherapeutic drug candidates that will target human diseases that are in need of improved therapeutic interventions. Similarly, we believe that we can deploy our platform technology to improve specific characteristics of a customer's pre-existing biotherapeutic drug candidate, such as its activity, stability or immunogenicity. Most notable is our lead program for the potential treatment of PKU in humans. PKU is an inherited metabolic disorder in which the enzyme that converts the essential amino acid phenylalanine into tyrosine is deficient.

We have also developed a pipeline of other biotherapeutic drug candidates, which are in preclinical development, and in which we expect to continue to make additional investments with the aim of advancing additional product candidates targeting other therapeutic areas. In March 2020 we entered into the Takeda Agreement with Takeda under which we will research and develop protein sequences for use in gene therapy products for certain diseases.

Factors considered in determining the two reportable segments of the Company include the nature of business activities, the management structure directly accountable to our CODM for operating and administrative activities, availability of discrete financial information and information presented to the Board of Directors. Our CODM regularly reviews our segments and the approach provided by management for performance evaluation and resource allocation.

Operating expenses that directly support the segment activity are allocated based on segment headcount, revenue contribution or activity of the business units within the segments, based on the corporate activity type provided to the segment. The expense allocation excludes certain corporate costs that are separately managed from the segments. This provides the CODM with more meaningful segment profitability reporting to support operating decisions and allocate resources.

The following tables provide financial information by our reportable business segments along with a reconciliation to consolidated loss before income taxes (in thousands):

	Year Ended December 31, 2020			Year Ended December 31, 2019		
	Performance Enzymes	Novel Biotherapeutics	Total	Performance Enzymes	Novel Biotherapeutics	Total
Revenues:						
Product revenue	$ 30,220	$ —	$ 30,220	$ 29,465	$ —	$ 29,465
Research and development revenue	17,886	20,950	38,836	28,691	10,302	38,993
Total revenues	48,106	20,950	69,056	58,156	10,302	68,458
Costs and operating expenses:						
Cost of product revenue	13,742	—	13,742	15,632	—	15,632
Research and development [1]	20,923	21,705	42,628	19,380	13,278	32,658
Selling, general and administrative[1]	9,597	2,355	11,952	8,462	2,222	10,684
Total segment costs and operating expenses	44,262	24,060	68,322	43,474	15,500	58,974
Income (loss) from operations	$ 3,844	$ (3,110)	734	$ 14,682	$ (5,198)	9,484
Corporate costs [2]			(22,306)			(19,624)
Depreciation and amortization			(2,099)			(1,778)
Loss before income taxes			$ (23,671)			$ (11,918)

[1] Research and development expenses and selling, general and administrative expenses exclude depreciation and amortization of finance leases.

[2] Corporate costs include unallocated selling, general and administrative expense, interest income, and other income and expenses.

	Year Ended December 31, 2019			Year Ended December 31, 2018		
	Performance Enzymes	Novel Biotherapeutics	Total	Performance Enzymes	Novel Biotherapeutics	Total
Revenues:						
Product revenue	$ 29,465	$ —	$ 29,465	$ 25,590	$ —	$ 25,590
Research and development revenue	28,691	10,302	38,993	21,483	13,521	35,004
Total revenues	58,156	10,302	68,458	47,073	13,521	60,594
Costs and operating expenses:						
Cost of product revenue	15,632	—	15,632	12,620	—	12,620
Research and development [1]	19,380	13,278	32,658	18,924	10,185	29,109
Selling, general and administrative[1]	8,462	2,222	10,684	7,538	771	8,309
Total segment costs and operating expenses	43,474	15,500	58,974	39,082	10,956	50,038
Income (loss) from operations	$ 14,682	$ (5,198)	9,484	$ 7,991	$ 2,565	10,556
Corporate costs [2]			(19,624)			(20,324)
Depreciation			(1,778)			(1,147)
Loss before income taxes			$ (11,918)			$ (10,915)

[1] For the year ended December 31, 2019, research and development expenses and selling, general and administrative expenses exclude depreciation and amortization of finance leases. For the year ended December 31, 2018, research and development expenses and selling, general and administrative expenses exclude depreciation.

[2] Corporate costs include unallocated selling, general and administrative expense, interest income, and other income and expenses.

The following table provides stock-based compensation expense included in income (loss) from operations (in thousands):

	Years Ended December 31,		
	2020	2019	2018
Performance Enzymes	$ 2,970	$ 2,303	$ 2,591
Novel Biotherapeutics	768	695	338
Corporate cost	3,990	3,945	4,960
Total	$ 7,728	$ 6,943	$ 7,889

Significant Customers

Customers that each accounted for 10% or more of our total revenues were as follows:

	Percentage of Total Revenues For the Years Ended December 31,		
	2020	2019	2018
Merck	26 %	28 %	29 %
Nestlé Health Science	11 %	15 %	22 %
Novartis	*	23 %	*
Tate & Lyle	*	*	13 %
Takeda Pharmaceutical Co. Ltd.	19 %	*	*

** Percentage was less than 10%*

Customers that each accounted for 10% or more of accounts receivable balances as of the periods presented as follows:

	Percentage of Accounts Receivables As Of December 31,	
	2020	2019
Merck & Co.	32 %	38 %
Nestlé Health Science	13 %	10 %
Novartis	25 %	*

** Percentage was less than 10%*

Geographical Information

Geographic revenues are identified by the location of the customer and consist of the following (in thousands):

	Year Ended December 31, 2020		
	2020	2019	2018
Revenues			
Americas	$ 24,352	$ 13,039	$ 15,370
EMEA	19,257	37,133	22,361
APAC	25,447	18,286	22,863
Total revenues	$ 69,056	$ 68,458	$ 60,594

Identifiable long-lived assets by location was as follows (in thousands):

	December 31,	
	2020	2019
United States	$ 31,176	$ 30,387

Identifiable goodwill was as follows (in thousands):`

	Year Ended December 31, 2020			Year Ended December 31, 2019		
	Performance Enzymes	Novel Biotherapeutics	Total	Performance Enzymes	Novel Biotherapeutics	Total
Goodwill	$ 2,463	$ 778	$ 3,241	$ 2,463	$ 778	$ 3,241

Note 16. Allowance for Credit Losses

The following summarizes the financing receivables allowance for credit losses (in thousands):

	Year Ended December 31, 2020
Beginning Balance, January 1, 2020	$ 34
Current year provision	40
Ending Balance, December 31, 2020	$ 74

The following tables below summarizes accounts receivable by aging category (in thousands):

	December 31, 2020					
	31-60 Days	61-90 Days	91 Days and over	Total over 31 Days	Current	Total balance
Accounts receivable	$ 688	$ 7	$ 27	$ 722	$ 13,172	$ 13,894

	December 31, 2019					
	31-60 Days	61-90 Days	91 Days and over	Total over 31 Days	Current	Total balance
Accounts receivable	$ 191	$ 8	$ 62	$ 261	$ 8,802	$ 9,063

Note 17. Subsequent Events

In the first quarter of 2021, we entered into a lease agreement with ARE-San Francisco No. 63, LLC ("ARE") to lease a portion of a facility comprising approximately 36,593 rentable square feet in San Carlos, California to serve as additional office and research and development laboratory space (the "San Carlos Space"). We expect to commence occupancy of the San Carlos Space in November 2021 once tenant improvements are substantially completed by ARE in accordance with the construction plan. The construction plan includes Codexis-specific improvements necessary for operations at the lease commencement date. The budget provides a net tenant improvement allowance of $6.3 million plus an additional allowance of up to $2.7 million. If we use the additional allowance, ARE will have an enforceable right to payment by us in the form of equal monthly additional rent payments at a certain interest rate through the lease term. The useful life of improvements made under the additional allowance are the lesser of useful life or lease term. The terms include an initial annualized base rent of approximately $2.5 million which are subject to scheduled 3% annual rent increases, plus certain operating expenses. The lease has a 10-year term with one option to extend the term for an additional period of 5 years. We have provided ARE with an approximately $0.4 million security deposit in the form of a letter of credit. We have the right to sublease the facility, subject to landlord consent.

An estimated maturity analyses of the annual undiscounted cash flows of the operating lease is as follows (in thousands):

Years ending December 31,	Operating lease
2021	$ 208
2022	2,091
2023	2,582
2024	2,659
2025	2,739
Thereafter	17,690
Total minimum lease payments	27,969
Less: imputed interest	5,328
Lease obligations	$ 22,641

Selected Quarterly Financial Data (Unaudited)

The following table provides the selected quarterly financial data for 2020 and 2019:

Condensed Consolidated Statements of Operations
(In Thousands, Except Per Share Amounts)

	Quarter Ended [1]							
	December 31, 2020 [3]	September 30, 2020	June 30, 2020	March 31, 2020	December 31, 2019 [3]	September 30, 2019	June 30, 2019	March 31, 2019
Revenues:								
Product revenue	$ 12,215	$ 8,401	$ 4,504	$ 5,100	$ 4,877	$ 10,351	$ 6,249	$ 7,988
Research and development revenue	8,819	9,984	10,463	9,570	13,773	11,555	6,070	7,595
Total revenues	$ 21,034	$ 18,385	$ 14,967	$ 14,670	$ 18,650	$ 21,906	$ 12,319	$ 15,583
Costs and operating expenses:								
Cost of product revenue	$ 5,860	$ 3,642	$ 1,699	$ 2,541	$ 3,402	$ 5,067	$ 2,772	$ 4,391
Research and development	10,355	12,010	10,853	10,967	8,872	8,711	8,274	8,016
Selling, general and administrative	8,741	8,797	8,522	8,989	7,322	7,869	7,896	8,415
Total costs and operating expenses	$ 24,956	$ 24,449	$ 21,074	$ 22,497	$ 19,596	$ 21,647	$ 18,942	$ 20,822
Income (loss) from operations	$ (3,922)	$ (6,064)	$ (6,107)	$ (7,827)	$ (946)	$ 259	$ (6,623)	$ (5,239)
Income (loss) before income taxes	$ (3,912)	$ (6,075)	$ (6,037)	$ (7,647)	$ (630)	$ 336	$ (6,491)	$ (5,133)
Net income (loss)	$ (3,920)	$ (6,094)	$ (6,344)	$ (7,652)	$ (635)	$ 343	$ (6,507)	$ (5,136)
Net income (loss) per share, basic	$ (0.06)	$ (0.10)	$ (0.11)	$ (0.13)	$ (0.01)	$ 0.01	$ (0.12)	$ (0.09)
Net income (loss) per share, diluted	$ (0.06)	$ (0.10)	$ (0.11)	$ (0.13)	$ (0.01)	$ 0.01	$ (0.12)	$ (0.09)
Weighted average common shares used in computing net income (loss) per share, basic [2]	60,483	59,061	59,000	58,888	58,620	58,287	54,954	54,170
Weighted average common shares used in computing net income (loss) per share, diluted [2]	60,483	59,061	59,000	58,888	58,620	61,412	54,954	54,170

[1] Amounts were computed independently for each quarter, and the sum of the quarters may not total the annual amounts due to rounding differences.

[2] The full year net loss per share of common stock, basic and diluted, may not equal the sum of the quarters due to weighting of outstanding shares.

[3] PSUs, PBOs, and cash bonus awards are granted to certain employees and executives and are subject to our performance in achieving pre-determined criteria approved by our board of directors. Based on the actual achievement of the annual goals, we updated the calculation of the annual expense in the fourth quarter which resulted in estimate revisions of approximately $(0.1) million in 2020 and $(0.9) million in 2019, primarily in selling, general and administrative expense.

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURES

None.

ITEM 9A. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

Our management, under the supervision of our Chief Executive Officer and Chief Financial Officer and with the participation of our disclosure committee, evaluated the effectiveness of the design and operation of our disclosure controls and procedures as of December 31, 2020. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, as appropriate, to allow timely decisions regarding required disclosure. Based on this evaluation, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective as of December 31, 2020 at the reasonable assurance level.

Management's Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Exchange Act Rules 13a-15(f) and 15d-15(f). Internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external reporting purposes in accordance with United States generally accepted accounting principles.

Under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting as of December 31, 2020 based on the guidelines established in *Internal Control-Integrated Framework* (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). Based on the results of our evaluation, our management concluded that our internal control over financial reporting was effective as of December 31, 2020. We reviewed the results of management's assessment with our Audit Committee.

Our internal control over financial reporting as of December 31, 2020 has been audited by BDO USA, LLP, an independent registered public accounting firm, as stated in their report which is included in Item 8 of this Annual Report.

Inherent Limitations on Effectiveness of Controls

In designing and evaluating the disclosure controls and procedures, management recognizes that any controls and procedures, even if determined effective and no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives to prevent or detect misstatements. In addition, the design of disclosure controls and procedures must reflect the fact that there are resource constraints and that management is required to apply judgment in evaluating the benefits of possible controls and procedures relative to their costs. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting (as defined in Rule 13a-15(f) of the Exchange Act) identified in connection with the evaluation required by paragraph (d) of Rule 13a-15 or 15d-15 of the Exchange Act, which occurred during the fourth fiscal quarter of the year ended December 31, 2020, which has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting. Because of the impact of COVID-19 shelter-in-place orders, we have made minor modifications to existing controls involving evidence of review-type controls. Further, we implemented internal controls to ensure we adequately evaluated impairment of financial instruments and goodwill, respectively, in properly assessing and facilitating the impact and adoption on January 1, 2020 of ASU 2016-13, *Financial Instruments - Credit Losses (Topic 326)* and ASU No. 2017-04, *Intangibles - Goodwill and Other (Topic 350): Simplifying the Test for Goodwill Impairment.* There were no significant changes to our internal control over financial reporting due to the adoption of new standards.

ITEM 9B. OTHER INFORMATION

Not applicable.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

The information required by this item concerning our directors, executive officers, compliance with Section 16 of the Exchange Act, our code of ethics and our Nominating and Corporate Governance Committee, and our Audit Committee is incorporated by reference from the information that will be set forth in the sections under the headings "Election of Directors," "Other Matters—Section 16(a) Beneficial Ownership Reporting Compliance" and "Corporate Governance Matters" in the 2021 Proxy Statement.

ITEM 11. EXECUTIVE COMPENSATION

The information required by this item concerning executive compensation is incorporated by reference from the information that will be set forth in the 2021 Proxy Statement under the headings "Executive Compensation," and "Corporate Governance Matters."

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

The information required by this item concerning securities authorized for issuance under equity compensation plans and security ownership of certain beneficial owners and management is incorporated by reference from the information that will be set forth in the 2021 Proxy Statement under the headings "Executive Compensation—Equity Compensation Plan Information" and "Information Concerning Voting and Solicitation—Security Ownership of Certain Beneficial Owners and Management."

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

The information required by this item concerning transactions with related persons and director independence is incorporated by reference from the information that will be set forth in the 2021 Proxy Statement under the headings "Certain Relationships and Related Transactions" and "Corporate Governance Matters."

ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES

The information required by this item is incorporated by reference from the information that will be set forth in the 2021 Proxy Statement under the heading "Ratification of Independent Registered Public Accounting Firm—Principal Accounting Fees and Services."

PART IV

ITEM 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES

1. Financial Statements: See “Index to Consolidated Financial Statements” in Part II, Item 8 of this Annual Report on Form 10-K

2. Exhibits: The exhibits listed in the accompanying index to exhibits are filed or incorporated by reference as part of this Annual Report on Form 10-K.

EXHIBIT INDEX

Exhibit No.	Description
3.1	Amended and Restated Certificate of Incorporation of Codexis, Inc. filed with the Secretary of the State of the State of Delaware on April 27, 2010 and effective as of April 27, 2010 (incorporated by reference to Exhibit 3.1 to the Company's Quarterly Report on Form 10-Q for the quarter ended March 31, 2010, filed on May 28, 2010).
3.2	Certificate of Designations of Series A Junior Participating Preferred Stock of Codexis, Inc., filed with the Secretary of State of the State of Delaware on September 4, 2012 (incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K, filed on September 4, 2012).
3.3	Amended and Restated Bylaws of Codexis, Inc. effective as of April 27, 2010 (incorporated by reference to Exhibit 3.2 to the Company's Quarterly Report on Form 10-Q for the quarter ended March 31, 2010, filed on May 28, 2010).
4.1	Reference is made to Exhibits 3.1 through 3.3.
4.2	Form of the Company's Common Stock Certificate (incorporated by reference to Exhibit 4.1 to the Company's Quarterly Report on Form 10-Q for the quarter ended June 30, 2012, filed on August 9, 2012).
4.3	Description of the Common Stock of Codexis, Inc. (incorporated by reference to Exhibit 4.3 to the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2019, filed on February 28, 2020).
10.1A*	Lease Agreement by and between the Company and Metropolitan Life Insurance Company dated as of February 1, 2004.
10.1B*	Amendment to Lease Agreement by and between the Company and Metropolitan Life Insurance Company dated as of June 1, 2004.
10.1C*	Amendment to Lease Agreement by and between the Company and Metropolitan Life Insurance Company dated as of March 9, 2007.
10.1D*	Amendment to Lease Agreement by and between the Company and Metropolitan Life Insurance Company dated as of March 31, 2008.
10.1E	Fourth Amendment to Lease Agreement by and between the Company and Metropolitan Life Insurance Company dated as of September 17, 2010 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2010, filed on November 4, 2010).
10.1F	Fifth Amendment to Lease Agreement by and between the Company and Metropolitan Life Insurance Company dated as of March 16, 2011 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the quarter ended March 31, 2011, filed on May 6, 2011).
10.1G	Sixth Amendment to Lease by and between the Company and Metropolitan Life Insurance Company dated as of September 27, 2012 (incorporated by reference to Exhibit 10.6 to the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2012, filed on November 7, 2012).
10.1H	Seventh Amendment to Lease by and between the Company and Metropolitan Life Insurance Company dated as of October 11, 2016 (incorporated by reference to Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2016, filed on November 8, 2016).

Exhibit No.	Description
10.1I***	Eighth Amendment to Lease, dated as of February 8, 2019, by and between the Company and Metropolitan Life Insurance Company (incorporated by reference to Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q for the quarter ended March 31, 2019, filed on May 8, 2019).
10.2+*	Codexis, Inc. 2010 Equity Incentive Award Plan and Form of Stock Option Agreement.
10.3A+	Codexis, Inc. 2019 Incentive Award Plan (incorporated by reference to Exhibit 99.1 to the Company's Registration Statement on Form S-8 (File No. 333-232262) filed with the SEC on June 21, 2019).
10.3B+	Form of Restricted Stock Unit Award Grant Notice and Restricted Stock Unit Award Agreement under 2019 Incentive Award Plan (incorporated by reference to Exhibit 99.2 to the Company's Registration Statement on Form S-8 (File No. 333-232262) filed with the SEC on June 21, 2019).
10.3C+	Form of Stock Option Grant Notice and Stock Option Agreement under 2019 Incentive Award Plan (incorporated by reference to Exhibit 99.3 to the Company's Registration Statement on Form S-8 (File No. 333-232262) filed with the SEC on June 21, 2019).
10.3D+	Form of Stock Option Grant Notice and Stock Option Agreement under 2019 Incentive Award Plan (incorporated by reference to Exhibit 99.4 to the Company's Registration Statement on Form S-8 (File No. 333-232262) filed with the SEC on June 21, 2019).
10.3E+	Form of Performance Stock Unit Award Grant Notice and Performance Stock Unit Award Agreement under 2019 Incentive Award Plan (incorporated by reference to Exhibit 99.5 to the Company's Registration Statement on Form S-8 (File No. 333-232262) filed with the SEC on June 21, 2019).
10.3F+	Form of Restricted Stock Award Grant Notice and Restricted Stock Award Agreement under 2019 Incentive Award Plan (incorporated by reference to Exhibit 99.6 to the Company's Registration Statement on Form S-8 (File No. 333-232262) filed with the SEC on June 21, 2019).
10.4*	Form of Indemnification Agreement between the Company and each of its directors, officers and certain employees.
10.5+	Form of Amended and Restated Change in Control Severance Agreement between the Company and certain of its officers (incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2019, filed on November 6, 2019).
10.6	Asset Purchase Agreement, dated October 28, 2010, by and among the Company, Codexis Mayflower Holdings, LLC and Maxygen, Inc. (incorporated by reference to Exhibit 2.1 to the Company's Current Report on Form 8-K, filed on October 28, 2010).
10.7A†	Manufacture and Supply Agreement, dated May 16, 2011, by and between the Company and Lactosan GmbH & Co. KG (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the quarter ended June 30, 2011, filed on August 3, 2011).
10.7B	Amendment No. 1 to the Manufacture and Supply Agreement by and between the Company and Lactosan GmbH & Co. KG dated as of March 9, 2012 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the quarter ended March 31, 2012, filed on May 10, 2012).
10.8+	Employment Agreement by and between the Company and Ross Taylor effective as of August 4, 2019(incorporated by reference to Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2019, filed on November 6, 2019).
10.9A+	Employment Agreement by and between the Company and John Nicols effective as of May 28, 2012 (incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q for the quarter ended June 30, 2012, filed on August 9, 2012).

Exhibit No.	Description
10.9B+	John Nicols Stock Option Grant Notice and Stock Option Agreement dated June 13, 2012 between John J. Nicols and the Company (incorporated by reference to Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q for the quarter ended June 30, 2012, filed on August 9, 2012).
10.9C+	Amendment to Employment Agreement between the Company and John Nicols, dated April 21, 2016 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the quarter ended June 30, 2016, filed on August 9, 2016).
10.9D+	Amendment to Employment Agreement between the Company and John Nicols, dated November 16, 2017 (incorporated by reference to Exhibit 10.8E to the Company's Annual Report on Form 10-K for the year ended December 31, 2017, filed on March 15, 2018).
10.9E+	Amendment to Employment Agreement between the Company and John Nicols, effective as of June 28, 2019 (incorporated by reference to Exhibit 10.4 to the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2019, filed on November 6, 2019).
10.10A†	Sitagliptin Catalyst Supply Agreement by and between Merck Sharp and Dohme Corp. and the Company dated as of February 1, 2012 (incorporated by reference to Exhibit 10.25 to the Company's Annual Report on Form 10-K for the year ended December 31, 2012, filed on April 2, 2013).
10.10B†	Amendment to Sitagliptin Catalyst Supply Agreement between Merck Sharp and Dohme Corp. and the Company dated as of October 1, 2013 (incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2013, filed on November 12, 2013).
10.10C	Amendment No. 2 to Sitagliptin Catalyst Supply Agreement between Merck Sharp and Dohme Corp. and the Company dated as of February 25, 2015 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the quarter ended March 31, 2015, filed on May 7, 2015).
10.10D	Amendment No. 3 to Sitagliptin Catalysts Supply Agreement between Merck Sharp and Dohme Corp. and the Company dated as of December 17, 2015 (incorporated by reference to Exhibit 10.11D to the Company's Annual Report on Form 10-K for the year ended December 31, 2015, filed on March 8, 2016).
10.10E	Amendment No. 4 to Sitagliptin Catalysts Supply Agreement, effective as of January 1, 2016, by and between the Company and Merck Sharp and Dohme Corp. (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2016, filed on November 8, 2016).
10.11A†	Global Development, Option and License Agreement by and among the Company,Societé des Produits Nestlé S.A., formerly known as Nestec Ltd. ("Nestlé Health Science"), effective as of October 12, 2017 (incorporated by reference to Exhibit 10.10 to the Company's Annual Report on Form 10-K for the year ended December 31, 2017, filed on March 15, 2018).
10.11B†	Amendment No. 1 to Global Development, Option and License Agreement by and among the Company, Nestec Ltd. and Nestlé Amendment No. 1 to Global Development, Option and License Agreement by and among the Company, Nestec Ltd. and Nestlé Health Science S.A., effective as of July 26, 2018.(incorporated by reference to Exhibit 10.12B to the Company's Annual Report on Form 10-K for the year ended December 31, 2018, filed on March 3, 2019). Science S.A., effective as of July 26, 2018.
10.11C†	Letter Agreement to Global Development, Option and License Agreement by and among the Company, Nestec Ltd. and Nestlé Health Science S.A., effective as of December 12, 2018. (incorporated by reference to Exhibit 10.12C to the Company's Annual Report on Form 10-K for the year ended December 31, 2018, filed on March 3, 2019).
10.12A†	Platform Technology Transfer, Collaboration and License Agreement by and between the Company and GlaxoSmithKline Intellectual Property Limited, effective as of July 10, 2014 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the quarter ended September 31, 2014, filed on November 6, 2014).

Exhibit No.	Description
10.12B†	Letter Agreement, effective as of February 21, 2020, by and between Codexis, Inc. and GlaxoSmithKline Intellectual Property Development Limited (incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q for the quarter ended March 31, 2020, filed on May 8, 2020).
10.13A†	Platform Technology Transfer and License Agreement by and between the Company and Merck Sharp & Dohme Corp., dated as of August 3, 2015 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the quarter ended September 31, 2015, filed on November 6, 2015).
10.13B†	Amendment No. 1 to Platform Technology Transfer and License Agreement by and between the Company and Merck Sharp & Dohme Corp., dated as of October 10, 2018, incorporated by reference to Exhibit 10.14A to the Company's Annual Report on Form 10-K for the year ended December 31, 2018, filed on March 3, 2019).
10.13C***	Amendment No. 2 to Platform Technology Transfer and License Agreement by and between Merck and the Company dated as of January 1, 2019 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the quarter ended March 31, 2019, filed on May 8, 2019).
10.14***	Platform Technology Transfer and License Agreement, dated May 2, 2019, by and between the Company and Novartis Pharma AG (incorporated by reference to Exhibit 10.4 to the Company's Quarterly Report on Form 10-Q for the quarter ended June 30, 2019, filed on August 6, 2019).
10.15***	Strategic Collaboration and License Agreement by and between Shire Human Genetic Therapies, Inc., a wholly-owned subsidiary of Takeda Pharmaceutical Company Limited and the Company, dated March 23, 2020 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the quarter ended March 31, 2020, filed on May 8, 2020).
10.16A†	Loan and Security Agreement effective as of June 30, 2017 by and between the Company and Western Alliance Bank (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the quarter ended June 30, 2017, filed on August 9, 2017).
10.16B†	First Amendment to Loan and Security Agreement effective as of September 28, 2017 by and between the Company and Western Alliance Bank (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2017, filed on November 9, 2017).
10.16C†	Second Amendment to Loan and Security Agreement effective as of November 7, 2017 by and between the Company and Western Alliance Bank (incorporated by reference to Exhibit 10.15B to the Company's Annual Report on Form 10-K for the year ended December 31, 2017, filed on March 15, 2018).
10.16D†	Third Amendment to Loan and Security Agreement by and between the Company and Western Alliance Bank dated as of June 29, 2018 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the quarter ended June 30, 2018, filed on August 9, 2018).
10.16E†	Fourth Amendment to Loan and Security Agreement effective as of September 28, 2018 by and between the Company and Western Alliance Bank (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2018, filed on November 9, 2018).
10.16F	Fifth Amendment to Loan and Security Agreement effective as of January 23, 2019 by and between the Company and Western Alliance Bank (incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q for the quarter ended March 31, 2019, filed on May 8, 2019).
10.16G	Sixth Amendment to Loan and Security Agreement by and between the Company and Western Alliance Bank dated as of July 11, 2019 (incorporated by reference to Exhibit 10.1A to the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2019, filed on November 6, 2019).

Exhibit No.	Description
10.16H	Seventh Amendment to Loan and Security Agreement by and between the Company and Western Alliance Bank dated as of September 30, 2019 (incorporated by reference to Exhibit 10.1B to the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2019, filed on November 6, 2019).
10.16I	Eighth Amendment to Loan and Security Agreement by and between the Company and Western Alliance Bank dated as of September 30, 2020 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2020, filed on November 6, 2020.)
23.1	Consent of BDO USA, LLP, independent registered public accounting firm.
24.1	Power of Attorney (see signature page to this Annual Report on Form 10-K).
31.1	Certification of Principal Executive Officer Required Under Rule 13a-14(a) and 15d-14(a) of the Securities Exchange Act of 1934, as amended.
31.2	Certification of Principal Financial Officer Required Under Rule 13a-14(a) and 15d-14(a) of the Securities Exchange Act of 1934, as amended.
32.1**	Certification of Principal Executive Officer and Principal Financial Officer Required Under Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, and 18 U.S.C. §1350.
101	The following materials from Registrant's Annual Report on Form 10-K for the fiscal year ended December 31, 2020 formatted in Inline Extensible Business Reporting Language (iXBRL) includes: (i) Consolidated Balance Sheets at December 31, 2020 and December 31, 2019, (ii) Consolidated Statements of Operations for the years ended December 31, 2020, December 31, 2019 and December 31, 2018, (iii) Consolidated Statements of Cash Flows for the years ended December 31, 2020, December 31, 2019 and December 31, 2018, (vi) Consolidated Statements of Stockholders' Equity for the years ended December 31, 2020, December 31, 2019 and December 31, 2018 and (vii) Notes to Consolidated Financial Statements.
101.SCH	Inline XBRL Taxonomy Extension Schema Document
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104	The cover page from the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2020, formatted in Inline XBRL and contained in Exhibit 101.

+ Indicates a management contract or compensatory plan or arrangement.

† Confidential treatment has been granted for certain information contained in this exhibit. Such information has been omitted and filed separately with the Securities and Exchange Commission.

* Filed as exhibits to the registrant's Registration Statement on Form S-1 (File No. 333-164044), effective April 21, 2010, and incorporated herein by reference.

** Pursuant to Item 601(b)(32) of Regulation S-K this exhibit is furnished rather than filed with this report.

*** Portions of the exhibit, marked by brackets, have been omitted because the omitted information is (i) not material and (ii) would be competitively harmful if publicly disclosed.

ITEM 16. FORM 10-K SUMMARY

Not applicable.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

CODEXIS, INC.

Date: March 1, 2021

By: /s/ John J. Nicols
President and Chief Executive Officer
(Principal Executive Officer)

POWER OF ATTORNEY

Each person whose individual signature appears below hereby authorizes and appoints John J. Nicols, Ross Taylor and Richard A. Sabalot, and each of them, with full power of substitution and resubstitution and full power to act without the other, as his or her true and lawful attorney-in-fact and agent to act in his or her name, place and stead and to execute in the name and on behalf of each person, individually and in each capacity stated below, and to file any and all amendments to this annual report on Form 10-K and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing, ratifying and confirming all that said attorneys-in-fact and agents or any of them or their or his substitute or substitutes may lawfully do or cause to be done by virtue thereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the Registrant and in the capacities and on the dates indicated.

SIGNATURE	TITLE		DATE
/s/ John J. Nicols John J. Nicols	President, Chief Executive Officer and Director (Principal Executive Officer)	Date:	March 1, 2021
/s/ Ross Taylor Ross Taylor	Senior Vice President and Chief Financial Officer (Principal Financial and Accounting Officer)	Date:	March 1, 2021
/s/ Bernard J. Kelley Bernard J. Kelley	Chairman of the Board of Directors	Date:	March 1, 2021
/s/ Jennifer Aaker Jennifer Aaker	Director	Date:	March 1, 2021
/s/ Stephen Dilly Stephen Dilly	Director	Date:	March 1, 2021
/s/ Byron L. Dorgan Byron L. Dorgan	Director	Date:	March 1, 2021
/s/ Esther Martinborough Esther Martinborough	Director	Date:	March 1, 2021
/s/ Alison Moore Alison Moore	Director	Date:	March 1, 2021
/s/ David V. Smith David V. Smith	Director	Date:	March 1, 2021
/s/ Dennis P. Wolf Dennis P. Wolf	Director	Date:	March 1, 2021
/s/ Patrick Y. Yang Patrick Y. Yang	Director	Date:	March 1, 2021

Consent of Independent Registered Public Accounting Firm

Codexis, Inc.
Redwood City, California

We hereby consent to the incorporation by reference in the Registration Statements on Form S-8 (Nos. 333-167752, 333-172166, 333-179903, 333-187711, 333-194524, 333-202596, 333-210022, 333-216587, 333-223693, 333-224885, 333-230037, and 333-232262) and Form S-3ASR (No. 333-228693) of Codexis, Inc. of our reports dated March 1, 2021, relating to the consolidated financial statements and the effectiveness of Codexis, Inc.'s internal control over financial reporting, which appear in this Form 10K.

/s/BDO USA, LLP
San Jose, California
March 1, 2021

R-221 (11/20)

Exhibit 31.1

CERTIFICATION

I, John J. Nicols, certify that:

1. I have reviewed this Annual Report on Form 10-K of Codexis, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 1, 2021

/s/John J. Nicols

John J. Nicols

President and Chief Executive Officer

Exhibit 31.2

CERTIFICATION

I, Ross Taylor, certify that:

1. I have reviewed this Annual Report on Form 10-K of Codexis, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 1, 2021

/s/Ross Taylor

Ross Taylor
Senior Vice President and Chief Financial Officer

Exhibit 32.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report of Codexis, Inc. (the "Company") on Form 10-K for the fiscal year ended December 31, 2020, as filed with the Securities and Exchange Commission (the "Report"), John J. Nicols, President and Chief Executive Officer of the Company and Ross Taylor, Senior Vice President and Chief Financial Officer of the Company, respectively, do each hereby certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that:

- The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
- The information in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 1, 2021

/s/John J. Nicols
John J. Nicols
President and Chief Executive Officer

/s/Ross Taylor
Ross Taylor
Senior Vice President and Chief Financial Officer