

RAFAEL HOLDINGS, INC.

RAFAEL
Holdings, Inc.

2023 ANNUAL REPORT

Dear Fellow Stockholders:

In fiscal 2023, Rafael Holdings Inc. made significant progress toward our goal of further transitioning our focus toward clinical stage biotechnology assets. We started the fiscal year by completing the sale of our real estate assets in Newark, New Jersey for \$49 million with net proceeds of \$33 million (after payment of mortgage, taxes and commissions). We ended the fiscal year in a strong cash position with \$79 million in cash and cash equivalents.

Our balance sheet position enables us to opportunistically pursue strategic business development, given the distressed valuations that characterize much of the current biotech market. While we have evaluated many opportunities during the fiscal year, we remain committed to a disciplined approach given the continued pressure on the biotechnology market. Approximately 70% of the public companies that make up the biotech industry are trading at market capitalizations below \$100 million and over 200 companies have less than 12 months of cash runway. These numbers have been increasing for most of 2023. There were record levels of funding for biotechnology companies in 2020 and 2021. More recently, inflation, the significant increase in interest rates, and other factors have negatively impacted biotech valuations. We continue to be disciplined in selecting opportunities that have promising technologies in indications with real unmet medical need and where we believe our investment can advance the company's ability to achieve meaningful milestones that enhances value for our shareholders.

During the fiscal year, we made investments in two such companies, Cyclo Therapeutics, Inc. (Nasdaq: CYTH) and Day Three Labs, Inc. Cyclo Therapeutics is a clinical-stage biotechnology company whose lead drug candidate is Trappsol[®] Cyclo[™] (hydroxypropyl beta cyclodextrin), a treatment for Niemann-Pick Type C disease ("NPC"). NPC is a rare and fatal autosomal recessive genetic disease resulting in disrupted cholesterol metabolism that impacts the brain, lungs, liver, spleen, and other organs. Trappsol[®] Cyclo[™] is currently being evaluated in a Phase III Clinical Trial in Pediatric and Adult Patients with Niemann-Pick Disease Type C1.

Day Three Labs is a company which reimagines existing cannabis offerings with pharmaceutical-grade technology and innovation like Unlokt[™] to bring to market better, cleaner, more precise and predictable products in the cannabis industry. We believe that this emerging technology has the potential to deliver long term shareholder value through the development of treatments for patients suffering with disease.

We continue to believe in the potential represented by Lipomedix and Cornerstone Pharmaceuticals. During the fiscal year, Lipomedix progressed by overcoming earlier manufacturing challenges with Prometil[®] to move closer to starting a clinical trial in BRCA mutated cancers which we expect to initiate in 2024. Cornerstone Pharmaceuticals is progressing through a recapitalization to help it achieve financial flexibility to invest in its future. Cornerstone is anticipating data from an investigator-initiated phase I/II clinical trial of gemcitabine and cisplatin with or without CPI-613 as first line treatment for advanced unresectable biliary tract cancer in the coming months.

We expect the challenging market environment for biotechnology companies to persist through the coming year. We will allocate capital to existing investment companies as needed and appropriate and will continue to opportunistically vet and invest in opportunities that fit our strategic interests. We appreciate the support you have demonstrated during the year and remain confident that we will generate long term value for our shareholders.

Sincerely,



Bill Conkling
Chief Executive Officer

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

FORM 10-K

Annual report pursuant to section 13 or 15(d) of the Securities Exchange Act of 1934
for the year ended July 31, 2023.

or

Transition report pursuant to section 13 or 15(d) of the Securities Exchange Act of 1934.

Commission File Number: 000-55863

RAFAEL HOLDINGS, INC.
(Exact name of registrant as specified in its charter)

Delaware

82-2296593

(State or other jurisdiction of
incorporation or organization)

(I.R.S. Employer
Identification No.)

520 Broad Street, Newark, New Jersey 07102
(Address of principal executive offices, zip code)

(212) 658-1450
(Registrant's telephone number, including area code)

Securities registered pursuant to Section 12(b) of the Act:

<u>Title of each class</u>	<u>Trading Symbol</u>	<u>Name of each exchange on which registered</u>
Class B common stock, par value \$0.01 per share	RFL	New York Stock Exchange

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, smaller reporting company, or an emerging growth company. See definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	<input type="checkbox"/>	Accelerated filer	<input type="checkbox"/>
Non-accelerated filer	<input checked="" type="checkbox"/>	Smaller reporting company	<input checked="" type="checkbox"/>
Emerging growth company	<input checked="" type="checkbox"/>		

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.

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements.

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b).

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 the voting and non-voting stock held by non-affiliates of the registrant, based on the closing price on January 31, 2023 (the last business day of the registrant's most recently completed second fiscal quarter) of the Class B common stock of \$4.14 per share, as reported on the New York Stock Exchange, was approximately \$70.2 million.

The number of shares outstanding of the registrant's common stock as of October 27, 2023 was:

Class A common stock, par value \$0.01 per share:	787,163 shares
Class B common stock, par value \$0.01 per share:	23,719,472 shares (excluding 162,536 treasury shares)

DOCUMENTS INCORPORATED BY REFERENCE

The definitive proxy statement relating to the registrant's Annual Meeting of Stockholders, to be held January 10, 2024, is incorporated by reference into Part III of this Form 10-K to the extent described therein.

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RAFAEL HOLDINGS, INC.

Annual Report on Form 10-K

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This Annual Report contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934, including statements that contain the words “believes,” “anticipates,” “expects,” “plans,” “intends” and similar words and phrases. These forward-looking statements are subject to risks and uncertainties that could cause actual results to differ materially from the results projected in any forward-looking statement. In addition to the factors specifically noted in the forward-looking statements, other important factors, risks and uncertainties that could result in those differences include, but are not limited to, those discussed under Item 1A to Part I “Risk Factors” in this Annual Report. The forward-looking statements are made as of the date of this Annual Report, and we assume no obligation to update the forward-looking statements, or to update the reasons why actual results could differ from those projected in the forward-looking statements. Investors should consult all of the information set forth in this report and the other information set forth from time to time in our reports filed with the Securities and Exchange Commission pursuant to the Securities Act of 1933 and the Securities Exchange Act of 1934, including our reports on Forms 10-Q and 8-K.

Our business, operating results or financial condition could be materially adversely affected by any of the following risks associated with any one of our businesses, as well as the other risks highlighted elsewhere in this document. The trading price of our common stock could decline due to any of these risks. Note that references to “our”, “us”, “we”, “the Company”, etc. used in each risk factor below refers to the business about which such risk factor is provided.

Our business is subject to numerous risks as described in this section. Some of these risks include:

- *Preclinical and clinical drug development is a lengthy and expensive process, with an uncertain outcome. Our and the Pharmaceutical Companies’ preclinical and clinical programs may experience delays or may never advance, which would adversely affect the ability to obtain regulatory approvals or commercialize product candidates on a timely basis or at all, which could have an adverse effect on our business*
- *Our future success may depend on prospects for Cornerstone’s lead product candidate devimistat (CPI-613[®]) and results of Cyclo Therapeutics’ Phase III trial for Trappsol[®] Cyclo[™]. If either company is unable to gain regulatory approval or commercialize its product candidates or experiences significant delays in doing so, our business will be materially harmed.*
- *We and the companies in which we hold interests may expend our and their limited resources to pursue a particular product candidate or an indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.*
- *Results of preclinical studies and early clinical trials may not be predictive of results of future clinical trials.*
- *The companies in which we hold interests face substantial competition, and if competitors develop and market technologies or products more rapidly than those companies do or that are more effective, safer or less expensive than the product candidates that those companies develop, our commercial opportunities will be negatively impacted.*
- *Rafael Medical Devices’ device candidates may cause significant adverse events, toxicities or other undesirable side effects when used alone or in combination with other approved or cleared devices or investigational or approved drugs that may result in a safety profile that could prevent regulatory approval, prevent market acceptance, limit their commercial potential, result in significant negative consequences, or potential product liability claims.*
- *We rely significantly on information technology and any failure, inadequacy, interruption or security lapse of that technology, including any cyber security incidents, could harm our ability to operate our business and that of the companies in which we hold interests effectively.*
- *We may not be able to consummate any investment, business combination or other transaction.*
- *We are controlled by our principal stockholder, which limits the ability of other stockholders to affect the management of the Company.*

- *If the companies in which we hold interests are unable to adequately protect their proprietary technology and product candidates, if the scope of the patent protection obtained is not sufficiently broad, or if the terms of patents are insufficient to protect product candidates for an adequate amount of time, competitors could develop and commercialize technology and products similar or identical to that technology or those product candidates and the ability to successfully commercialize technology or product candidates may be materially impaired*
- *Public health threats could have an adverse effect on the Company's operations and financial results.*

As used in this Annual Report, unless the context otherwise requires, the terms the "Company," "Rafael Holdings," "we," "us," and "our" refer to Rafael Holdings, Inc., a Delaware corporation, and its subsidiaries, collectively. Each reference to a fiscal year in this Annual Report refers to the fiscal year ending in the calendar year indicated (for example, fiscal 2023 refers to the fiscal year ended July 31, 2023).

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Item 1. Business.

OVERVIEW

Rafael Holdings, Inc. (NYSE:RFL), (“Rafael Holdings”, “we” or the “Company”), a Delaware corporation, is a holding company with interests in clinical and early-stage pharmaceutical companies (the “Pharmaceutical Companies”), including an investment in Cornerstone Pharmaceuticals, Inc., formerly known as Rafael Pharmaceuticals Inc., a cancer metabolism-based therapeutics company, a majority equity interest in LipoMedix Pharmaceuticals Ltd. (“LipoMedix”), a clinical stage pharmaceutical company, the Barer Institute Inc. (“Barer”), a wholly-owned preclinical cancer metabolism research operation, an investment in Cyclo Therapeutics, Inc. (Nasdaq: CYTH) (“Cyclo Therapeutics” or “Cyclo”), a clinical-stage biotechnology company dedicated to developing life-changing medicines for patients and families living with challenging diseases through its lead therapeutic asset, Trappsol® Cyclo™, an investment in Day Three Labs, Inc. (“Day Three”), a company which reimagines existing cannabis offerings with pharmaceutical-grade technology and innovation like Unlokt™ to bring to market better, cleaner, more precise and predictable products in the cannabis industry, and a majority interest in Rafael Medical Devices, LLC, an orthopedic-focused medical device company developing instruments to advance minimally invasive surgeries (“Rafael Medical Devices” and Day Three Labs together with the Pharmaceutical Companies, represent our “Investment Companies”). In November 2022, the Company resolved to curtail its early-stage development efforts, including pre-clinical research at Barer. The decision was taken to reduce spending as the Company focuses on exploring strategic opportunities. The Company’s primary focus is to expand our investment portfolio through opportunistic and strategic investments including therapeutics which address high unmet medical needs.

Historically, the Company owned multiple real estate assets. In 2020, the Company sold an office building located in Piscataway, New Jersey and, on August 22, 2022, the Company sold the building at 520 Broad Street in Newark, New Jersey that serves as headquarters for the Company and several tenants and an associated public garage (the “520 Property”). See Note 3 for further details on the sale transaction. Currently, the Company holds a portion of a commercial building in Jerusalem, Israel as its remaining real estate asset.

The Company holds debt and equity investments in Cornerstone Pharmaceuticals that includes preferred and common equity interests and a warrant to purchase additional equity. On June 17, 2021, the Company entered into a merger agreement to acquire full ownership of Cornerstone Pharmaceuticals in exchange for issuing Company Class B common stock to the other stockholders of Cornerstone Pharmaceuticals. On October 28, 2021, the Company announced that the AVENGER 500 Phase 3 clinical trial for CPI-613® (devimistat), Cornerstone Pharmaceuticals’ lead product candidate, did not meet its primary endpoint of significant improvement in overall survival in patients with metastatic adenocarcinoma of the pancreas. In addition, following a pre-specified interim analysis, the independent data monitoring committee for the ARMADA 2000 Phase 3 study for devimistat recommended the trial to be stopped due to a determination that it was unlikely to achieve the primary endpoint (the “Data Events”). In connection with the preparation of the Company’s financial statements for the first quarter ended October 31, 2021, accounting principles generally accepted in the United States of America (“U.S. GAAP”) required that the Company assess the impact of the Data Events and determine whether the carrying values of the Company’s assets were impaired based upon the Company’s expectations to realize future value. In light of the Data Events, the Company concluded that the likelihood of further development of and prospects for CPI-613 is uncertain and fully impaired in the first quarter ended October 31, 2021 the value of its loans, receivables, and investment in Cornerstone Pharmaceuticals based upon its valuation of Cornerstone Pharmaceuticals. On February 2, 2022, the Company terminated the Merger Agreement with Cornerstone Pharmaceuticals, effective immediately, in accordance with its terms. Subsequently, on February 2, 2022, the Company withdrew its Registration Statement on Form S-4 related to the proposed Merger. Cornerstone is in the process of a comprehensive restructuring transaction as discussed more fully below and in Note 4 to the Consolidated Financial Statements.

Cyclo Therapeutics, Inc. is a clinical stage biotechnology company that develops cyclodextrin-based products for the treatment of neurodegenerative diseases. Cyclo’s lead drug candidate is Trappsol® Cyclo™ (hydroxypropyl beta cyclodextrin), a treatment for Niemann-Pick Type C disease (“NPC”). NPC is a rare and fatal autosomal recessive genetic disease resulting in disrupted cholesterol metabolism that impacts the brain, lungs, liver, spleen, and other organs. In January 2017 the FDA granted Fast Track designation to Trappsol® Cyclo™ for the treatment of NPC. Initial patient enrollment in the U.S. Phase I study commenced in September 2017, and in May 2020 Cyclo announced Top Line data showing a favorable safety and tolerability profile for Trappsol® Cyclo™ in this study. Cyclo is currently conducting a Phase 3 Clinical Trial Evaluating Trappsol® Cyclo™ in Pediatric and Adult Patients with Niemann-Pick

Disease Type C1. In May 2023, we purchased 2,514,970 shares of common stock and warrants to purchase an additional 2,514,970 shares of common stock of Cyclo. The purchase price for one share of common stock and a warrant to purchase one share of common stock was \$0.835. The warrants have an exercise price of \$0.71 and have a term of seven years.

In 2019, the Company established Barer, a wholly owned preclinical cancer metabolism research operation, to focus on developing a pipeline of novel therapeutic compounds, including compounds to regulate cancer metabolism with potentially broader application in other indications beyond cancer. In addition to its own internal discovery efforts, Barer pursued collaborative research agreements and in-licensing opportunities with leading scientists from top academic institutions. Barer's subsidiary, Farber Partners, LLC ("Farber"), was formed around one such agreement with Princeton University's Office of Technology Licensing for technology from the laboratory of Professor Joshua Rabinowitz, in the Department of Chemistry, Princeton University, for an exclusive worldwide license to its SHMT (serine hydroxymethyltransferase) inhibitor program. In November 2022, the Company resolved to curtail its early-stage development efforts, including pre-clinical research at the Barer Institute.

In 2016, the Company first invested in LipoMedix Pharmaceuticals Ltd. ("LipoMedix"), a clinical stage pharmaceutical company and holds a majority of the common stock.

In April 2023, the Company invested in Day Three Labs, the majority-owner of Day three Labs Manufacturing, a company which reimagines existing cannabis offerings with pharmaceutical-grade technology and innovation like Unlokt™ to bring to market better, cleaner, more precise and predictable products in the cannabis industry.

In May 2021, we formed Rafael Medical Devices, an orthopedic-focused medical device company developing instruments to advance minimally invasive surgeries.

Financial information by segment is presented in Note 15 in the Notes to our Consolidated Financial Statements in Item 8 of this Annual Report.

Our headquarters are located at 520 Broad Street, Newark, New Jersey 07102. The main telephone number at our headquarters is (212) 658-1450 and our corporate web site's home page is www.rafaelholdings.com.

We make available free of charge our Annual Report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and all amendments to these reports, and all beneficial ownership reports on Forms 3, 4 and 5 filed by directors, officers and beneficial owners of more than 10% of our equity through the investor relations page of our web site (<https://rafaeholdings.irpass.com>) as soon as reasonably practicable after such material is electronically filed with the Securities and Exchange Commission. Our web site also contains information not incorporated into this Annual Report on Form 10-K or our other filings with the Securities and Exchange Commission.

RECENT DEVELOPMENTS

On October 20, 2023, we exercised a warrant to purchase 2,514,970 shares of common stock of Cyclo and received a new warrant to purchase an additional 2,766,467 shares of common stock for an aggregate purchase price of \$1,785,629. The new warrants have an exercise price of \$0.95 per share and a term of four years.

On August 2, 2023, we increased our investment in Cyclo by purchasing 4,000,000 shares of common stock of Cyclo and warrants to purchase an additional 4,000,000 shares of common stock of Cyclo for an aggregate purchase price of \$5,000,000. The warrants have an exercise price of \$1.25 and a term of seven years.

In August 2023, Rafael Medical Devices raised \$925,000 from third parties after which we maintain approximately 53% of Rafael Medical Devices on a fully diluted basis

BUSINESS DESCRIPTION

We work to advance the pipeline development of our Investment Companies, including Cornerstone Pharmaceuticals, LipoMedix Cyclo Therapeutics, Rafael Medical Devices and Day Three Labs. We also further seek to expand our investment portfolio through opportunistic investments including therapeutics which address high unmet medical needs. Historically, the Company owned real estate assets. In 2020, the Company sold an office building located in Piscataway, New Jersey and following the end of Fiscal 2022, the Company sold the 520 Property. Currently, the Company holds a portion a commercial building in Jerusalem, Israel as its remaining real estate asset.

Investment Companies

Overview

We are a company with interests in clinical and early-stage pharmaceutical companies, through an investment in Cornerstone Pharmaceuticals, Inc., a clinical stage cancer metabolism-based therapeutics company, and a majority equity interest in LipoMedix Pharmaceuticals, a clinical stage pharmaceutical company. Our wholly-owned Barer Institute, is a preclinical cancer metabolism research operation formed in 2019 to focus on developing a pipeline of novel therapeutic compounds, including compounds to regulate cancer metabolism with potentially broader application in other indications beyond cancer. In addition to its own internal discovery efforts, Barer pursued collaborative research agreements and in-licensing opportunities with leading scientists from top academic institutions. Barer's majority owned subsidiary, Farber Partners, LLC ("Farber"), was formed around one such agreement with Princeton University's Office of Technology Licensing for technology from the laboratory of Professor Joshua Rabinowitz, in the Department of Chemistry, Princeton University, for an exclusive worldwide license to its SHMT (serine hydroxymethyltransferase) inhibitor program. In November 2022, the Company resolved to curtail its early-stage development efforts, including pre-clinical research at Barer. We are invested in Cyclo Therapeutics, Inc. (Nasdaq: CYTH) ("Cyclo Therapeutics" or the "Cyclo"), a clinical-stage biotechnology company dedicated to developing life-changing medicines for patients and families living with challenging diseases through its lead therapeutic asset, Trappsol® Cyclo™. Our focus to date has been to invest in and fund, discover, and develop novel therapies, and we further seek to expand our investment portfolio through opportunistic investments including therapeutics which address high unmet medical needs.

Cornerstone

We own our interest in Cornerstone through a 90%-owned non-operating subsidiary, Pharma Holdings, LLC ("Pharma Holdings"). Pharma Holdings owns 50% of CS Pharma Holdings, LLC ("CS Pharma"), a non-operating entity that owns equity interests in Cornerstone, including 44.0 million shares of Cornerstone Series D Convertible Preferred Stock and 979,617 common shares. Accordingly, the Company holds an effective 90% interest in its Cornerstone interests held by Pharma Holdings directly and an effective 45% indirect interest in its interest held by CS Pharma.

Cornerstone is in the process of a comprehensive restructuring transaction including, the conversion of the debt under a line of credit agreement and the promissory note held by the Company, the conversion and modification of other Cornerstone debt obligations, the extension of the Cornerstone debt held by RP Finance, a reverse stock split, the conversion of all outstanding preferred stock of Cornerstone into common stock and the adoption of certain governance measures. This transaction is subject to a number of conditions which are beyond the Company's control.

Science and Preclinical:

CPI-613[®] (devimistat) is a stable analog of normally transient, acylated catalytic intermediates of lipoate. The CPI-613[®] intermediates are designed to disrupt mitochondrial function and thereby decrease the TCA cycle function; thus, CPI-613[®] (devimistat) misinforms these tumor systems, triggering mitochondrial stress and turning off the cancer cell TCA cycle. CPI-613[®] is designed to broadly affect tumor metabolism, including disrupting mitochondria and potentially intercalating in cancer cell membranes. The metabolic and mitochondrial stress have been found to trigger apoptotic and necrotic cell death pathways in tumor cells (Zachar et al., J Mol Med, 2011, 89:1137-48; Stuart et al., Cancer Metab. 2014, 2, 4: reviewed in Bingham et al., Expert Rev Clin Pharmacol. 2014, 7:837-46 and Hammoudi et al., Chin J Cancer. 2011, ;30:508-25). Therefore CPI-613[®] is believed to have anti-cancer activity. Combining CPI-613[®] with generalized metabolic stressors like chemotherapy holds the potential to result in the effective killing of even the most intractable tumors like pancreatic cancer. These effects were observed in Cornerstone Pharmaceuticals' Phase 1/2 trials to date (Alistar, et al., 2017; Pardee et al., 2018). CPI-613[®] has been found to be selectively accumulated in tumors in animal studies. CPI-613 is a lipoic acid analog with a fatty acid tail that may be able to utilize fatty acid transporters. Cancer cells have been shown to up-regulate fatty acid metabolism to support tumorigenesis. Cornerstone continues to study devimistat and its potential mechanism of action.

There are potential advantages of CPI-613[®] (devimistat) over alternative anti-metabolism and anti-cancer drugs. It is believed to be selectively taken up by cancer cells. Therefore, CPI-613[®] (devimistat) is anticipated to be minimally toxic to healthy cells (i.e., safe, and well tolerated), potentially allowing extended treatment courses. Moreover, its toxicity profile may allow CPI-613[®] (devimistat) to be used in combination with other drugs and in older patients. These potential combination regimens include established standards of care for major malignancies, allowing potential

treatment of surgically unresectable cancers. Additionally, this toxicity profile could support the administration of cocktails of anti-cancer drugs that may work synergistically with CPI-613[®]. Thus, CPI-613[®] (devimistat) is being investigated for broad-spectrum activity, and the potential to treat diverse tumor types, including difficult-to-treat cancers, high-risk cancers, solid tumors as well as hematologic malignancies and advanced-stage cancers by targeting cancer metabolism.

Several pre-clinical pharmacology and toxicology studies (including good laboratory practice toxicology (GLP Tox) studies) were conducted to investigate the pharmacokinetics (PK), drug metabolism, safety, and anticancer activity of CPI-613[®] (devimistat). In *in vitro* and *ex vivo* studies, CPI-613[®] (devimistat) exhibited anticancer activities against tumor cell lines and cells. CPI-613[®] (devimistat) was taken up less in non-malignant cells. In vivo animal models bearing diverse tumor types were used to evaluate dose-response, PK, and metabolism of CPI-613[®] (devimistat). The drug was well tolerated in animal models studied. Prolonged survival was observed when compared to untreated controls in these animal models. GLP toxicology studies showed that any adverse events related to CPI-613[®] (devimistat) were considered transient and mostly observed during acute dosing; animals returned to normal post-dose (i.e., toxicities were reversible or recoverable). Toxicokinetic (TK) exposures of C_{max} (peak concentration) and area under curve (AUC) of CPI-613[®] (devimistat) from GLP Tox studies in rats and minipigs have shown safety margins expected to cover PK exposures of C_{max} and AUC of CPI-613[®] (devimistat) in AML and pancreatic cancer patients at doses studied.

Clinical Highlights:

More than 890 patients have been dosed with CPI-613[®] (devimistat) to date in 24 ongoing or completed clinical trials.

In a phase IB/II study of gemcitabine and cisplatin with or without CPI-613[®] (devimistat) as first-line therapy for patients with advanced biliary tract cancer (BiLT-04), in phase 1B portion, the objective response rate is 45% (1 complete response and 8 partial responses). Median progression-free survival is 10.0 months.

Currently, 4 clinical trials are enrolling participants:

- *A Multi-Center Randomized Phase IB/II Study of Gemcitabine and Cisplatin With or Without CPI-613[®] as First Line Therapy for Patients With Advanced Unresectable Biliary Tract Cancer (BiLT-04)*
- *Pilot Study of CPI-613[®], in Combination With Bendamustine, in Patients With Relapsed or Refractory T-Cell Non-Hodgkin Lymphoma*
- *A Phase I Dose-Escalation Study of CPI-613[®] in Combination With Chemoradiation in Patients With Pancreatic Adenocarcinoma*
- *Phase II Open-Label Multi-Cohort Study Evaluating CPI-613[®] in Combination With Hydroxychloroquine and 5-fluorouracil or Gemcitabine in Patients With Advanced Chemorefractory Colorectal, Pancreatic, or Other Solid Cancers*

Cornerstone is also contemplating additional clinical trials for devimistat in combination with other compounds for different indications.

In March 2023, Cornerstone purchased all assets and rights of telaglenastat (CB-839), a glutaminase inhibitor, from Calithera Biosciences, Inc. Cornerstone is currently exploring the options to develop telaglenastat in different oncology indications.

Barer

In 2019, the Company established Barer, as an early-stage small molecule research operation focused on developing a pipeline of novel therapeutic targets. The Barer programs are largely focused on new approaches to treat oncology including the regulation of cancer metabolism, synthetic lethal pathways, T-cell nutrients, and autoimmunity. Barer pursued collaborative research agreements and in-licensing opportunities with leading scientists from top academic institutions. Farber, a majority owned subsidiary of Barer, was formed around one such agreement with Princeton University's Office of Technology Licensing for technology from the laboratory of Professor Joshua Rabinowitz, in the Department of Chemistry, Princeton University, for an exclusive worldwide license to its SHMT (serine hydroxymethyltransferase) inhibitor program. In November 2022, the Company resolved to curtail its early-stage development efforts, including pre-clinical research at Barer.

LipoMedix

LipoMedix is a clinical stage Israeli company focused on the development of a product candidate that holds the potential to be innovative, safe, and effective cancer therapy based on liposome delivery. As of July 31, 2022, the Company's ownership interest in LipoMedix was approximately 95%.

About Promitil®:

LipoMedix was established to advance the pharmaceutical and clinical development of a patented prodrug of mitomycin-C (MMC) and its efficient delivery in liposomes to cancer cells. This proprietary molecule, known as Promitil — Pegylated Liposomal Mitomycin-C Lipidic Prodrug (PL-MLP) — is designed to overcome the toxicity associated with the clinical use of mitomycin-C and turns it into a targeted, anticancer therapeutic that could potentially become the treatment of choice in a variety of cancers with high unmet need. The inventor and scientific founder, of LipoMedix is Alberto Gabizon, M.D., Ph.D., of the Hebrew University — Shaare Zedek Medical Center, Israel. He is the co-inventor and co-developer of Doxil® (pegylated liposomal doxorubicin), a successful and widely used anticancer product based on a similar drug development strategy. Prof. Gabizon is one of the few scientists intimately familiar with the successful development and commercialization process of liposomal drugs.

Promitil® is designed for the targeted delivery of MMC in a proprietary prodrug form. Promitil® confers tumor targeting advantage due to the enhanced permeability and retention effect (EPR) of liposomes. Once in the tumor cells, the prodrug is converted to the active drug (MMC) by thiolytic agents abundantly present in tumor tissues, and MMC induces DNA cross-linking leading to tumor cell death. In preclinical studies, Promitil® inhibited cancer cells growth in animal models (pancreatic, colorectal, stomach, breast, ovarian, melanoma, bladder), including multidrug resistant tumors, as monotherapy as well as in combination with radiotherapy and/or approved cancer drugs. In these studies, Promitil® was found to be more efficacious and less toxic than MMC by a 3-fold factor.

LipoMedix has completed 3 clinical studies with Promitil® including:

1. Phase 1A, a dose escalation study of Promitil in patients with advanced cancers. (Golan et al., “Pegylated liposomal mitomycin C prodrug enhances tolerance of mitomycin C: a Phase 1 study in advanced solid tumor patients.” *Cancer Medicine*, 4:1472 – 1483, 2015).
2. Phase IB in advanced colorectal cancer patients with Promitil as single agent and in combination with capecitabine and/or bevacizumab. (Gabizon et al, “Pharmacokinetics of mitomycin-c lipidic prodrug entrapped in liposomes and clinical correlations in metastatic colorectal cancer patients” *Investigational New Drugs*, 38(5):1411 – 1420, 2020).
3. Phase 1B of Promitil-based chemo-radiotherapy in patients with advanced cancers. These study results have been presented at the ESTRO-2022 meeting in poster form.

Over 100 patients were treated with Promitil® as a single agent or in combination with other anticancer drugs or radiotherapy in three clinical studies under a United States IND to assess the safety, PK profile, and preliminary efficacy, as well as 40 patients treated as named-patient for compassionate use. Promitil® was given by intravenous infusion once every 3 or 4 weeks and appears to be well-tolerated at a dose up to 2 mg/kg. Except for mild myelosuppression, no other toxicities such as skin irritation, mouth ulcers, neuropathic pain, diarrhea, or hair loss were reported. Promitil® was stable in plasma with a half-life of approximately 20 hours (vs 40-50 minutes for naked MMC).

Next Steps for Clinical Development:

Homologous recombination (HR) is an evolutionarily conserved process for repairing DNA double-strand breaks with high fidelity, and the BRCA1 and BRCA2 proteins play essential roles in this process. Patients harboring germline mutations in the BRCA1 and/or BRCA2 genes have significantly increased life-time risk of developing breast, ovarian cancer, pancreatic, and prostate cancer. Tumors with BRCA mutations are susceptible to platinum-based chemotherapy and hypersensitive to agents that inhibit poly(ADP-ribose) polymerase (PARP). However, despite their initial anti-tumor activity, multiple resistance mechanisms have been described and the development of resistance limits the clinical utility of platinum based and PARP inhibitor (PARPi) therapies. Overall, it remains a challenge in treating cancers associated with deleterious germline mutation in HR, such as BRCA1, BRCA2, and PALB2 (Partner and Localizer of BRCA2).

Preclinical studies have shown that MMC was effective in killing of BRCA2 mutant tumors. Clinical efficacy of MMC has also been reported in heavily pretreated ovarian cancer patients with BRCA1 mutations and patient with advanced, gemcitabine-resistant, pancreatic cancer who had PALB2 gene mutation. Pancreatic ductal adenocarcinoma (PDAC) continues to be one of the most lethal malignant neoplasms, with a 5-year survival rate of only 5%. Surgery is considered the sole potentially curative treatment; however, only 20% of patients diagnosed with PDAC are candidates for surgery at the time of diagnosis and is frequently followed by recurrence and therapeutic resistance. Despite advances made in the development of systemic combination chemotherapies in the last two decades, progress in improving survival outcomes in patients with PDAC is stagnant.

Based on the reported preclinical and clinical efficacy of MMC in BRCA mutated tumors together with the demonstrated improved safety profile of Promitil in humans, LipoMedix believes that Promitil could offer an important therapeutic option for patients with pancreatic cancer. Thus, a clinical trial is planned to evaluate the safety, tolerability, and effects of Promitil in cancer patients who have deleterious germline mutation in BRCA1, BRCA2, or PALB2.

Promitil®-based pipeline products:

In addition to Promitil®, LipoMedix has developed other Promitil®-based products with potentially important applications:

- Folate-targeted Promitil® (Promi-Fol), aimed at local treatment (intravesical) of superficial bladder cancer. Decorating Promitil with folate ligands is designed to exploit the frequent overexpression of folate receptors in urothelial cancers for selective and enhanced delivery of Promitil® to cancer cells. Promi-Fol holds the potential to be a safe and effective therapeutic alternative to widely used instillation of mitomycin-c for local treatment of the growing elderly patient population with superficial bladder cancer (Patil Y, et al.: “Targeting of pegylated liposomal mitomycin-C prodrug to the folate receptor of cancer cells: Intracellular activation and enhanced cytotoxicity.” *Journal of Controlled Release*, 225:87-95, 2016). A patent application to cover the use of Promi-Fol was granted in May 2020 by the European Patent Office.
- Promi-Dox, a highly potent dual drug liposome with MLP and doxorubicin targeting a potential basket of tumors (Gabizon et al., “Liposome co-encapsulation of anti-cancer agents for pharmacological optimization of nanomedicine-based combination chemotherapy.” *Cancer Drug Resistance*, 4:463-484, 2021). There are several possible cancer settings with substantial patient numbers and significant unmet need where Promi-Dox potentially could be utilized. This formulation requires further product development. A patent application covering the formulation of Promi-Dox has been granted by the USPTO.

Cyclo Therapeutics Inc.

Cyclo is a clinical stage biotechnology company that develops cyclodextrin-based products for the treatment of neurodegenerative diseases. Cyclo filed a Type II Drug Master File with the U.S. Food and Drug Administration (“FDA”) in 2014 for its lead drug candidate, Trappsol® Cyclo™ (hydroxypropyl beta cyclodextrin) as a treatment for Niemann-Pick Type C disease (“NPC”). NPC is a rare and fatal autosomal recessive genetic disease resulting in disrupted cholesterol metabolism that impacts the brain, lungs, liver, spleen, and other organs. In 2015, Cyclo launched an International Clinical Program for Trappsol® Cyclo™ as a treatment for NPC. In 2016, Cyclo filed an Investigational New Drug application (“IND”) with the FDA, which described its Phase I clinical plans for a randomized, double blind, parallel group study at a single clinical site in the U.S. The Phase I study evaluated the safety and pharmacokinetics of Trappsol® Cyclo™ along with markers of cholesterol metabolism and markers of NPC during a 12-week treatment period of intravenous administration of Trappsol® Cyclo™ every two weeks to participants 18 years of age and older. The IND was approved by the FDA in September 2016, and in January 2017 the FDA granted Fast Track designation to Trappsol® Cyclo™ for the treatment of NPC. Initial patient enrollment in the U.S. Phase I study commenced in September 2017, and in May 2020, Cyclo announced Top Line data showing a favorable safety and tolerability profile for Trappsol® Cyclo™ in this study.

Cyclo has also completed a Phase I/II clinical study approved by European regulatory bodies with clinical trial centers in the United Kingdom, Sweden, and in Israel. The Phase I/II study evaluated the safety, tolerability and efficacy of Trappsol® Cyclo™ through a range of clinical outcomes, including neurologic, respiratory, and measurements of cholesterol metabolism and markers of NPC. Consistent with the 12-week phase I study (single US site), the European/Israel study administered Trappsol® Cyclo™ intravenously to NPC patients every two weeks in a double-blind,

randomized trial, but differs in that the study period was for 48 weeks (24 doses). In March of 2021, Cyclo announced that 100% of patients who completed the trial (9 out of 12) improved or remained stable, and 89% met the efficacy outcome measure of improvement in at least two domains of the 17-domain NPC severity scale.

Additionally, in February 2020, Cyclo had a face-to-face “Type C” meeting with the FDA with respect to the initiation of a pivotal Phase III clinical trial of Trappsol® Cyclo™ based on the clinical data obtained to date. At that meeting, Cyclo also discussed with the FDA submitting a New Drug Application (NDA) under Section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act for the treatment of NPC in pediatric and adult patients with Trappsol® Cyclo™. A similar request was submitted to the European Medicines Agency (“EMA”) in February 2020, seeking scientific advice and protocol assistance from the EMA for proceeding with a Phase III clinical trial in Europe. In October 2020, Cyclo received a “Study May Proceed” notification from the FDA with respect to the proposed Phase III clinical trial, and in June of 2021, Cyclo commenced enrollment in TransportNPC, a pivotal Phase III study of Trappsol® Cyclo™ for the treatment of NPC.

Preliminary data from their completed clinical studies suggest that Trappsol® Cyclo™ clears toxic deposits of cholesterol and other lipids from cells, has a consistent pharmacokinetic profile peripherally, and crosses the blood-brain-barrier in individuals suffering from NPC, and results in neurological and neurocognitive benefits and other clinical improvements in NPC patients. The full significance of these findings will be determined as part of the final analysis of data derived from our clinical trials (both completed and ongoing).

On May 17, 2010, the FDA designated Trappsol® Cyclo™ as an orphan drug for the treatment of NPC, which would provide Cyclo with the exclusive right to sell Trappsol® Cyclo™ for the treatment of NPC for seven years following FDA drug approval. In April 2015, Cyclo also obtained Orphan Drug Designation for Trappsol® Cyclo™ in Europe, which will provide Cyclo with 10 years of market exclusivity following regulatory approval, which period will be extended to 12 years upon acceptance by the EMA’s Pediatric Committee of our pediatric investigation plan (PIP) demonstrating that Trappsol® Cyclo™ addresses the pediatric population. On January 12, 2017, Cyclo received Fast Track Designation from the FDA, and on December 1, 2017, the FDA designated NPC a Rare Pediatric Disease.

Cyclo also continues to operate its legacy fine chemical business, consisting of the sale of cyclodextrins and related products to the pharmaceutical, nutritional, and other industries, primarily for use in diagnostics and specialty drugs.

Cyclo’s core business has transitioned to a biotechnology company primarily focused on the development of cyclodextrin-based biopharmaceuticals for the treatment of disease.

Global Phase III Clinical Study (TransportNPC)

Cyclo’s ongoing Phase III clinical trial (CTD-TCNPC-301), TransportNPC, is a prospective, randomized, double-blind, placebo controlled therapeutic study for up to 93 patients age three and older with confirmed diagnosis of NPC1. The objective of this study is to evaluate the safety, tolerability and efficacy of 2000 mg/kg doses of Trappsol® Cyclo™ (hydroxypropyl betacyclodextrin) administered intravenously by slow infusion every two weeks as compared to placebo. Patients will be randomized to receive Trappsol® Cyclo™ or placebo at a 2:1 ratio. The study duration is 96 weeks, with an unblinded interim analysis at 48 weeks. An open-label extension of up to 96 weeks follows the interventional study. Patients whose disease progression worsens by two levels in the Clinical Global Impression of Severity scale over 12 weeks, starting at week 36, may be moved to open label treatment. Efficacy will be measured at week 48 and week 96 by a composite score of major disease features. A sub-study is ongoing and being conducted outside of the U.S. for up to 12 patients age 0-3 years who may be asymptomatic. Outcomes for the sub-study are safety, clinical and caregiver impression of disease.

European and Israeli Phase I/II Clinical Study

Cyclo completed a Phase I/II clinical study in Europe, the United Kingdom and Sweden. This study evaluated the safety, tolerability and efficacy of Trappsol® Cyclo™ through a range of clinical outcomes, including neurologic, and respiratory, in addition to measurements of cholesterol metabolism and markers of NPC, in three dose groups (1500 mg/kg, 2000 mg/kg and 2500 mg/kg). The first patient was dosed in this study in July 2017, and in February 2020, Cyclo announced completion of enrollment of 12 patients in this study. The efficacy outcome measures and results from this study are as follows:

Efficacy Outcome Measure 1: At least a one-point reduction (or improvement) in two or more of the 17 domains measured under the NPC Clinical Severity Scale.

Results:

- Six of seven patients met this endpoint (86% of those who completed).
- Improvements seen in swallow, ambulation, ability to manage seizures, saccadic eye movements, fine motor skills, and cognition. (Individual patient profiles differed, i.e. patients improved differently.)
- Patients not receiving any intervention beyond standard of care would be expected to worsen in total score by 1.5 points over one year.

Efficacy Outcome Measure 2: Change from baseline in “Global Impression of Disease” at 48 weeks.

Results:

- Using the Clinician’s Global Impression of Improvement scale, five of seven patients who completed the trial improved, and the other 2 patients stabilized.
- five of seven improved in at least one of these features: walking, speaking, swallowing, fine motor and cognition. These five features are determined by NPC patients and their caregivers to be the most important for quality of life. A composite in improvement in these five features will be the primary outcome measure for our pivotal Phase III trial.

Additional Data:

- As a group, the first seven patients to complete the clinical trial meet both efficacy outcome measures for the study.
- Individual patients showed improvements in all dose groups.
- Trappsol® Cyclo™ demonstrated a highly favorable safety profile.
- Trappsol® Cyclo™ was shown to cross the blood brain barrier.
- Successive administration of Trappsol® Cyclo™ decreased tau levels, suggesting neuroprotective benefit.
- Trappsol® Cyclo™ improves neurological features of NPC, including ataxia, and quality of life for patients.
- Based on data provided, Cyclo selected the 2000 mg/kg dose for its pivotal Phase III trial.

US Phase I Clinical Study

In September 2016, the FDA approved Cyclo’s Phase I clinical plans for a randomized, double blind, parallel group study in the U.S. The Phase I study evaluated the safety of Trappsol® Cyclo™ along with markers of cholesterol metabolism and markers of NPC during a 14-week treatment period of intravenous administration of Trappsol® Cyclo™ every two weeks to participants 18 years of age and older in two dose groups (1500 mg/kg and 2500 mg/kg). Enrollment in this study was completed in October 2019, and in May 2020 Cyclo announced Top Line data showing a favorable safety and tolerability profile for Trappsol® Cyclo™ in this study. Additional data from this study includes the following data:

- Liver biopsies and biochemical data on cholesterol homeostasis demonstrated that Trappsol® Cyclo™ removes trapped cholesterol from liver cells and impacts cholesterol homeostasis.
- Tau decreased after seven doses in a majority of patients, suggesting that IV administration of Trappsol® Cyclo™ is preventing neurodegeneration in NPC patients.
- Efficacy signals from Trappsol® Cyclo™ include neurological improvements, higher energy, and greater focus exhibited by the patient.
- All eligible patients requested continuation of Trappsol® Cyclo™ administration in the extension protocol via home infusion.
- In January 2021, Cyclo reported positive efficacy data on all eight patients participating in the protocol.

Day Three Labs

Day Three Labs is a technology company focused on creating solutions for increased bioavailability of hydrophobic compounds, with a specific focus on compounds used as active ingredients in pharmaceutical and food supplement products. Day Three Labs maintains its manufacturing, sales and marketing activities in the United States, and research and development activities in Israel. Day Three Labs' majority-owned subsidiary, Day Three Labs Manufacturing, is dedicated to the commercialization of technology in the cannabis and hemp industries and has developed technological solutions specifically engineered for increased bioavailability of cannabinoids.

The Day Three Labs team, as well as that of its subsidiary Day Three Labs Manufacturing, has expertise in drug development, consumer product manufacturing and distribution, and product engineering, including pharmaceutical and food technology development. Day Three Labs as a group is positioning itself to target large addressable markets in the food supplement and pharmaceutical spaces, focusing its research and development on active ingredients with maximum addressable scope.

Rafael Medical Devices

Rafael Medical Devices is an orthopedic-focused medical device company currently concentrating on developing surgical and procedural devices designed to provide meaningful advantages to patients and healthcare providers. One of its current lead products is an orthopedic arthroscopy instrumentation.

Rafael Medical Devices has assembled an in-house team with expertise in engineering, quality, design discovery, and device development who have created successful commercial medical devices in the past. It has begun to expand its expert network of experienced device creators, key opinion leaders, and hoped to begin generating a commercial presence.

Orthopedics comprise a large addressable market. Rafael Medical Devices is seeking to assemble a portfolio of Class I, II and III devices to mitigate risk across a portfolio of devices with overlapping needs and markets. This strategy is designed to minimize supply chain requirements while maximizing market potential.

OUR STRATEGY

We are a company with interests in clinical and early-stage Investment Companies, through our investment in Cornerstone Pharmaceuticals, our majority equity interest in LipoMedix, Barer Institute, interests in Cyclo Therapeutics and Day Three Labs, and a majority interest in Rafael Medical Devices. Historically, our focus was on investing in and funding entities to discover and develop novel cancer therapies.

The focus of our efforts is subject to change with market conditions, results of our internal development efforts, the availability of investment opportunities on acceptable terms, the investment and acquisition opportunities we may pursue, and developments at those targets. More recently, we have expanded our focus to opportunities in the pharmaceutical industry not exclusively focused on cancer therapies, other healthcare-related investments and opportunities outside of biopharma.

Our goal within biopharma is to expand our portfolio and develop and bring to market therapeutics which address high unmet medical needs, opportunistic investments, acquisitions and in-licensing of assets.

We plan to continue to invest in pre-clinical and clinical stage healthcare opportunities, including those in which we already own interests, when determined to be consistent with our goals, and move toward clinical stage programs as research and development results warrant, while being ready to exploit other opportunities that may arise.

Our internal and external investment decisions will be based on the progress and results of our development and pre-clinical activities and other operational developments, and the availability of targets for investment, acquisition or licensing.

GOVERNMENT REGULATION AND COMPLIANCE

Our operations, products, and potential future customers are subject to extensive government regulation by the FDA and other federal and state authorities in the United States, as well as comparable authorities in foreign jurisdictions. The global regulatory environment is increasingly stringent, unpredictable, and complex. There is a global trend toward increased regulatory activity related to medical products.

In the U.S., our product candidates and device candidates are regulated as either drugs or biological products under the Federal Food, Drug and Cosmetic Act, or FDCA, and the Public Health Service Act, or PHSA, and their implementing regulations, or as medical devices under the FDCA and its implementing regulations, each as amended and enforced by the FDA. These laws govern the processes by which our product candidates and device candidates would be brought to market. The FDA has enacted extensive regulations that control all aspects of the development, design, non-clinical and clinical research, manufacturing, safety, efficacy, labeling, packaging, storage, installation, servicing, recordkeeping, premarket clearance or approval, adverse event reporting, advertising, promotion, marketing and distribution, postmarket surveillance, and import and export of drugs, biological products, and medical devices. In addition, the FDA controls the access of products to market through processes designed to ensure that only products that are safe and effective for their intended use(s) and otherwise meet the applicable requirements of the FDCA and/or PHSA before they are made available to the public.

Review And Approval Of Drugs In The United States

In the United States, the FDA approves and regulates drugs under the FDCA, and its implementing regulations. The failure to comply with requirements under the FDCA and other applicable laws at any time during the product development process, approval process or after approval may subject an applicant and/or sponsor to a variety of administrative or judicial sanctions, including refusal by the FDA to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters and other types of compliance letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement of profits, or civil or criminal investigations and penalties brought by the FDA and the Department of Justice or other governmental entities.

Each of Cornerstone's, LipoMedix's, Cyclo Therapeutics', and Barer's (collectively referred to as the "Pharmaceutical Companies") product candidates must be approved by the FDA through a New Drug Application, or NDA. An applicant seeking approval to market and distribute a new drug product in the United States must typically undertake the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice, or GLP, regulations;
- submission to the FDA of an Investigational New Drug, or IND, application, which must take effect before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practices, or GCP, to establish the safety and efficacy of the proposed drug product for each indication;
- preparation and submission to the FDA of an NDA requesting marketing for one or more proposed indications;
- review by an FDA advisory committee, where appropriate if applicable;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the product, or components thereof, are produced to assess compliance with current Good Manufacturing Practices, or cGMP, requirements and to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;
- satisfactory completion of FDA audits of clinical trial sites to assure compliance with GCP and the integrity of the clinical data;
- payment of user fees and securing FDA approval of the NDA; and
- compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy, or REMS, and the potential requirement to conduct post-approval studies.

Before an applicant begins testing a compound with potential therapeutic value in humans, the drug candidate enters the preclinical testing stage. Preclinical studies include laboratory evaluation of product chemistry, toxicity and formulation, and the purity and stability of the drug substance, as well as *in vitro* and animal studies to assess the potential safety and activity of the drug for initial testing in humans and to establish a rationale for therapeutic use. The conduct of the preclinical tests must comply with federal regulations and requirements including good laboratory practices, or GLP, requirements. The sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. An IND is an exemption from the FDCA that allows an unapproved drug to be shipped in interstate commerce for use in an investigational clinical trial and a request for FDA authorization to administer an investigational drug to humans. Such authorization must be secured prior to interstate shipment and administration of any new drug that is not the subject of an approved NDA. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA places the clinical trial on a clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. The FDA may also impose clinical holds on a drug candidate at any time before or during clinical trials due to safety concerns or non-compliance.

A sponsor may choose, but is not required, to conduct a foreign clinical study under an IND. When a foreign clinical study is conducted under an IND, all FDA IND requirements must be met unless waived. When the foreign clinical study is not conducted under an IND, the sponsor must ensure that the study complies with certain FDA regulatory requirements to use the study as support for an IND or application for regulatory approval. Such studies must be conducted in accordance with GCP, including review and approval by an independent ethics committee, or IEC, and informed consent from subjects. The GCP requirements encompass both ethical and data integrity standards for clinical studies. The FDA's regulations are intended to help ensure the protection of human subjects enrolled in non-IND foreign clinical studies, as well as the quality and integrity of the resulting data. They further help ensure that non-IND foreign studies are conducted in a manner comparable to that required for IND studies.

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research subjects provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written study protocols detailing, among other things, the objectives of the study, inclusion and exclusion criteria, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. Each protocol must be submitted to the FDA as part of the IND before a clinical trial can begin in the US. In addition, an IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at each institution, and the IRB must conduct continuing review and reapprove the study at least annually. The IRB must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects.

Human clinical trials are typically conducted in four sequential phases, which may overlap or be combined under certain limited circumstances when authorized by FDA:

Phase 1. The drug is initially introduced into a small number of healthy human subjects or, in certain indications such as cancer, patients with the target disease or condition (e.g., cancer) and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness and to determine optimal dosage.

Phase 2. The drug is administered to a limited number of patients in the target patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for a specific targeted disease and to determine dosage tolerance and optimal dosage.

Phase 3. These clinical trials are commonly referred to as “pivotal” studies, which denotes a study or studies that present the pivotal data (but not the only data) that the FDA or other relevant regulatory agency will use to determine whether or not to approve a drug. The drug is administered to an expanded number of patients in the target patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product, and to provide adequate information for the labeling of the product.

Phase 4. Post-approval studies may be required to be conducted, or a sponsor may decide on its own to conduct them, in order to collect additional data after initial regulatory approval. These studies are used to gain additional experience and additional safety and/or efficacy data from the treatment of patients in the intended therapeutic indication.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur. In addition, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions; findings from other studies or animal or in vitro testing that suggest a significant risk in humans exposed to the drug; and any clinically important increase in the case of a serious suspected adverse reaction over that listed in the investigator brochure.

Concurrent with clinical trials, companies often complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and, among other things, the sponsor must develop methods for testing the identity, strength, quality, purity, and potency of the final drug. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration in that packaging over its shelf life.

If clinical trials are successful, the next step in the drug development process is the preparation and submission to the FDA of an NDA or BLA, Biologics License Application. The NDA or BLA is the vehicle through which drug applicants formally propose that the FDA approve a new drug or biologic for marketing and sale in the United States for one or more indications. The results of product development, preclinical studies, and clinical trials, along with detailed descriptions of the manufacturing process, analytical tests conducted on the chemistry of the drug, proposed labeling, and other relevant information are submitted to the FDA as part of an NDA or BLA requesting approval to market the product. The submission of an NDA or BLA is subject to the payment of substantial user fees; a waiver of such fees may be obtained under certain limited circumstances. For example, products with orphan drug designation are not subject to user fees.

The FDA reviews all NDAs and BLAs submitted to identify if there are any deficiencies before it can officially accept the applications for in-depth review, also known as “filing” of the NDA or BLA. The FDA may also request additional information before deciding whether to accept an NDA or BLA for filing. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA or BLA.

After the NDA or BLA submission is accepted for filing, the FDA reviews the NDA or BLA to determine, among other things, whether the proposed product is safe and effective for its intended use, whether the product is being manufactured in accordance with cGMP to assure and preserve the product’s identity, strength, quality, and purity, and whether the product has appropriate labeling for its intended use. There is a two-tiered system of review times — standard review and priority review. A priority review designation means FDA’s goal is to take action on an application within six months (compared to 10 months under standard review) in addition to the 2-month filing period. During the approval process, the FDA also will determine whether a risk evaluation and mitigation strategy, or REMS, is necessary to assure the safe use of the drug or biologic following its approval. If the FDA concludes that a REMS is needed, the sponsor of the NDA must submit a proposed REMS; the FDA will not approve the NDA without a REMS, if a REMS is deemed to be required.

Before approving an NDA or BLA, the FDA will typically inspect the facilities at which the product is to be manufactured. These preapproval inspections may cover all facilities associated with an NDA or BLA submission, including drug component manufacturing (e.g., active pharmaceutical ingredients), finished drug product manufacturing, and control testing laboratories. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA or BLA, the FDA will typically inspect one or more clinical trial sites to assure compliance with GCP.

The FDA is required to refer an application for a novel drug to an advisory committee or explain why such referral was not made. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions about the approval of the drug.

On the basis of the FDA's evaluation of the NDA or BLA and accompanying information, including the results of the inspection of the manufacturing facilities and clinical trial sites, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for a specific indication or indications. A complete response letter generally outlines the deficiencies in the application and may require the sponsor to undertake substantial additional testing or gather significant additional data and information in order for the FDA to reconsider the application. If a complete response letter is issued, the applicant may either resubmit the application, addressing all of the deficiencies identified in the complete response letter, or withdraw the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA or BLA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included and the FDA's classification of the resubmission. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

If a product receives regulatory approval, the approval may be limited to a specific disease(s) and dosage(s) or the indication(s) for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling. In addition, the FDA may require phase 4 testing, which involves post-approval clinical trials designed to further assess a product's safety and/or effectiveness, and also may require testing and surveillance programs to monitor the safety of approved products that have been commercialized.

Fast track, breakthrough therapy, and priority review designations

The FDA is authorized to designate certain products for expedited review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs are fast track designation, breakthrough therapy designation, and priority review designation.

Accelerated approval pathway

The FDA may grant accelerated approval to a product for a serious or life-threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. The FDA may also grant accelerated approval for such a condition when the product has an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality, or IMM, and that is reasonably likely to predict an effect on IMM or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. Products granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval. If post-marketing clinical studies fail to verify clinical benefit, FDA may withdraw approval.

Post-Approval Requirements

Any drug that receives FDA approval is subject to continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion, and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, by submitting supplemental NDAs, are subject to prior FDA review and approval. There also are continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers, packagers or distributors that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. 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; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, suspension of the approval, product recalls, or complete withdrawal of the product from the market;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or BLAs or supplements to approved NDAs or BLAs, or suspension or revocation of product approvals;
- product seizure or detention, or refusal to permit the import or export of products; and/or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising, and promotion of products that are placed on the market. Drugs may be promoted only for the approved indication(s) and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting false or misleading promotion and the promotion of off-label uses, which require that promotion is truthful, not misleading, fairly balanced and provides adequate directions for use, and that all claims are substantiated, and which also prohibit the promotion of products for unapproved or “off-label” uses and impose other restrictions on labeling, in accordance with FDA guidance on off-label dissemination of information and responding to unsolicited requests for information. A company that is found to have improperly promoted off-label uses or engaged in any other false or misleading promotion may be subject to significant liability and enforcement actions.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, and its implementing regulations, as well as the Drug Supply Chain Security Act, or DSCA, which regulate the distribution and tracing of prescription drugs and prescription drug samples at the federal level, and set minimum standards for the regulation of drug distributors by the states. The PDMA, its implementing regulations, and state laws limit the distribution of prescription pharmaceutical product samples, and the DSCA imposes requirements to ensure accountability in distribution and to identify and remove counterfeit and other illegitimate products from the market.

Abbreviated new drug applications for generic drugs

In 1984, with passage of the Hatch-Waxman Amendments to the FDCA, Congress established an abbreviated regulatory scheme authorizing the FDA to approve generic drugs that are shown to contain the same active ingredients as, and to be bioequivalent to, drugs previously approved by the FDA pursuant to NDAs. To obtain approval of a generic drug, an applicant must submit an abbreviated new drug application, or ANDA, to the agency. An ANDA is a comprehensive submission that contains, among other things, data and information pertaining to the active pharmaceutical ingredient, bioequivalence, drug product formulation, specifications, and stability of the generic drug, as well as analytical methods, manufacturing process validation data, and quality control procedures. ANDAs are “abbreviated” because they generally do not include preclinical and clinical data to demonstrate safety and effectiveness. Instead, in support of such applications, a generic manufacturer may rely on the FDA’s prior determination of safety and effectiveness based upon the preclinical and clinical testing previously conducted for a drug product previously approved under an NDA, known as the reference-listed drug, or RLD.

505(b)(2) NDAs

As an alternative path to FDA approval for modifications to formulations or uses of products previously approved by the FDA pursuant to an NDA, an applicant may submit an NDA under Section 505(b)(2) of the FDCA. Section 505(b)(2) was enacted as part of the Hatch-Waxman Amendments and permits the filing of an NDA where at least some of the information required for approval comes from studies not conducted by, or for, the applicant. If the 505(b)(2) applicant can establish that reliance on FDA’s previous finding of safety and effectiveness of the RLD is scientifically and legally appropriate, it may eliminate the need to conduct certain preclinical or clinical

studies of the new product. The FDA may also require companies to perform additional studies or measurements, including clinical trials, to support the change from the previously approved RLD. The FDA may then approve the new product candidate for all, or some, of the label indication(s) for which the RLD has been approved, as well as for any new indication(s) for which approval is sought by the 505(b)(2) applicant.

Pediatric studies and exclusivity

Under the Pediatric Research Equity Act, an NDA or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the drug product for the claimed indication(s) in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. With enactment of FDASIA 2012, sponsors must also submit pediatric study plans prior to the assessment data. Those plans must contain an outline of the proposed pediatric study or studies the applicant plans to conduct, including study objectives and design, any deferral or waiver requests, and any other information required by regulation. The applicant, the FDA, and the FDA's internal review committee must then review the information submitted, consult with each other, and agree upon a final plan. The FDA or the applicant may request an amendment to the plan at any time. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. Additional requirements and procedures relating to waiver requests, deferral requests and requests for extension of deferrals are contained in FDASIA. Unless and until FDA promulgates a regulation stating otherwise, the pediatric data requirements do not apply to products with orphan designation. However, in accordance with FDARA 2017, certain orphan designated cancer drugs are no longer exempt from having to conduct pediatric studies. FDARA requires that any original NDA or BLA submitted on or after August 18, 2020, for a new active ingredient, must contain studies of molecularly targeted pediatric cancers, unless a deferral or a waiver is granted, if the drug that is the subject of the application is intended for the treatment of an adult cancer and directed at a molecular target that the FDA determines to be substantially relevant to the growth or progression of a pediatric cancer.

Orphan drug designation and exclusivity

Under the Orphan Drug Act, the FDA may designate a drug product as an "orphan drug" if it is intended to treat a rare disease or condition, generally meaning that it affects fewer than 200,000 individuals in the United States, or more in cases in which there is no reasonable expectation that the cost of developing and making a drug product available in the United States for treatment of the disease or condition will be recovered from sales of the product. A company must request orphan drug designation before submitting an NDA or BLA for the drug for the rare disease or condition. If the request is granted, the FDA will disclose the identity of the therapeutic agent and its potential use(s). Orphan drug designation does not shorten the PDUFA goal dates for the regulatory review and approval process, although it does convey certain advantages such as tax benefits and exemption from the PDUFA application fee. The first applicant to obtain approval of an orphan drug is eligible for seven years of exclusivity for a drug, or twelve years of exclusivity for a biologic, during which FDA may not approve the same drug for the same approved orphan indication unless the subsequent product is shown to be clinically superior or if the FDA withdraws exclusive approval or revokes orphan drug designation, or if the marketing application (NDA or BLA) for the orphan drug is withdrawn for any reason, or if the holder of the orphan exclusive approval fails to assure a sufficient quantity of the orphan drug.

Patent term restoration and extension

A patent claiming a new drug product or its method of use may be eligible for a limited patent term extension, also known as patent term restoration, under the Hatch-Waxman Act, which permits a patent restoration of up to five years for patent term lost during product development and the FDA regulatory review process. Patent term extension is generally available only for drug products whose active ingredient has not previously been approved by the FDA. The restoration period granted is typically one-half the time between the effective date of an IND and the submission date of an NDA, plus the time between the submission date of an NDA and the ultimate approval date, up to a maximum of five years. Patent term extension cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date. Only one patent applicable to an approved drug product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent in question. A patent that covers multiple drugs for which approval is sought can only be extended in connection with one of the approvals. The United States Patent and Trademark Office, or PTO, reviews and approves the application for any patent term extension in consultation with the FDA upon PTO's determination that the requirements for an extension have been met.

FDA approval and regulation of companion diagnostics

If safe and effective use of a therapeutic depends on a diagnostic, a medical device that is often an *in vitro* diagnostic or IVD, then the FDA generally will require approval or clearance of that diagnostic, known as a companion diagnostic, at the same time that the FDA approves the therapeutic product. In August 2014, the FDA issued final guidance clarifying the requirements that will apply to approval of therapeutic products and *in vitro* companion diagnostics. According to the guidance, for novel drugs, a candidate IVD companion diagnostic and its corresponding therapeutic should be co-developed and approved or cleared contemporaneously by the FDA for the use indicated in the therapeutic product's labeling. In July 2016, the FDA issued a draft guidance detailing general principles to guide co-development of an *in vitro* companion diagnostic device with a therapeutic product.

Review And Approval Or Clearance Of Medical Devices In The United States

Unless an exemption applies, each medical device commercially distributed in the United States requires either FDA clearance of a Premarket Notification, or 510(k), FDA approval of a Premarket Approval, or PMA, application, or FDA marketing authorization in response to a De Novo request. Under the FDCA, medical devices are classified into one of three classes — Class I, Class II or Class III — depending on the degree of risk associated with each medical device and the extent of manufacturer and regulatory control needed to ensure the device's safety and effectiveness. Devices deemed by the FDA to pose the greatest risks, such as life sustaining, life supporting or some implantable devices, or devices that have a new intended use, or that use advanced technology which is not substantially equivalent to that of a legally marketed device, are generally placed into Class III.

While most Class I devices are exempt from the 510(k) premarket notification requirement, manufacturers of most Class II devices are required to submit to the FDA a premarket notification under Section 510(k) of the FDCA requesting permission to commercially distribute the device. The FDA's permission to commercially distribute a device subject to a 510(k) premarket notification is generally known as 510(k) clearance. Class III devices require approval of a PMA evidencing safety and effectiveness of the device. Certain novel devices of low to moderate risk, for which the FDA can make a risk-based classification of the device into Class I or II, can receive marketing authorization in response to a De Novo request.

To obtain 510(k) clearance, a manufacturer must submit a 510(k) premarket notification demonstrating to the FDA's satisfaction that the proposed device is at least as safe and effective as, that is, "substantially equivalent" to, another legally marketed device that itself does not require PMA approval, or a predicate device. A predicate device is a legally marketed device that is not subject to premarket approval, *i.e.*, a device that was legally marketed prior to May 28, 1976 (pre-amendments device) and for which a PMA is not required, a device that has been reclassified from Class III to Class II or I, or a device that was found substantially equivalent through the 510(k) process. The sponsor must submit information that supports its substantial equivalency claims. The FDA's 510(k) clearance process usually takes from three to twelve months, but often takes longer. FDA may require additional information, including clinical data, to make a determination regarding substantial equivalence. In addition, the FDA collects user fees for certain medical device submissions and annual fees for medical device establishments.

Before the sponsor can market a new device that is the subject of a 510(k) premarket notification, the sponsor must receive an order from the FDA finding substantial equivalence and clearing the new device for commercial distribution in the US. If the FDA agrees that the device is substantially equivalent to a lawfully marketed predicate device, it will grant 510(k) clearance to authorize the device for commercialization. If the FDA determines that the device is "not substantially equivalent," the device is automatically designated as a Class III device. The device sponsor then must either fulfill the more rigorous PMA requirements, or the sponsor can submit a De Novo request seeking a risk-based classification determination for the device in accordance with the FDA's De Novo classification process, which is a route to market for novel medical devices that are low to moderate risk and are not substantially equivalent to a predicate device. A sponsor also can submit a De Novo classification request directly, without first submitting a 510(k), if the sponsor determines that there is no legally marketed predicate device upon which to base a determination of substantial equivalence.

After a device receives 510(k) clearance, any modification that could significantly affect its safety or effectiveness, or that would constitute a major change or modification in its intended use, will require a new 510(k) clearance or, depending on the modification, PMA approval or De Novo classification. The FDA requires each manufacturer to determine in the first instance whether the proposed change requires submission of a 510(k), a De Novo classification request or a PMA, but the FDA can review any such decision and disagree with a sponsor's determination. If the FDA

disagrees with a manufacturer's determination not to seek a new 510(k) or other form of marketing authorization for a modification to a 510(k)-cleared product, the FDA can require the manufacturer to cease marketing and/or request the recall of the modified device until 510(k) clearance or PMA approval is obtained or a De Novo classification is granted.

The PMA process is more demanding than either the 510(k) premarket notification process or the De Novo classification process and includes stringent clinical investigation and other requirements. In a PMA, the manufacturer must demonstrate that the device is safe and effective, and the PMA must be supported by extensive data, including data from preclinical studies and human clinical trials. All clinical investigations of devices to determine safety and effectiveness must be conducted in accordance with the FDA's investigational device exemption, or IDE, regulations, which govern investigational device labeling, prohibit promotion of investigational devices, and specify an array of recordkeeping, reporting, and monitoring responsibilities of study sponsors and study investigators. If the device presents a "significant risk" to human health, as defined by the FDA, the FDA requires the device sponsor to submit an IDE application to the FDA, which must become effective prior to commencing human clinical trials. A significant risk device is one that presents a potential for serious risk to the health, safety or welfare of a patient and either is implanted, used in supporting or sustaining human life, substantially important in diagnosing, curing, mitigating or treating disease or otherwise preventing impairment of human health, or otherwise presents a potential for serious risk to a subject. In addition, the study must be approved by, and conducted under the oversight of, an Institutional Review Board, or IRB, for each clinical site. The IRB is responsible for the initial and continuing review of the IDE, and the IRB may impose additional requirements for the conduct of the clinical trial. If the device presents a non-significant risk to the patient, a sponsor may begin the clinical trial after obtaining approval for the trial by one or more IRBs without separate approval from the FDA, but must still follow abbreviated IDE requirements, such as monitoring the investigation, ensuring that the investigators obtain informed consent, and labeling and recordkeeping requirements.

In addition to clinical and preclinical data, the PMA must contain a full description of the device and its components, a full description of the methods, facilities, and controls used for manufacturing, and proposed labeling. Following receipt of a PMA, the FDA determines whether the application is sufficiently complete to permit a substantive review. If FDA accepts the PMA for review, FDA has 180 days under the FDCA to complete its review of a PMA, although in practice, the FDA's review often takes significantly longer, and can take up to several years. An advisory panel of experts from outside the FDA may be convened to review and evaluate the application and provide recommendations to the FDA as to the approvability of the device. The FDA may or may not accept the panel's recommendation. In addition, the FDA generally will conduct a pre-approval inspection of the applicant and/or its third-party manufacturers' or suppliers' facilities to ensure compliance with the FDA's Quality System Regulation codified in 21 CFR Part 820, or QSR.

The FDA will approve the new device for commercial distribution if the FDA determines that the data and information in the PMA constitute valid scientific evidence and that there is reasonable assurance that the device is safe and effective for its intended use(s). The FDA may approve a PMA with post-approval conditions intended to ensure the safety and effectiveness of the device, including, among other things, restrictions on labeling, promotion, sale and distribution, and collection of long-term follow-up data from patients in the clinical study that supported PMA approval or requirements to conduct additional clinical studies post-approval. The FDA may condition PMA approval on some form of post-market surveillance when deemed necessary to protect the public health or to provide additional safety and efficacy data for the device in a larger population or for a longer period of use. In such cases, the manufacturer might be required to follow certain patient groups for a number of years and to make periodic reports to the FDA on the clinical status of those patients. Failure to comply with the conditions of approval can result in material adverse enforcement action, including withdrawal of the approval. Certain changes to an approved device, such as changes in manufacturing facilities, methods, or quality control procedures, or changes in the design performance specifications, which affect the safety or effectiveness of the device, require submission of a PMA supplement, or in some cases a new PMA.

Both before and after a medical device is commercially released, the sponsor has ongoing responsibilities under FDA regulations. The FDA reviews design and manufacturing practices, labeling and record keeping, and manufacturers' required reports of adverse experiences and other information to identify potential problems with marketed medical devices. Sponsors are also subject to periodic inspection by the FDA for compliance with the FDA's QSR, among other FDA requirements, such as requirements for advertising and promotion of medical devices. The sponsor's manufacturing operations, and those of any third-party manufacturers, are required to comply with the QSR, which require manufacturers, including third-party manufacturers and suppliers, to follow stringent design, testing, control, maintenance of records and documentation, and other quality assurance procedures during all aspects of the design

and manufacturing process both before and after receiving device clearance or approval. The QSR requires that each manufacturer establish a quality system by which the manufacturer monitors the manufacturing process and maintains records that show compliance with the FDA regulations and the manufacturer's written specifications and procedures relating to each device. QSR compliance is necessary to receive and maintain FDA clearance or approval to market new and existing medical devices, and it is also necessary for distributing in the United States certain devices exempt from FDA clearance and approval requirements. The FDA conducts announced and unannounced periodic and ongoing inspections of medical device manufacturers, including third-party manufacturers and suppliers, to determine compliance with the QSR. If in connection with these inspections the FDA believes the manufacturer has failed to comply with applicable regulations and/or procedures, the FDA may issue inspectional observations on Form FDA-483, or Form 483, that would necessitate prompt corrective action. If the FDA inspectional observations are not addressed and/or corrective action is not taken in a timely manner and to the FDA's satisfaction, the FDA may issue a warning letter (which would similarly necessitate prompt corrective action) and/or proceed directly to other forms of enforcement action, including the imposition of operating restrictions, including a ceasing of operations, on one or more facilities, enjoining and restraining certain violations of applicable law pertaining to products, mandating recall of products, seizure of products, and assessing civil or criminal penalties against the manufacturer and its officers and employees. The FDA could also issue a corporate warning letter or a recidivist warning letter or negotiate the entry of a consent decree of permanent injunction with the manufacturer. The FDA may also recommend prosecution to the U.S. Department of Justice, or DOJ. Any adverse regulatory action, depending on its magnitude, may restrict a manufacturer from effectively manufacturing, marketing, and selling any medical device(s) and could have a material adverse effect on the manufacturer's business, financial condition, and results of operations.

After a device is cleared, receives marketing authorization, or approved for marketing, numerous pervasive regulatory requirements continue to apply unless a device is explicitly exempt from them. These include, among other things:

- establishment registration and device listing with the FDA;
- continued adherence to the QSR requirements;
- marketing, labeling, advertising, and promotion regulations, which require that promotion is truthful, not misleading, fairly balance and provides adequate directions for use, and that all claims are substantiated and in accordance with the provisions of the approved label, and which also prohibit the promotion of products for unapproved or "off-label" uses and impose other restrictions on labeling, in accordance with FDA guidance on off-label dissemination of information and responding to unsolicited requests for information;
- clearance or approval of product modifications to 510(k)-cleared, De Novo classified or PMA-approved devices that could significantly affect safety or effectiveness or that would constitute a major change in intended use of a cleared device;
- medical device reporting regulations, which require that a manufacturer report to the FDA if a device it markets may have caused or contributed to a death or serious injury, or has malfunctioned and the device or a similar device that it markets would be likely to cause or contribute to a death or serious injury if the malfunction were to occur;
- correction, removal, and recall reporting regulations, which require that manufacturers report to the FDA field corrections and product recalls or removals if undertaken to reduce a risk to health posed by the device or to remedy a violation of the FFDCA that may present a risk to health;
- complying with requirements governing Unique Device Identifiers on devices and also requiring the submission of certain information about each device to the FDA's Global Unique Device Identification Database;
- the FDA's recall authority, whereby the agency can order device manufacturers to recall from the market a product that is in violation of governing laws and/or regulations; and
- post-market surveillance activities and regulations, which apply when deemed by the FDA to be necessary to protect the public health or to provide additional safety and effectiveness data for the device.

Review And Approval Of Drugs In Europe And Other Foreign Jurisdictions

In addition to regulations in the US, a manufacturer of drugs is subject to a variety of regulations in foreign jurisdictions to the extent they choose to sell any drug products in those foreign countries. Even if a manufacturer obtains FDA approval of a product, it must still obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. To obtain regulatory approval of an investigational drug or biological product in the European Union, or the EU, a manufacturer must submit a marketing authorization application, or MAA, to the European Medicines Agency or EMA. For other countries outside of the EU, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical trials, product licensing, pricing, and reimbursement vary from country to country. In all cases, clinical trials are to be conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. The time required to obtain approval by a foreign country may be longer or shorter than that required for FDA approval, and the requirements may differ significantly.

Review And Approval Of Medical Devices In Europe And Other Foreign Jurisdictions

In addition to regulations in the US, a manufacturer of medical devices is subject to a variety of regulations in foreign jurisdictions, which vary substantially from country to country, to the extent a manufacturer chooses to sell any medical devices in those foreign countries. In those countries, a manufacturer can be subject to supranational, national, regional, and local regulations affecting, among other things, the development, design, manufacturing, product standards, packaging, advertising, promotion, labeling, marketing, and postmarket surveillance of medical devices. In order to market a medical device in other countries, the sponsor must obtain regulatory approvals or certifications and comply with extensive safety and quality regulations enforced in those countries. The time required to obtain approval or certification by a foreign country may be longer or shorter than that required for FDA approval or clearance, and the requirements may differ significantly.

The EU has adopted specific directives and regulations regulating the design, manufacture, clinical investigation, conformity assessment, labeling, and adverse event reporting for medical devices. Until May 25, 2021, medical devices were regulated by Council Directive 93/42/EEC, the EU Medical Devices Directive, or MDD, which had created a single set of medical device regulations for devices marketed in all EU member countries. Compliance with the MDD and certification to a quality system (e.g., ISO 13485 certification) enabled a manufacturer to place a CE mark on its products. To obtain authorization to affix the CE mark to a product, a recognized European Notified Body had to assess a manufacturer's quality system and the product's conformity to the requirements of the MDD.

The MDD has been repealed and replaced by Regulation (EU) No 2017/745, the EU Medical Devices Regulation, or MDR, which imposes significant additional premarket and postmarket requirements on medical devices. The MDR entered into application on May 26, 2021. Under a corrigendum to the MDR finalized in December 2019, some low-risk medical devices being up-classified as a result of the MDR, including low-risk instruments, may receive a transitional period to comply by May 2024.

The MDR establishes a uniform, transparent, predictable, and sustainable regulatory framework across the EU for medical devices and ensures a high level of safety and health while supporting innovation. Unlike the MDD, the MDR is directly applicable in EU member states without the need for member states to implement the MDR into national law, with the aim of increasing harmonization across the EU. The MDR, among other things:

- strengthens the rules on placing devices on the market (e.g., reclassification of certain devices and wider scope than the MDD) and reinforces surveillance once the devices are commercially available;
- establishes explicit provisions on manufacturers' responsibilities for follow-up on the quality, performance, and safety of devices placed on the market;
- establishes explicit provisions on importers' and distributors' obligations and responsibilities;
- imposes an obligation to identify a responsible person who is ultimately responsible for all aspects of compliance with the requirements of the new regulation;
- improves the traceability of medical devices throughout the supply chain to the end-user or patient through the introduction of a unique identification number, to increase the ability of manufacturers and regulatory authorities to trace specific devices through the supply chain and to facilitate the prompt and efficient recall of medical devices that have been found to present a safety risk;

- sets up a central database (MDR EUDAMED or EUDAMED), which is collaborative and interoperable and functions as a registration system, and a collaborative and a dissemination system (partially open to the public) that can, among other things, provide patients, healthcare professionals, and the public with information on products available in the EU; and
- strengthens rules for the assessment of certain high-risk devices, such as implants, which may have to undergo a clinical evaluation consultation procedure by experts before they are placed on the market.

Devices lawfully placed on the market pursuant to the MDD prior to May 26, 2021 may generally continue to be made available on the market or put into service until May 26, 2025, provided that the requirements of the MDR's transitional provisions are fulfilled. In particular, the certificate in question must still be valid. However, even in this case, manufacturers must comply with a number of new or reinforced requirements set forth in the MDR, in particular the obligations described below.

The MDR requires that before placing a device, other than a custom-made device, on the market, manufacturers (as well as other economic operators such as authorized representatives and importers) must register by submitting identification information to the electronic system (EUDAMED), unless they have already registered. The information to be submitted by manufacturers (and authorized representatives) also includes the name, address, and contact details of the person or persons responsible for regulatory compliance. The MDR also requires that, before placing a device, other than a custom-made device, on the market, manufacturers must assign a unique identifier to the device and provide it along with other core data to the unique device identifier, or UDI, database. These new requirements aim at ensuring better identification and traceability of medical devices. Each device — and, as applicable, each package — will have a UDI composed of two parts: a device identifier, or UDI-DI, specific to a device, and a production identifier, or UDI-PI, to identify the unit producing the device. Manufacturers are also responsible for entering the necessary data on EUDAMED, which includes the UDI database, and for keeping it up to date. The obligations for registration in EUDAMED and other mandatory uses of the system will start when the entire EUDAMED system (including all six modules) has been declared fully functional following an independent audit and an EU Commission notice to be published in the Official Journal and in accordance with the transitional provisions set out in the medical devices regulations. Until EUDAMED is fully functional, the corresponding provisions of the MDD continue to apply for the purpose of meeting the obligations laid down in the provisions regarding exchange of information, including, and in particular, information regarding registration of devices and economic operators.

All manufacturers placing medical devices into the market in the EU must comply with the EU medical device vigilance system. Under this system, serious incidents and Field Safety Corrective Actions, or FSCAs, must be reported to the relevant authorities of the EU member states. Manufacturers are required to take FSCAs, which are defined as any corrective action for technical or medical reasons to prevent or reduce a risk of a serious incident associated with the use of a medical device that is made available on the market. An FSCA may include the recall, modification, exchange, destruction or retrofitting of the device.

The advertising and promotion of medical devices in the EU is subject to some general principles set forth in EU legislation. Under the MDR, only devices that are CE marked may be marketed and advertised in the EU in accordance with their intended purpose. Directive 2006/114/EC concerning misleading and comparative advertising and Directive 2005/29/EC on unfair commercial practices, while not specific to the advertising of medical devices, also apply to the advertising of medical devices and contain general rules, for example, requiring that advertisements are evidenced, balanced, and not misleading. Specific requirements are defined at a national level. EU member states' laws related to the advertising and promotion of medical devices, which vary between jurisdictions, may limit or restrict the advertising and promotion of products to the general public and may impose limitations on promotional activities with healthcare professionals.

Many EU member states have adopted specific anti-gift statutes that further limit commercial practices for medical devices, in particular with respect to healthcare professionals and organizations. Additionally, there has been a recent trend of increased regulation of payments and transfers of value provided to healthcare professionals or entities, and many EU member states have adopted national "Sunshine Acts" which impose reporting and transparency requirements (often on an annual basis), similar to the requirements in the US, on medical device manufacturers. Certain countries also mandate implementation of commercial compliance programs.

The aforementioned EU requirements are generally applicable in the European Economic Area, or EEA, which consists of the 27 EU member states plus Norway, Liechtenstein, and Iceland.

Many other countries have specific requirements for classification, registration, and post-marketing surveillance that are independent of the countries discussed above. This landscape is constantly evolving. Rafael Medical Devices could be found in violation if it interprets the laws incorrectly or fails to keep pace with changes in laws and regulations. In the event of either of these occurrences, Rafael Medical Devices could be instructed to recall any products that it is marketing, cease distribution, and/or be subject to civil or criminal penalties.

Pharmaceutical Coverage, Pricing, And Reimbursement

In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Patients are unlikely to use our products unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our products. Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Even if one of the Pharmaceutical Companies' product candidates is approved, sales of the Pharmaceutical Companies' products will depend, in part, on the extent to which third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers, and managed care organizations, provide coverage, and establish adequate reimbursement levels for, such products. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity, and reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the approved products for a particular indication.

There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal, and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. Such reforms could have an adverse effect on anticipated revenue from product candidates that the Pharmaceutical Companies may successfully develop and for which they may obtain regulatory approval and may affect their overall financial condition and ability to develop product candidates.

Healthcare Law And Regulation

In addition to FDA restrictions on marketing of drug products and medical devices, other supranational, national, regional, federal, state, and local laws concerning healthcare fraud and abuse, including false claims and anti-kickback laws, healthcare professional payment transparency laws, and privacy laws restrict business practices in the pharmaceutical and medical device industries. These laws have been subject to increased enforcement activities with respect to medical products manufacturers in recent years. Violations of these laws are punishable by criminal and/or civil sanctions, including, in some instances, fines, imprisonment and, within the US, exclusion from participation in government healthcare programs, including Medicare, Medicaid, Department of Defense, and Veterans Administration health programs. Restrictions under applicable federal and state and analogous foreign healthcare laws and regulations include the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce or in return for purchasing, leasing, ordering, or arranging for or recommending the purchase, lease, or order of any item or service reimbursable under Medicare, Medicaid or other federal healthcare programs;
- the federal False Claims Act, which prohibits any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government or knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal laws that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and their respective implementing regulations, including the Final Omnibus Rule published in January 2013, which impose obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security, and transmission of individually identifiable protected health information, including breach notification regulations;
- analogous state data privacy and security laws and regulations that govern the collection, use, disclosure, transfer, storage, disposal, and protection of personal information, such as social security numbers, medical and financial information, and other information, including data breach laws that require timely notification to individuals, and at times regulators, the media or credit reporting agencies, if a company has experienced the unauthorized access or acquisition of personal information, as well as the California Consumer Privacy Act or CCPA, which, among other things, contains new disclosure obligations for businesses that collect personal information about California residents and affords those individuals numerous rights relating to their personal information that may affect companies' ability to use personal information or share it with business partners, and the California Privacy Rights Act, or CPRA, which expands the scope of the CCPA, imposes new restrictions on behavioral advertising and establishes a new California Privacy Protection Agency that will enforce the law and issue regulations, and is scheduled to become "operative" on January 1, 2023, with a 12-month "lookback provision," and the various state laws and regulations may be more restrictive and not preempted by United States federal laws;
- analogous foreign data protection laws, including among others the EU General Data Protection Regulation, or the GDPR, and EU member states' implementing legislation, which imposes data protection requirements that include strict obligations and restrictions on the ability to collect, analyze, and transfer EU personal data, a requirement for prompt notice of data breaches to data subjects and supervisory authorities in certain circumstances, and possible substantial fines for any violations (including possible fines for certain violations of up to the greater of 20 million Euros or 4% of total worldwide annual turnover of the preceding financial year), with legal requirements in foreign countries relating to the collection, storage, processing, and transfer of personal data continuing to evolve;
- the United States civil monetary penalties statute, which imposes penalties against any person who is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent;
- the federal Physician Payments Sunshine Act, which requires certain manufacturers of drugs, devices, biologics, and medical supplies to report annually to the Centers for Medicare & Medicaid Services information related to payments and other transfers of value made by that entity to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members;
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to healthcare items or services that are reimbursed by non-governmental third-party payors, including private insurers; and
- state laws requiring pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

In addition, our operations in foreign countries are subject to the extraterritorial application of the United States Foreign Corrupt Practices Act, or FCPA. Our global operations are also subject to foreign anti-corruption laws, such as the United Kingdom Bribery Act, among others. As part of our global compliance program, we seek to address anti-corruption risks proactively.

COMPETITION

We and the Investment Companies operate in highly competitive segments. We and the Investment Companies face competition from many different sources, including commercial pharmaceutical and biotechnology and medical device enterprises, academic institutions, government agencies, and private and public research institutions. Many of our and the Investment Companies' competitors have significantly greater financial, product development, manufacturing and marketing resources than we and the Investment Companies possess. Large pharmaceutical companies and medical device companies have extensive experience in clinical testing and obtaining regulatory approval for drugs and devices. In addition, many universities and private and public research institutes are active in research in direct competition with us and the Investment Companies. We and the Investment Companies also may compete with these organizations to recruit scientists and clinical development personnel. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

Our and the Investment Companies competitors are pursuing the development and/or acquisition of pharmaceuticals, medical devices and over-the-counter ("OTC") products that target the same diseases, conditions and unmet needs that we and the Investment Companies are targeting. If competitors introduce new products, delivery systems or processes with therapeutic or cost advantages, our and the Investment Companies' products can be subject to progressive price reductions or decreased volume of sales, or both. Most new products that we and the Investment Companies would introduce must compete with other products already on the market or products that are later developed by competitors. The principal methods of competition for our and the Investment Companies' products include quality, efficacy, market acceptance, price, and marketing and promotional efforts, patient access programs and product insurance coverage and reimbursement.

INTELLECTUAL PROPERTY

Licenses

Cornerstone maintains an exclusive license agreement with the Research Foundation of the State University of New York at Stony Brook, or RF, granting Cornerstone the exclusive right to make, use and sell products covered under specified technology relating to lipoic acid derivatives with the right to grant sublicenses. This license agreement was subsequently amended in 2004, 2007 and 2017 and relates to Cornerstone's class of compounds. Cornerstone maintains a low single-digit royalty agreement with Altira Capital and Consulting, LLC (of which we own 66.66%) ("Altira"), pursuant to which Cornerstone is granted sole ownership of certain patents directed to lipoic acid derivatives and other technology held by Altira.

Cornerstone maintains an exclusive license agreement with Ono Pharmaceutical Co., Ltd, or Ono, whereby Cornerstone granted Ono an exclusive right to make, use and sell CPI-613[®] (devimistat) and related products in Japan, South Korea, Taiwan, and certain countries in Southeast Asia under specified intellectual property held by Cornerstone. Ono granted to Cornerstone a non-exclusive right under intellectual property held by Ono to make, use, and sell CPI-613[®] (devimistat) and related products in countries other than Japan, South Korea, Taiwan, and certain countries in Southeast Asia. Under the license agreement, Ono is required to use commercially reasonable efforts to develop the licensed products in territories licensed to Ono. The agreement may be terminated without cause by Ono or by Cornerstone for material breach by Ono.

LipoMedix maintains an exclusive license agreement with Yissum Research and Development Company, the technology transfer arm of the Hebrew University of Jerusalem granting LipoMedix the exclusive right to make, use and sell products covered under specified patents relating to the mitomycin lipophilic prodrug and its liposomal formulation (Promitil[®]) with the right to grant sublicenses. LipoMedix also maintains an exclusive license agreement with Shaare Zedek Scientific Company, the technology transfer arm of Shaare Zedek Medical Center ("SZMC") granting LipoMedix the exclusive right to license any new intellectual property developed at SZMC relating to the mitomycin lipophilic prodrug and its liposomal formulation (Promitil[®]) with the right to grant sublicenses.

Barer's subsidiary, Farber Partners, LLC ("Farber"), has formed agreements with Princeton University's Office of Technology Licensing for technology from the laboratory of Professor Joshua Rabinowitz, in the Department of Chemistry, Princeton University, for an exclusive worldwide license to its SHMT (serine hydroxymethyltransferase) inhibitor program and use of Methanol and prodrugs in therapy.

Patents

Cornerstone patents its technology, inventions, and improvements that it considers important to the development of its business. A patent gives the patent holder the right to exclude any unauthorized use of the subject matter of the patent in those jurisdictions in which a patent is granted. As of September 2023, Cornerstone owns or in-licenses more than one dozen U.S. patents, more than thirty (30) foreign patents registered in various countries, and many pending U.S. and foreign patent applications. Additional patent applications are anticipated to be filed as studies progress. Patents that Cornerstone has obtained for its platform technologies and patents that may issue in the future based on Cornerstone's currently pending patent applications are scheduled to expire in years 2028 through 2042. These dates do not include potential patent term extensions. Cornerstone has obtained U.S. orphan drug designation for CPI-613[®] (devimistat) in the treatment of pancreatic cancer, AML, MDS, Burkitt's Lymphoma, Peripheral T-cell Lymphoma (PTCL), soft tissue sarcoma, and biliary cancer.

Cornerstone maintains U.S. and international trademarks covering its lead development compounds (CPI-613[®] (devimistat) and Telaglenastat (CB-839)). U.S. and international trademarks are also maintained for potential brand names of devimistat in the event that it was to receive regulatory approval permitting commercialization.

Barer has filed patents for its novel inventions, and has entered into licensing agreements for other intellectual property. Patent applications have been filed in the name of Farber Partners, LLC (Barer's subsidiary) in the areas of T-cell nutrients to enhance checkpoint inhibition and one-carbon metabolism, and serine hydroxymethyltransferase (SHMT) inhibitors for therapies directed to treatment of cancer, autoimmune disease and fibrotic disease. In the area of T-cell nutrients, a Patent Cooperation Treaty Application (PCT) was filed on July 15, 2022, claiming priority to two US provisional applications that were filed in July and December of 2021. In the area of SHMT inhibitors, a US provisional application was filed on May 19, 2023.

As of October 9, 2020, LipoMedix owns or in-licenses several families of U.S. patents. Additional patent applications may be filed as studies continue. Patents that LipoMedix has obtained and patents that may issue in the future based on LipoMedix's currently pending patent applications for its platform technologies are scheduled to expire in years 2032 through 2035. These dates do not include potential patent term extensions.

Four new patent applications covering the use of Promitil[®], in combination with other chemotherapies and with radiotherapy, targeting of Promitil with a folate ligand, and a reformulation of Promitil with co-encapsulated mitomycin prodrug and doxorubicin have been approved by the USPTO or EPO in 2018-2020. The patent portfolio is currently comprised of five granted families of patents and one application under review.

Rafael Medical Devices patents its technology, inventions, and improvements that it considers important to the development of its business and seeks to expand its intellectual property portfolio. As of September 16, 2023, Rafael Medical Devices had filed the following patent application related to its devices filed with the USPTO and PCT: Patent application entitled, Devices, Instruments, Implants and Methods of Assembly and Use, and patent application entitled Videoscopic Arthroscopic Instruments, Devices, and Systems and Methods of Use and Assembly.

The designation of Trappsol[®] Cyclo[™] as an orphan drug for the treatment of NPC by the FDA and European regulators would provide Cyclo with seven years, and 10 to 12 years, of market exclusivity, respectively, following regulatory approval. Cyclo also protected its Trappsol[®] and Aquaplex[®] trademarks by registering them with the U.S. Patent and Trademark Office.

Day Three Labs Manufacturing, a majority-owned subsidiary of Day Three Labs, owns several families of US and international patents and patent applications related to increased bioavailability of cannabinoids. Day Three Labs Manufacturing has also filed for trademark protection over the use of the term UNLOKT, which it uses as the brand name for the cannabinoids processed using its technology.

Additional patent applications may be filed as development progresses across the Investment Companies as deemed to be in its best interest.

MANUFACTURING

The Investment Companies do not own or operate, and currently have no plans to establish, any manufacturing facilities or fill-and-finish facilities. The Pharmaceutical Companies currently rely, and expect to continue to rely, on third parties for the manufacture of their product candidates for preclinical and clinical testing, as well as for commercial

manufacture of any products that they may commercialize. The Pharmaceutical Companies obtain supplies from these established contract manufacturers on a purchase-order basis and do not have long-term supply arrangements in place. The Pharmaceutical Companies do not currently have arrangements in place for a redundant supply of bulk drug substance or drug product, however, they may seek to add that capability if they move toward commercialization of specific candidates. For all of the product candidates, the Pharmaceutical Companies intend to identify and qualify additional manufacturers to provide the active pharmaceutical ingredient and the formulation and fill-and-finish.

Cornerstone's compounds are organic compounds of low molecular weight, generally called small molecules. They can be manufactured in reliable and reproducible synthetic processes from readily available starting materials. The chemistry is amenable to scale-up and does not require unusual equipment in the manufacturing process. Cornerstone expects to continue to develop drug candidates that can be produced relatively cost-effectively at contract manufacturing facilities.

LipoMedix's Promitil[®] and other pipeline candidates are based on an active pharmaceutical ingredient (API) referred to as MLP (abbreviation of mitomycin-C lipid-based prodrug) that is formulated into customized nanoparticles. These nanoparticles consist of lipids and a polyethylene-glycol (PEG) polymer and are known as pegylated liposomes. LipoMedix obtains bulk drug substance and drug product supplies from established contract manufacturers on a purchase order basis and does not have long-term supply arrangements in place. LipoMedix does not currently have arrangements in place for commercial supply or redundant supply for bulk drug substance or drug product.

Rafael Medical Devices optimizes supply chains and manufacturing on a device per device basis focusing on quality, time, and cost. At present Rafael Medical Devices does not own or operate manufacturing facilities. Rafael Medical Devices management has relationships with top tier manufacturers on an as-needed basis.

Cyclo is developing its lead product Trappsol[®] Cyclo[™] for the treatment of Niemann-Pick Disease Type C. The company owns all manufacturing and commercial rights to the product and manufactures using a validated, commercial-scale process using a team of contract manufacturing service providers.

Day Three Labs Manufacturing, a majority-owned subsidiary of Day Three Labs, processes cannabinoids together with proteins using commercially available filtration equipment. Proteins used by Day Three Labs Manufacturing are obtained from established commercial manufacturers, and cannabinoids are obtained from licensed growers and extractors. All processing activities take place at licensed cannabis facilities, and Day Three Labs Manufacturing does not take ownership over the cannabinoids being processed, but rather provides the processing as a service.

Barer Institute, a wholly owned subsidiary of Rafael, does not own or operate manufacturing facilities.

Real Estate

Our current commercial real estate holdings consist of a portion of a building in Israel. Prior to its sale in August 2022, we also owned the 520 Property.

On August 22, 2022, the Company completed the sale of 520 Property for a purchase price of \$49.4 million.

The 520 Property was encumbered by a mortgage securing a \$15 million loan which was paid off in this transaction. After repaying the loan, and paying commissions, taxes, and other costs, the Company received a net amount of approximately \$33 million at closing.

The 520 Property serves as the headquarters of the Company and affiliated entities, IDT Corporation ("IDT"), and Genie Energy, Ltd. ("Genie"), who occupy the second through fourth floors.

Our holding in Israel is a condominium portion of an office building built in 2004 located in the Har Hotzvim section of Jerusalem, Israel. The condominium is one floor comprising approximately 12,400 square feet. Har Hotzvim is a high-tech industrial park located in northwest Jerusalem. It is the city's main zone for science-based and technology companies, among them Intel, Teva and Mobileye. As of July 31, 2023, the space is fully leased to two tenants; one of which is an IDT subsidiary.

Depreciation expense of property, plant and equipment was \$78 thousand and \$72 thousand in fiscal 2023 and fiscal 2022, respectively.

COMPETITION

With respect to our real estate business, we compete for commercial (office and retail) tenants in Jerusalem, Israel. The commercial real estate market is highly competitive. Numerous commercial properties compete with us for tenants based on location, rental rates, tenant allowances, operating expenses and the quality and design of the property. Other factors tenants consider are; quality and breadth of tenant services provided, onsite amenities and reputation of the owner and property manager.

OUR STRATEGY

Our strategy related to our real estate business is to continue to operate and maximize the value of our real estate holding in Israel.

EMPLOYEES

As of October 30, 2023, Rafael Holdings and its subsidiaries had 13 full-time employees, including 1 employee dedicated to the real estate group.

Item 1A. Risk Factors

RISK FACTORS

Our business, operating results or financial condition could be materially adversely affected by any of the following risks associated with any one of our businesses, as well as the other risks highlighted elsewhere in this document. The trading price of our common stock could decline due to any of these risks. Note that references to “our”, “us”, “we”, “the Company”, etc. used in each risk factor below refers to the business about which such risk factor is provided.

Risks Related to Our Financial Condition and Capital Needs

We have limited resources and could find it difficult to raise additional capital.

We may need to raise additional capital for operations and in order for stockholders to realize increased value on our securities. Given the current global economy and other factors, if we need to raise additional capital there can be no assurance that we will be able to obtain the necessary funding on commercially reasonable terms in a timely fashion or at all. Failure to receive the funding could have a material adverse effect on our business, prospects, and financial condition.

Our limited operating history makes it difficult to evaluate our business and prospects and may increase your investment risk.

We have only a limited operating history upon which our business and prospects can be evaluated. We expect to encounter risks and difficulties frequently encountered by early-stage companies in the industries in which we operate.

We have not yet demonstrated our ability to successfully complete any clinical trials, including large-scale, pivotal clinical trials, obtain regulatory approvals, manufacture a commercial scale medicine, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful commercialization. Typically, it takes about ten to fifteen years to develop one new medicine from the time it is discovered to when it is available for treating patients. Consequently, any predictions made about our future success or viability may not be as accurate as they could be if we had a longer operating history.

In addition, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors and risks frequently experienced by clinical stage biopharmaceutical companies in rapidly evolving fields. We will also need to transition from a company with a research focus to a company capable of supporting commercial activities. If we do not adequately address these risks and difficulties or successfully make such a transition, our business will suffer, our future revenue potential may be impacted, and our ability to pursue our growth strategy and attain profitability could be compromised.

We hold significant cash, cash equivalents, restricted cash and investments that are subject to various market risks.

As of July 31, 2023, we held approximately \$21.5 million in cash and cash equivalents, approximately \$57.7 million in short-term available-for-sale securities, \$2.5 million in third-party and related party receivables and interest receivable (net of allowance for doubtful accounts), approximately \$5.0 million in interests in hedge funds and approximately \$0.1 million in securities in another entity that are not liquid. Investments in hedge funds carry a degree of risk, as there can be no assurance that we will be able to redeem any hedge fund investments at any time or that our investment managers will be able to accurately predict the course of price movements of securities and other instruments and, in general, the securities markets have in recent years been characterized by great volatility and unpredictability. Our passive interests in other entities are not currently liquid, and we cannot assure that we will be able to liquidate them when we desire, or ever. As a result of these different market risks, our holdings of cash, cash equivalents, and investments could be materially and adversely affected.

We may not be able to consummate any investment, business combination or other transaction.

While we are actively seeking corporate development opportunities, we may not be able to find any suitable target businesses and consummate an investment, business combination or other transaction. Our ability to complete any such transactions may be negatively impacted by general market conditions, volatility in the debt and equity markets, decreased market liquidity, and third-party financing being unavailable on terms acceptable to us or at all.

Risks Related to our Pharmaceuticals Business

Our future success may depend on prospects for Cornerstone's lead product candidate devimistat (CPI-613[®]) and results of Cyclo Therapeutics' Phase III trial for Trappsol[®] Cyclo[™]. If either company is unable to gain regulatory approval or commercialize its product candidates or experiences significant delays in doing so, our business will be materially harmed.

We have invested a significant amount of capital into Cornerstone's development program. All of Cornerstone's current and any future product candidates will require preclinical and clinical development, regulatory review and approval, substantial investment, access to sufficient commercial manufacturing capacity, and significant marketing efforts before Cornerstone can generate any revenue from product sales.

The success of CPI-613[®] (devimistat) and Trappsol[®] Cyclo[™] is beyond our, Cornerstone's or Cyclo's control, and the drug development and regulatory approval processes could cause significant delay or prevent Cornerstone and/or Cyclo from obtaining regulatory approval or commercializing CPI-613[®] (devimistat), Trappsol[®] Cyclo[™] or any other product candidates. If either Cornerstone or Cyclo is unable to develop, obtain regulatory approval for, or, if approved, successfully commercialize its product candidates, we may not be able to generate sufficient revenue to continue our business.

The Pharmaceutical Companies may not be successful in their efforts to identify or discover potential product candidates.

Our business strategy includes elements for our subsidiaries and entities in which we invest to identify, create and test compounds, and to advance clinical testing of those and other compounds. A significant portion of the research that the Pharmaceutical Companies are conducting involves new compounds and drug discovery methods and suitable drug delivery systems, including the Pharmaceutical Companies' proprietary technology. The drug discovery that the Pharmaceutical Companies are conducting using the Pharmaceutical Companies' proprietary technology may not be successful in identifying compounds that are useful in treating cancer or other ailments. The Pharmaceutical Companies' research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for a number of reasons, including:

- the research methodology used may not be successful in identifying appropriate biomarkers, potential product candidates or effective carrier systems to confer a drug delivery advantage.
- potential product candidates may, on further study, be shown to not be effective, have harmful side effects or other characteristics that indicate that they are unlikely to be medicines that will receive regulatory approval and achieve market acceptance.

Research programs to identify new product candidates require substantial technical, financial, and human resources. The Pharmaceutical Companies may choose to focus the Pharmaceutical Companies' efforts and resources on a potential product candidate that ultimately proves to be unsuccessful.

If the Pharmaceutical Companies are unable to identify suitable compounds for preclinical and clinical development, and/or are unable to successfully secure regulatory approval for any such compounds, the Pharmaceutical Companies will not be able to obtain product revenue in future periods, which likely would result in significant harm to the Pharmaceutical Companies' financial position and adversely impact the Pharmaceutical Companies' valuation and our business.

We and the companies in which we hold interests may expend our and their limited resources to pursue a particular product candidate or an indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because the Pharmaceutical Companies have limited financial and managerial resources, their focus on research programs and product candidates that they may or will identify for specific indications may not be exhaustive. As a result, the Pharmaceutical Companies may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. The Pharmaceutical Companies' resource allocation decisions may cause them to fail to capitalize on viable commercial medicines or profitable market opportunities. The Pharmaceutical Companies' spending on current and future research and development programs

and product candidates for specific indications may not yield any commercially viable medicines. If the Pharmaceutical Companies do not accurately evaluate the commercial potential or target market for a particular product candidate, they may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for them to retain sole development and commercialization rights to such product candidate.

Preclinical and clinical drug development is a lengthy and expensive process, with an uncertain outcome. Our and the Pharmaceutical Companies' preclinical and clinical programs may experience delays or may never advance, which would adversely affect the ability to obtain regulatory approvals or commercialize product candidates on a timely basis or at all, which could have an adverse effect on our business.

In order to obtain FDA approval to market a new drug, the product sponsor must demonstrate the safety and efficacy of the new drug in humans to the satisfaction of the FDA. To meet these requirements, the Pharmaceutical Companies will have to conduct extensive studies, including pre-clinical studies and adequate and well-controlled clinical trials. Clinical testing is very expensive, time-consuming, and subject to uncertainty.

Before the Pharmaceutical Companies can commence clinical trials for a product candidate, they must complete extensive nonclinical and preclinical studies that support their planned and future INDs in the United States. We cannot be certain of the timely completion or outcome of the Pharmaceutical Companies' nonclinical and preclinical studies and cannot predict if the FDA will allow their proposed clinical programs to proceed or if the outcome of their nonclinical and preclinical studies will ultimately support further development of their programs. We also cannot be sure that the Pharmaceutical Companies will be able to submit INDs or similar applications with respect to their product candidates on the timelines we expect, if at all, and we cannot be sure that submission of IND or similar applications will result in the FDA or other regulatory authorities allowing clinical trials to begin.

Conducting nonclinical and preclinical testing and clinical trials represents a lengthy, time-consuming, and expensive process. The length of time may vary substantially according to the type, complexity, and novelty of the program, and often can be several years or more per development program. Delays associated with programs for which the Pharmaceutical Companies are conducting nonclinical and preclinical studies may cause them to incur additional operating expenses. The commencement and rate of completion of nonclinical and preclinical studies and clinical trials for a product candidate may be delayed by many factors, including, for example:

- inability to generate sufficient nonclinical and preclinical or other in vivo or in vitro data to support the initiation of clinical studies;
- timely completion of nonclinical and preclinical laboratory tests, animal studies, and formulation studies in accordance with FDA's good laboratory practice requirements and other applicable regulations;
- approval by an independent Institutional Review Board, or IRB, ethics committee at each clinical site before each trial may be initiated;
- delays in reaching a consensus with regulatory agencies on study design and obtaining regulatory authorization to commence clinical trials;
- delays in reaching agreement on acceptable contractual 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 clinical trial sites;
- delays in identifying, recruiting and training suitable clinical investigators;
- delays in recruiting eligible patients to participate in clinical trials;
- delays in manufacturing, testing, releasing, validating or importing/exporting sufficient stable quantities of product candidates for use in clinical trials;
- 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;
- imposition of a temporary or permanent clinical hold by regulatory authorities;

- developments on trials conducted by competitors for related technology or medical products that raise FDA or foreign regulatory authority concerns about risk to patients of the technology broadly, or if the FDA or a foreign regulatory authority finds that the investigational protocol or plan is clearly deficient to meet its stated objectives;
- delays in recruiting, screening and enrolling patients and delays caused by patients withdrawing from clinical trials or failing to return for post-treatment follow-up;
- difficulty collaborating with patient groups and investigators;
- failure by CROs, other third parties or the Pharmaceutical Companies to adhere to clinical trial protocols;
- failure by CROs, other third parties or the Pharmaceutical Companies to perform in accordance with the FDA's or any other regulatory authority's good laboratory practices, or GLPs, good clinical practice requirements, or GCP, or other applicable regulatory guidelines in other countries;
- occurrence of adverse events associated with the product candidate that are viewed to outweigh its potential benefits, or occurrence of adverse events in a clinical trial of the same class of agents conducted by other companies; changes to the clinical trial protocols;
- clinical sites deviating from trial protocols or dropping out of a trial;
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols;
- changes in the standard of care on which a clinical development plan was based, which may require new or additional trials;
- selection of clinical endpoints that require prolonged periods of observation or analyses of resulting data;
- the cost of clinical trials of the Pharmaceutical Companies' product candidates being greater than anticipated;
- interruptions of and/or delays in the clinical trials of the Pharmaceutical Companies' product candidates and the potential impact of such interruptions or delays on a product candidate's development program and the validity of clinical data result from a product candidate's development program;
- clinical trials of the Pharmaceutical Companies' product candidates producing negative or inconclusive results, which may result in our or their deciding, or regulators requiring us, to conduct additional clinical trials or abandon development of such product candidates;
- transfer of manufacturing processes to larger-scale facilities operated by a contract manufacturing organization, or CMO, and delays or failure by CMOs or the Pharmaceutical Companies to make any necessary changes to such manufacturing processes; and
- third parties being unwilling or unable to satisfy their contractual obligations to us or the Pharmaceutical Companies.

In addition, disruptions caused by the COVID-19 pandemic and subsequent variants may increase the likelihood that the Pharmaceutical Companies encounter difficulties or delays in initiating, enrolling, conducting or completing any planned and ongoing nonclinical and preclinical studies and clinical trials. Any inability by the Pharmaceutical Companies to successfully initiate or complete nonclinical and preclinical studies or clinical trials could result in additional costs or impair our ability to generate revenue from future product sales of any product candidates that were thought to be on track to receive regulatory approval. In addition, if the Pharmaceutical Companies make manufacturing or formulation changes to their product candidates that already have undergone or are undergoing clinical evaluation, they may be required to or may elect to conduct additional studies to bridge modified product candidates to earlier versions. Clinical trial delays could also shorten any periods during which any marketed products have patent protection and may allow our competitors to bring products to market before we do, which could impair our ability to successfully commercialize the Pharmaceutical Companies' product candidates and may seriously harm our business.

Further, conducting clinical trials in foreign countries, as the Pharmaceutical Companies may do for their product candidates, presents additional risks that may delay completion of clinical trials. These risks include the failure of enrolled patients in foreign countries to adhere to clinical protocols as a result of differences in healthcare services or cultural customs, failure to conduct foreign clinical trials according to standards of care in foreign countries that FDA considers comparable to the standards of care in the US, failure of the Pharmaceutical Companies to persuade the FDA as to the scientific robustness and clinical acceptability of the data from any such foreign clinical trials, managing additional administrative burdens associated with foreign regulatory schemes, as well as political and economic risks relevant to such foreign countries.

Moreover, principal investigators for the Pharmaceutical Companies' clinical trials may serve as scientific advisors or consultants to the Pharmaceutical Companies from time to time and receive compensation in connection with such services. Under certain circumstances, the Pharmaceutical Companies may be required to report some of these relationships to the FDA or comparable foreign regulatory authorities. The FDA or comparable foreign regulatory authority may conclude that a financial relationship between the Pharmaceutical Companies and a principal investigator has created a conflict of interest or otherwise affected interpretation of the study. The FDA or comparable foreign regulatory authority may therefore question the integrity of the data generated at the applicable clinical trial site, and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of marketing applications by the FDA or comparable foreign regulatory authority, as the case may be, and may ultimately lead to the denial of regulatory approval of one or more product candidates.

Delays in the completion of any preclinical studies or clinical trials of the Pharmaceutical Companies' product candidates will increase our costs, slow down product candidate development and approval processes, and delay or potentially jeopardize our ability to commence product sales and generate product revenue from any product candidate that might receive regulatory approval. In addition, 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 a product candidate. Any delays to the Pharmaceutical Companies' preclinical studies or clinical trials that occur as a result could shorten any period during which they may have the exclusive right to commercialize such product candidates, and their competitors may be able to bring products to market before they do, and the commercial viability of any product candidates could be significantly reduced. Any of these occurrences may harm our business, financial condition, and prospects significantly.

If the Pharmaceutical Companies experience delays or difficulties in the enrollment of patients in clinical trials, the Pharmaceutical Companies' receipt of necessary regulatory approvals could be delayed or prevented.

The Pharmaceutical Companies or their collaborators may not be able to initiate or continue clinical trials for the Pharmaceutical Companies' product candidates if the Pharmaceutical Companies or such collaborators are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or analogous regulatory authorities outside the United States.

Enrollment may be particularly challenging for some of the orphan diseases the Pharmaceutical Companies target in the Pharmaceutical Companies' programs. In addition, there may be limited patient pools from which to draw for clinical studies. In addition to the rarity of some diseases, the eligibility criteria of the Pharmaceutical Companies' clinical studies will further limit the pool of available study participants as they may require that patients have specific characteristics that they can measure or to assure their disease is either severe enough or not too advanced to include them in a study. In addition, some of the Pharmaceutical Companies' competitors may have ongoing clinical trials for product candidates that are in development to treat the same indications as the Pharmaceutical Companies' product candidates, and patients who would otherwise be eligible for the Pharmaceutical Companies' clinical trials may instead enroll in clinical trials of the Pharmaceutical Companies' competitors' product candidates and therefore be ineligible or otherwise unwilling to enroll in the Pharmaceutical Companies' clinical trials.

Patient enrollment is also affected by other factors including:

- size and nature of the patient population;
- severity of the disease under investigation;
- availability and efficacy of approved drugs for the disease under investigation;
- patient eligibility criteria for the trial in question as defined in the protocol;

- perceived risks and benefits of the product candidate under study;
- clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new products that may be approved or future product candidates being investigated for the indications we are investigating;
- delays in or temporary suspension of the enrollment of patients in our planned clinical trials due to the COVID-19 pandemic;
- ability to obtain and maintain patient consents;
- patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment;
- proximity and availability of clinical trial sites for prospective patients; and
- the risk that patients enrolled in clinical trials will drop out of the trials before completion, including as a result of contracting COVID-19 or other health conditions or being forced to quarantine, or, because they may be late-stage cancer patients and will not survive the full durations of the clinical trials.

These factors may make it difficult for the Pharmaceutical Companies to enroll enough patients to complete their clinical trials in a timely and cost-effective manner. The Pharmaceutical Companies' inability to enroll a sufficient number of patients for their clinical trials would result in significant delays or may require them to abandon one or more clinical trials altogether. Enrollment delays in clinical trials may result in increased development costs for the Pharmaceutical Companies' product candidates and jeopardize their ability to obtain regulatory approval. Furthermore, even if the Pharmaceutical Companies are able to enroll a sufficient number of patients for their clinical trials, they may have difficulty maintaining participation in their clinical trials through the treatment and any follow-up periods.

The Pharmaceutical Companies' product candidates may cause significant adverse events, toxicities or other undesirable side effects when used alone or in combination with other approved products or investigational new drugs that may result in a safety profile that could prevent regulatory approval, prevent market acceptance, limit their commercial potential or result in significant negative consequences.

If the Pharmaceutical Companies' product candidates are associated with undesirable side effects or have unexpected characteristics in preclinical studies or clinical trials when used alone or in combination with other approved products or investigational new drugs, the Pharmaceutical Companies may need to interrupt, delay or abandon their development or limit development to more narrow uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Treatment-related side effects could also affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may prevent the Pharmaceutical Companies from achieving or maintaining market acceptance of the affected product candidate and may adversely affect our business, financial condition, and prospects significantly.

In addition, many compounds that initially showed promise in early-stage testing for treating cancer or other indications have later been found to cause side effects that prevented further development of the compound. Further, we expect that certain product candidates will be used in patients that have weakened immune systems, which may exacerbate any potential side effects associated with their use. Patients treated with oncology product candidates may also be undergoing surgical, radiation and chemotherapy treatments, which can cause side effects or adverse events that are unrelated to the product candidate but may still impact the success of clinical trials. The inclusion of critically ill patients in clinical trials may result in deaths or other adverse medical events due to other therapies or medications that such patients may be using or due to the gravity of such patients' illnesses. It may be very challenging, or even impossible, for the Pharmaceutical Companies to demonstrate that any such deaths or other adverse events are traceable to other therapies or medications that such patients may be using or to the gravity of such patients' illnesses, in which case the FDA or analogous regulatory authorities may attribute any such deaths or other adverse events to the Pharmaceutical Companies' product candidate being studied in the clinical trial.

If significant adverse events or other side effects are observed in any of the Pharmaceutical Companies' current or future clinical trials, the Pharmaceutical Companies may have difficulty recruiting patients to the clinical trials, patients may drop out of such trials, or they may be required to abandon the trials or our development efforts of a

product candidate altogether. The Pharmaceutical Companies, the FDA, other comparable regulatory authorities or an IRB may suspend clinical trials of a product candidate at any time for various reasons, including a belief that subjects in such trials are being exposed to inadequate clinical benefit and/or unacceptable health risks or adverse side effects.

Further, if any of the Pharmaceutical Companies' product candidates obtains regulatory approval, toxicities associated with such product candidates previously not seen during clinical testing may also develop after such approval and lead to a number of potentially significant negative consequences, including, but not limited to:

- regulatory authorities may suspend, limit or withdraw 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;
- the Pharmaceutical Companies may be required to change the way the product is administered or conduct additional clinical trials or post-approval studies;
- the Pharmaceutical Companies may be required to develop and implement a risk evaluation and mitigation strategy, or REMS, which could include, among other things, a medication guide outlining the risks of such side effects for distribution to patients, and potentially limitations or even restrictions on prescribing, dispensing, and/or distribution;
- the Pharmaceutical Companies may be subject to fines, injunctions or the imposition of criminal penalties;
- we or the Pharmaceutical Companies could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent the Pharmaceutical Companies from achieving or maintaining market acceptance of the particular product candidate, if approved, and could seriously harm our business.

Interim, "top-line," and preliminary data from clinical trials that we announce or publish from time to time may change as more patient 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 and/or the Pharmaceutical Companies may publicly disclose preliminary or top-line data from preclinical studies and clinical trials, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We and/or the Pharmaceutical Companies may also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we or they may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the top-line or preliminary results reported may differ significantly from future results of the same studies, or different conclusions or considerations may qualify such results and/or limit the clinical conclusions that can be drawn from them, once additional data have been received and fully evaluated. 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. In addition, the full study results from all clinical trials are subject to FDA review, and the FDA may draw materially different conclusions than those reached by us or the Pharmaceutical Companies. As a result, top-line data should be viewed with caution until the final data are available, and then, until the full study results have been completely evaluated by the FDA.

From time to time, we and/or the Pharmaceutical Companies may also disclose interim data from preclinical studies and clinical trials. Interim data from preclinical and clinical trials are subject to the risk that one or more of the preclinical or clinical outcomes may materially change as patient enrollment continues and more patient data become available or as patients from such clinical trials continue other treatments for their disease. Adverse differences between preliminary or interim data and final data could materially adversely affect our business prospects.

Further, others, including regulatory agencies, may not accept or agree with our or the Pharmaceutical Companies' 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 or they 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 material or otherwise appropriate information to include in our disclosure. If the interim, top-line, or preliminary data that we or the Pharmaceutical Companies report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, the Pharmaceutical Companies' ability to obtain approval for, and commercialize, their product candidates may be adversely affected, which could materially adversely affect our business, financial condition and results of operations.

Results of preclinical studies and early clinical trials may not be predictive of results of future preclinical studies or clinical trials.

The outcome of preclinical studies and early clinical trials may not be predictive of the success or failure of later preclinical studies or clinical trials, and interim results of preclinical studies or clinical trials do not necessarily predict success in future clinical trials. Many companies in the biopharmaceutical industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in earlier development, and the Pharmaceutical Companies could face similar setbacks. The design of a clinical trial can determine whether its results will support approval of a product, and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced or even completed. We and the Pharmaceutical Companies have limited experience in designing clinical trials and may be unable to design and execute a clinical trial to support regulatory approval. In addition, preclinical and clinical data are often susceptible to varying interpretations and analyses. Many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain regulatory approval for the product candidates. Even if we or the Pharmaceutical Companies, or future collaborators, believe that the results of clinical trials for the Pharmaceutical Companies' product candidates warrant regulatory approval, the FDA or comparable foreign regulatory authorities may disagree and may not grant regulatory approval of the Pharmaceutical Companies' product candidates.

In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the dosing regimen and other clinical trial protocols, and the rate of dropout among clinical trial participants. If the Pharmaceutical Companies fail to receive positive results in clinical trials of the Pharmaceutical Companies' product candidates, the development timeline and regulatory approval and commercialization prospects for the Pharmaceutical Companies' most advanced product candidates, and, correspondingly, our or the Pharmaceutical Companies' business and financial prospects would be negatively impacted.

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

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 the 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. We and the Pharmaceutical Companies have not obtained regulatory approval for any product candidate, and it is possible that any product candidates they may seek to develop in the future will never obtain regulatory approval. Neither we nor the Pharmaceutical Companies nor any future collaborator is permitted to market any new drug in the United States or abroad until they receive regulatory approval of an NDA, or other comparable submission, from the FDA or foreign regulatory agencies.

Prior to obtaining approval to commercialize a product candidate in the United States or abroad, the Pharmaceutical Companies or their collaborators must demonstrate with substantial evidence from, among other things, well-controlled clinical trials, and to the satisfaction of the FDA or foreign regulatory agencies, that such product candidates are safe and effective for their intended use(s). Results from nonclinical and preclinical studies and clinical trials can be interpreted in different ways. Even if we believe the nonclinical and preclinical or clinical data for the Pharmaceutical Companies' product candidates are promising, such data may not be sufficient to support approval by the FDA and other regulatory authorities. The FDA or foreign regulatory agencies may also require the Pharmaceutical Companies to conduct additional preclinical studies or clinical trials for their product candidates either prior to or post-approval, or they may object to elements of a proposed clinical development program.

The FDA or any foreign regulatory bodies can delay, limit or deny approval of the Pharmaceutical Companies' product candidates or require them to conduct additional nonclinical and preclinical or clinical testing or abandon a program for multiple reasons in their sole discretion, including the following:

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of clinical trials;
- the Pharmaceutical Companies 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;
- serious and unexpected drug-related side effects experienced by participants in clinical trials or by individuals using drugs similar to the Pharmaceutical Companies' product candidates may result in negative regulatory conclusions regarding a product candidate's safety profile;
- the Pharmaceutical Companies 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 the Pharmaceutical Companies' interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of the Pharmaceutical Companies' product candidates may not be acceptable or sufficient to support the submission of a NDA or other comparable submission or to obtain regulatory approval in the United States or elsewhere, and the Pharmaceutical Companies may be required to conduct additional clinical studies;
- the FDA's or the applicable foreign regulatory authority may disagree regarding the formulation, labeling, manufacturing, and/or the specifications of the Pharmaceutical Companies' product candidates;
- the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which the Pharmaceutical Companies contract for clinical and commercial supplies; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering clinical data insufficient for approval.

Of the large number of drugs in development, only a small percentage successfully complete the FDA or foreign regulatory approval processes and are commercialized. The lengthy approval process as well as the unpredictability of future clinical trial results may result in the Pharmaceutical Companies failing to obtain regulatory approval to market their product candidates, which would significantly harm our business, results of operations and prospects. In addition, even if the Pharmaceutical Companies were to obtain approval, regulatory authorities may approve any of their product candidates for fewer or more limited indications than requested, may grant approval contingent on the performance of costly post-marketing clinical trials, including Phase 4 clinical trials, and/or the implementation of a REMS, which may be required to assure safe use of the drug after approval. The FDA or the applicable foreign regulatory authority also may approve a product candidate for a more limited indication or patient population than originally requested, 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. Even if regulatory approval were to be secured, foreign authorities responsible for drug pricing determinations may not approve the prices the Pharmaceutical Companies intend to charge for any approved products. Any of the foregoing scenarios could materially harm the commercial prospects for the Pharmaceutical Companies product candidates.

If the FDA does not conclude that certain of the Pharmaceutical Companies' product candidates satisfy the requirements for the Section 505(b)(2) regulatory approval pathway, or if the requirements for such product candidates under Section 505(b)(2) are not as they expect, the approval pathway for those product candidates will likely take significantly longer, cost significantly more and entail significantly greater complications and risks than anticipated, and in either case may not be successful.

The Pharmaceutical Companies may develop product candidates for which they plan to seek approval under the 505(b)(2) regulatory pathway in the United States. For example, LipoMedix may ultimately seek FDA approval of Promitil through the 505(b)(2) pathway.

The Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Act, added Section 505(b)(2) to the FDCA. Section 505(b)(2) of the FDCA permits the submission of an NDA where at least some of the information required for approval comes from studies that were not conducted by or for the applicant and for which the applicant has not obtained a right of reference. Section 505(b)(2), if applicable under the FDCA, would allow an NDA submitted to the FDA to rely in part on data in the public domain and the FDA's prior conclusions regarding the safety and effectiveness of a previously-approved product, which could expedite the development program for certain of the Pharmaceutical Companies' product candidates by potentially decreasing the amount of nonclinical and preclinical and/or clinical data that they would need to generate in order to obtain FDA approval.

If the FDA does not allow any of the Pharmaceutical Companies' product candidates to pursue approval under the Section 505(b)(2) regulatory pathway as anticipated, the Pharmaceutical Companies may need to conduct additional nonclinical and preclinical studies and/or clinical trials, provide additional data and information, and meet additional standards for regulatory approval. If this were to occur, the time and financial resources required to obtain FDA approval for such product candidates, and complications and risks associated with such product candidates, would likely substantially increase. Moreover, inability to pursue approval under the Section 505(b)(2) regulatory pathway could result in new competitive products reaching the market more quickly than any product candidates the Pharmaceutical Companies are developing, which could adversely impact our and their competitive position and prospects. Even if the Pharmaceutical Companies are allowed to pursue approval under the Section 505(b)(2) regulatory pathway, we cannot assure you that any product candidates the Pharmaceutical Companies develop will receive the requisite approval for commercialization.

In addition, notwithstanding the approval of a number of products by the FDA under Section 505(b)(2), certain pharmaceutical companies and others have objected to the FDA's interpretation of Section 505(b)(2). If the FDA's interpretation of Section 505(b)(2) is successfully challenged, either generally or in connection with a Section 505(b)(2) submission by the Pharmaceutical Companies, the FDA may change its 505(b)(2) policies and practices, which could delay or even prevent the FDA from approving any NDA that the Pharmaceutical Companies submit under Section 505(b)(2). In addition, the pharmaceutical industry is highly competitive, and Section 505(b)(2) NDAs are subject to certain requirements designed to protect the patent rights of sponsors of previously approved drugs that are referenced in a Section 505(b)(2) NDA. These requirements may give rise to patent litigation and mandatory delays in approval of the Pharmaceutical Companies NDAs for up to 30 months or longer depending on the outcome of any litigation. It is not uncommon for a manufacturer of a previously approved product to file a citizen petition with the FDA seeking to delay approval of, or impose additional approval requirements for, pending competing products. If successful, such petitions can significantly delay, or even prevent, the approval of a new product. Even if the FDA ultimately denies such a petition, the FDA may substantially delay approval while it considers and responds to the petition. In addition, even if the Pharmaceutical Companies are able to utilize the Section 505(b)(2) regulatory pathway, there is no guarantee this would ultimately lead to streamlined product development or earlier approval.

The Pharmaceutical Companies may not be able to obtain orphan drug designation or obtain or maintain the benefits associated with orphan drug designation, such as orphan drug exclusivity and, even if they do, that exclusivity may not prevent the FDA or other comparable foreign regulatory authorities from approving competing products.

As part of their business strategy, the Pharmaceutical Companies may seek orphan drug designation, or ODD, for any eligible product candidates they develop, but they may be unsuccessful in obtaining or maintaining the benefits of such designations.

Regulatory authorities in some jurisdictions, including the United States, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing and making available the drug will be recovered from sales in the United States. Cornerstone has received ODD for CPI-613 (devimistat) for the treatment of pancreatic cancer, acute myeloid leukemia, myelodysplastic syndrome, Burkitt's lymphoma, peripheral T-cell lymphomas, soft tissue sarcoma, and biliary cancer. Cyclo received orphan drug for the treatment of NPC by the FDA for its Trappsol® product.

In the United States, ODD entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. In addition, if a product that has ODD subsequently receives the first FDA approval for a particular active ingredient for the rare disease for which it has such designation, the product is entitled to orphan drug exclusivity for that active ingredient for that rare disease. Orphan drug exclusivity in the United States provides that the FDA may not approve any other applications, including a full NDA or other comparable submission, to market the same drug for the same indication for seven years, except in limited circumstances such as a showing of clinical superiority to the product with orphan product exclusivity, or if the FDA withdraws exclusive approval or revokes orphan drug designation, or if the marketing application (NDA or BLA) for the orphan drug is withdrawn for any reason, or if the FDA finds that the holder of the orphan exclusivity has not shown that it can ensure the availability of sufficient quantities of the orphan product to meet the needs of patients with the disease or condition for which the product was designated.

Even if the Pharmaceutical Companies obtain ODD for a product candidate, they may not be able to obtain or maintain orphan drug exclusivity for that product candidate. The Pharmaceutical Companies may not be the first to obtain regulatory approval of any product candidate for which they have obtained ODD for the orphan-designated indication due to the uncertainties associated with developing pharmaceutical products. In addition, exclusive marketing rights in the United States may be limited if the Pharmaceutical Companies seek approval for an indication broader than the orphan-designated indication or may be lost if the FDA later determines that the request for designation was materially defective or if they are unable to ensure that they will be able to manufacture sufficient quantities of the product to meet the needs of patients with the rare disease or condition.

Further, even if the Pharmaceutical Companies obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs with different active ingredients be approved for the same condition, and competitors also potentially could secure approval of the same drug for different non-orphan conditions. Even after an orphan drug is approved, the FDA can subsequently approve the same drug for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care or the manufacturer of the product with orphan exclusivity is unable to maintain sufficient product quantity. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the product candidate any advantage in the regulatory review or approval process.

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, including a shutdown of the federal government. Average review times at the FDA have fluctuated in recent years. 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 drugs or modifications to approved drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, including for 35 days beginning on December 22, 2018, the United States federal 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. Additionally, on April 15, 2021, the FDA issued a guidance document in which the FDA described its plans to conduct voluntary remote interactive evaluations of certain drug manufacturing facilities and clinical research sites. According to the guidance, the FDA intends to request such remote interactive evaluations in situations where an in-person inspection would not be prioritized, deemed mission-critical, or where direct inspection is otherwise limited by travel restrictions, but where the FDA determines that remote evaluation would be appropriate. Regulatory authorities outside the United States may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic, subsequent variants or comparable public health emergencies. In addition, clinical trial sites, including hospitals and medical centers among others, may significantly limit or even halt clinical trials as a result of the COVID-19 pandemic, subsequent variants or comparable public health emergencies, which could significantly impede the ability to recruit for or even conduct clinical trials during such a public health emergency, which could have a material adverse effect on our and/or the Pharmaceutical Companies' business. 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 the Pharmaceutical Companies' regulatory submissions, which could have a material adverse effect on our business.

Even if the Pharmaceutical Companies receive regulatory approval for any product candidate, they will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense.

Any regulatory approvals that the Pharmaceutical Companies may receive for their product candidates will require the regular submission of reports to regulatory authorities and surveillance to monitor the safety and efficacy of the product, may contain significant limitations related to use restrictions for specified age groups, warnings, precautions or contraindications, and may include burdensome post-approval study or risk management requirements. For example, the FDA may require a REMS as a condition of approval of a product candidate, which could include requirements for a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries, and other risk minimization tools. In addition, if the FDA or a comparable foreign regulatory authority approves a product candidate, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, import, export, and recordkeeping for the Pharmaceutical Companies' products will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMP and GCP requirements for any clinical trials that are conducted post-approval. Manufacturers of approved products and their facilities are subject to continual review and periodic, unannounced inspections by the FDA and other regulatory authorities for compliance with cGMP regulations and standards. Later discovery of previously unknown problems with marketed products, including adverse events of unanticipated severity or frequency, or with third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing or manufacturing of our products, withdrawal of the product from the market or voluntary or mandatory product recalls;
- restrictions on product distribution or use, or requirements to conduct post-marketing studies or clinical trials;
- fines, restitutions, disgorgement of profits or revenue, warning letters, untitled letters or holds on clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us or suspension or revocation of approvals;
- product seizure or detention, or refusal to permit the import or export of our products; and
- injunctions or the imposition of civil or criminal penalties.

The occurrence of any event or penalty described above may inhibit our or the Pharmaceutical Companies' ability to commercialize their product candidates and generate revenue and could require the Pharmaceutical Companies to expend significant time and resources in response and could generate negative publicity.

The FDA's and other regulatory authorities' policies may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of the Pharmaceutical Companies' product candidates. We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. For example, the results of the 2020 United States Presidential Election impacted our business and industry. Namely, the Trump Administration took several Executive Actions, including the issuance of a number of Executive Orders, that imposed significant burdens on, or otherwise materially delayed, 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 rescinded and replaced under the Biden Administration. The policies and priorities of any administration are unknown and could materially impact the regulations governing the Pharmaceutical Companies' product candidates. If we or the Pharmaceutical Companies are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or they are not able to maintain regulatory compliance, we or they may be subject to enforcement action and we or they may not achieve or sustain profitability.

The FDA and other regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses.

If any of the Pharmaceutical Companies' product candidates are approved and if they are found to have been improperly promoted for unapproved uses of those products, we and/or the Pharmaceutical Companies may become subject to significant liability. The FDA and other regulatory agencies strictly regulate the promotional claims that may be made about prescription products, such as the Pharmaceutical Companies' product candidates, if approved. In particular, a product may not be promoted for uses or other conditions of labeling that are not approved by the FDA or such other regulatory agencies as reflected in the product's approved labeling. If the Pharmaceutical Companies receive regulatory approval for a product candidate, physicians may nevertheless prescribe it to their patients in a manner that is inconsistent with the approved label. If we or the Pharmaceutical Companies are found to have promoted such unapproved, or off-label, uses, we or they may become subject to significant liability. The U.S. federal government has levied large civil and criminal fines against companies for alleged improper promotion of off-label use and has enjoined several companies from engaging in off-label promotion. The FDA has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed. If we or the Pharmaceutical Companies cannot successfully manage the promotion of their product candidates, if approved, we and/or they could become subject to significant liability, which would materially adversely affect our business and financial condition.

Even if any of the Pharmaceutical Companies' product candidates receive regulatory approval, they may fail to achieve the degree of market acceptance by physicians, patients, healthcare payors and others in the medical community necessary for commercial success.

If any of the Pharmaceutical Companies' product candidates receive regulatory approval, they may nonetheless fail to gain sufficient market acceptance by physicians, patients, healthcare payors, and others in the medical community. For example, current cancer treatments like chemotherapy and radiation therapy are well established in the medical community, and doctors may continue to rely on these treatments. If the Pharmaceutical Companies' product candidates do not achieve an adequate level of acceptance, the Pharmaceutical Companies may not generate significant product revenue and may not become profitable. The degree of market acceptance of the Pharmaceutical Companies' product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy, safety profile, and any potential clinical advantages compared to alternative treatments;
- the approval, availability, market acceptance, and reimbursement for any companion diagnostic;
- the ability to offer the Pharmaceutical Companies' medicines for sale at competitive prices;
- convenience and ease of administration compared to alternative treatments;

- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- ensuring uninterrupted product supply;
- the strength of marketing and distribution support;
- sufficient third-party coverage and reimbursement; and
- the prevalence and severity of any side effects.

If any of the Pharmaceutical Companies' product candidates are approved but do not achieve an adequate level of acceptance by physicians, hospitals, healthcare payors and patients, they may not generate or derive sufficient revenue from that product candidate and our and their financial results could be negatively impacted.

We are dependent upon third parties for a variety of functions. These arrangements may not provide us with the benefits we expect.

We rely on third parties to perform a variety of functions. We are party to numerous agreements that place substantial responsibility on clinical research organizations, contract manufacturing organizations, consultants, and other service providers for the development of the Pharmaceutical Companies' product candidates. We also rely on medical and academic institutions to perform aspects of the Pharmaceutical Companies' clinical trials of product candidates. In addition, an element of our research and development strategy has been to in-license technology and product candidates from academic and government institutions in order to minimize or eliminate investments in early research. We may not be able to enter new arrangements without undue delays or expenditures or on favorable terms, if at all, and these arrangements may not allow us to compete successfully. Moreover, if third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct clinical trials in accordance with regulatory requirements or applicable protocols, the Pharmaceutical Companies' product candidates may not be approved for marketing and commercialization or such approval may be delayed. If that occurs, our collaborators will not be able, or may be delayed in their efforts, to seek regulatory approval for or commercialize the Pharmaceutical Companies' product candidates.

If, in the future, the Pharmaceutical Companies are unable to establish sales and marketing capabilities or enter into agreements with third parties to sell and market the Pharmaceutical Companies' product candidates, the Pharmaceutical Companies may not be successful in commercializing their product candidates if and when they are approved.

We and the Pharmaceutical Companies do not have a sales or marketing infrastructure and have little experience in the sale, marketing or distribution of pharmaceutical products. To achieve commercial success for any approved medicine for which the Pharmaceutical Companies retain sales and marketing responsibilities, they must either develop a sales and marketing organization or outsource these functions to other third parties. In the future, the Pharmaceutical Companies may choose to build a focused sales and marketing infrastructure to sell, or participate in sales activities with our or their collaborators for, some of their product candidates if and when they are approved.

There are risks involved with both establishing the Pharmaceutical Companies' own sales and marketing capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force is expensive and time consuming and could delay any product launch. If the commercial launch of a product candidate that has received regulatory approval for which the Pharmaceutical Companies recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, they would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if the Pharmaceutical Companies cannot retain or reposition their sales and marketing personnel.

Factors that may inhibit the Pharmaceutical Companies' efforts to commercialize their medicines on our their own include:

- the Pharmaceutical Companies' inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future medicines;

- the lack of complementary medicines to be offered by sales personnel, which may put them at a competitive disadvantage relative to companies with more extensive product lines;
- the Pharmaceutical Companies' inability to equip medical and sales personnel with effective materials, including medical and sales literature, to help them educate physicians and other healthcare providers regarding applicable diseases and any products that receive regulatory approval;
- the Pharmaceutical Companies' inability to develop or obtain sufficient operational functions to support our commercial activities; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If the Pharmaceutical Companies enter into arrangements with third parties to perform sales, marketing, reimbursement and distribution services, their product revenue or the profitability of product revenue to them are likely to be lower than if the Pharmaceutical Companies were to market and sell any medicines that they develop themselves. In addition, the Pharmaceutical Companies may not be successful in entering into arrangements with third parties to sell and market their product candidates or may be unable to do so on terms that are favorable. We and the Pharmaceutical Companies likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market the Pharmaceutical Companies' medicines effectively. If the Pharmaceutical Companies do not establish sales and marketing capabilities successfully, either on their own or in collaboration with third parties, the Pharmaceutical Companies will not be successful in commercializing their product candidates.

The companies in which we hold interests face substantial competition, and if competitors develop and market technologies or products more rapidly than those companies do or that are more effective, safer or less expensive than the product candidates that those companies develop, our commercial opportunities will be negatively impacted.

The biopharmaceutical industries are characterized by rapidly advancing technologies, intense competition, and a strong emphasis on proprietary and novel products and product candidates. The development and commercialization of new drug products is highly competitive. We and the Pharmaceutical Companies face competition with respect to current product candidates, and we and the Pharmaceutical Companies and our and their collaborators will face competition with respect to any product candidates that they or their collaborators may seek to develop or commercialize in the future, from major pharmaceutical companies and specialty biopharmaceutical companies worldwide. There are a number of large biopharmaceutical companies that currently market and sell products or are pursuing the development of products for the treatment of the disease indications for which the Pharmaceutical Companies are developing their product candidates, such as pancreatic cancer and acute myelogenous leukemia among others. Some of these competitive products and therapies are based on scientific approaches that are similar to our or the Pharmaceutical Companies' approach. Potential competitors also include academic institutions, government agencies, and other public and private research organizations that conduct research, seek patent protection, and establish collaborative arrangements for research, development, manufacturing and commercialization.

The Pharmaceutical Companies that are developing their product candidates for the treatment of cancer may compete against a variety of available drug therapies marketed for cancer. In many cases, these drugs are administered in combination to enhance efficacy, and cancer drugs are frequently prescribed off-label by healthcare professionals. Some of the currently approved drug therapies are branded and subject to patent protection, and others are available on a generic or biosimilar basis. Many of these approved drugs are well established therapies and are widely accepted by physicians, patients and third-party payors. Insurers and other third-party payors may also encourage the use of generic products. The Pharmaceutical Companies expect that if their product candidates are approved, they will be priced at a significant premium over competitive generic or biosimilar products. This may make it difficult for the Pharmaceutical Companies to achieve their business strategy of using their product candidates in combination with existing therapies or replacing existing therapies with their product candidates following any regulatory approvals.

Cornerstone is focused on an area known as cancer metabolism, and there are also a number of product candidates in preclinical or clinical development by third parties to treat cancer by targeting cancer metabolism. These companies include large pharmaceutical companies, including, but not limited to, AstraZeneca plc, Eli Lilly and Company, Roche Holdings Inc. and its subsidiary Genentech, Inc., GlaxoSmithKline plc, Merck & Co., Novartis, Pfizer, Inc., Novo Nordisk, and Genzyme, a Sanofi company. There are also biotechnology companies of various sizes that are developing therapies to target cancer metabolism, including, but not limited to, Sagiment Biosciences, Eleison Pharmaceuticals, BioMarin Pharmaceutical Inc., and Takeda.

Cyclo is focused on a cure for NPC and faces competition from Actelion, a subsidiary of Johnson & Johnson Orphazyme, a public company based in Denmark, Zevra Therapeutics, Inc., Mandos Health, azafaros and IntraBio among others.

LipoMedix faces competition from (i) other liposome and nanomedicine products in solid tumors (for example, Doxil (Janssen), Onivyde (Ipsen), and Abraxane (Celgene)); (ii) other non-liposomal chemotherapeutic drugs in gastrointestinal malignancies recently developed or under development (for example, TAS-102 (Taiho) in colorectal cancer); (iii) biological therapy (including small molecule kinase inhibitors) recently developed or under development for colon cancer (for example, Regorafenib (Bayer)); (iv) immunotherapy approaches in gastrointestinal malignancies (for example, Merck USA), antibodies and/or vaccinations; and (v) other companies such as Roche.

The Pharmaceutical Companies' competitors may develop products that are more effective, safer, more convenient or less costly than any that the Pharmaceutical Companies are developing or that would render their product candidates obsolete or non-competitive. In addition, our or the Pharmaceutical Companies' competitors may discover biomarkers that more efficiently and/or effectively measure metabolic pathways than the Pharmaceutical Companies' methods, which may give them a competitive advantage in developing potential products. The Pharmaceutical Companies' competitors may also obtain regulatory approval from the FDA or other regulatory authorities for their products more rapidly than the Pharmaceutical Companies may obtain approval, which could result in the Pharmaceutical Companies' competitors establishing a strong market position before they are able to enter the market.

Many of the Pharmaceutical Companies' competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals, and marketing approved products than the Pharmaceutical Companies do. Mergers and acquisitions in the biopharmaceutical industries may result in even more resources being concentrated among a smaller number of the Pharmaceutical Companies' competitors. Smaller and other clinical stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us and the Pharmaceutical Companies in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, the Pharmaceutical Companies' programs.

Even if the Pharmaceutical Companies or their collaborators are able to commercialize any product candidates, such products may become subject to unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives, which would harm our and the Pharmaceutical Companies' business.

The commercial success of the Pharmaceutical Companies' product candidates will depend substantially, both domestically and abroad, on the extent to which the costs of the Pharmaceutical Companies' product candidates will be paid following regulatory approval by third-party payors, including government health administration authorities and private health coverage insurers. If coverage and reimbursement is not available, or reimbursement is available only to limited levels, the Pharmaceutical Companies, or any future collaborators, may not be able to successfully commercialize the Pharmaceutical Companies' product candidates in the event they receive regulatory approval. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us, the Pharmaceutical Companies, or any future collaborators, to establish or maintain pricing sufficient to realize a sufficient return on our or the Pharmaceutical Companies' investments. In the United States, no uniform policy of coverage and reimbursement for products exists among third-party payors, and 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 and the Pharmaceutical Companies to provide scientific and clinical support for the use of their products to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance.

There is significant uncertainty related to third-party payor coverage and reimbursement of newly approved drugs. Regulatory approvals, pricing, and reimbursement for new drug products vary widely from country to country. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or regulatory approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, the Pharmaceutical Companies, or any future collaborators, might obtain regulatory approval for a product in a particular country, but then be subject to price regulations that delay commercial launch of the product, possibly for lengthy time periods, which may negatively impact the revenue the Pharmaceutical Companies are able to generate from the sale of

the product in that country. Adverse pricing limitations may hinder our or the Pharmaceutical Companies' ability or the ability of any future collaborators to recoup our or the Pharmaceutical Companies' or their investment in one or more product candidates, even if the Pharmaceutical Companies' product candidates obtain regulatory approval.

Patients who are provided medical treatment for their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Therefore, the Pharmaceutical Companies' ability, and the ability of any future collaborators, to commercialize any of the Pharmaceutical Companies' product candidates will depend in part on the extent to which coverage and reimbursement for these products and related treatments will be available from third-party payors. Third-party payors decide which medications they will cover and establish reimbursement levels. The healthcare industry is acutely focused on cost containment, both in the United States and elsewhere. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications, which could affect our or the Pharmaceutical Companies' ability or that of any future collaborators to sell the Pharmaceutical Companies' product candidates profitably following regulatory approval. These payors may not view the Pharmaceutical Companies' products, if any, as cost-effective, and coverage and reimbursement may not be available to our or the Pharmaceutical Companies' customers, or those of any future collaborators, or may not be sufficient to allow the Pharmaceutical Companies' products, if any, to be marketed on a competitive basis. Cost-control initiatives could cause us, or any future collaborators, to decrease the price the Pharmaceutical Companies, or they, might establish for products, which could result in lower than anticipated product revenue. If the prices for the Pharmaceutical Companies' products, if any, decrease or if governmental and other third-party payors do not provide coverage or adequate reimbursement, our and the Pharmaceutical Companies' prospects for revenue and profitability will suffer.

There may also be delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the indications for which the drug is approved by the FDA or comparable foreign regulatory authorities. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our or the Pharmaceutical Companies' costs, including research, development, manufacture, sale, and distribution. Reimbursement rates may vary, by way of example, according to the use of the product and the clinical setting in which it is used. Reimbursement rates may also be based on reimbursement levels already set for lower cost drugs or may be incorporated into existing payments for other services.

In addition, increasingly, third-party payors are requiring higher levels of evidence of the benefits and clinical outcomes of new technologies and are challenging the prices charged. We and the Pharmaceutical Companies cannot be sure that coverage will be available for any product candidate that they, or any future collaborator, commercializes and, if available, that the reimbursement rates will be adequate. Further, the net reimbursement for drug products may be subject to additional reductions if there are changes to laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. An inability to promptly obtain coverage and adequate reimbursement rates from both government-funded and private payors for any of the Pharmaceutical Companies' product candidates for which they, or any future collaborator, obtain regulatory approval could significantly harm our and the Pharmaceutical Companies' operating results, our and the Pharmaceutical Companies' ability to raise capital needed to commercialize products, and our and the Pharmaceutical Companies' overall financial condition.

Product liability lawsuits against us or the Pharmaceutical Companies or our or their collaborators could cause substantial liabilities and could limit commercialization of any medicines that the Pharmaceutical Companies or our or their collaborators may develop.

We and the Pharmaceutical Companies and their collaborators face an inherent risk of product liability exposure related to the testing of the Pharmaceutical Companies' product candidates in human clinical trials and will face an even greater risk if the Pharmaceutical Companies commercially sell any medicines that the Pharmaceutical Companies may develop that secure regulatory approval. If the Pharmaceutical Companies or us or their or our collaborators cannot successfully defend ourselves or themselves against claims that the Pharmaceutical Companies' product candidates or medicines caused injuries, the Pharmaceutical Companies and we could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates or medicines that the Pharmaceutical Companies may develop;
- injury to the Pharmaceutical Companies' reputation and significant negative media attention;

- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue;
- reduced resources of the Pharmaceutical Companies' management to pursue the Pharmaceutical Companies' business strategy; and diverted time and attention from executing on that strategy; and
- the inability to commercialize any medicines that the Pharmaceutical Companies may develop.

Although we and the Pharmaceutical Companies plan to maintain product liability insurance coverage, it may not be adequate to cover all liabilities that the Pharmaceutical Companies and we may incur. We anticipate that we and the Pharmaceutical Companies will need to increase our and their insurance coverage as they continue to run clinical trials and if they successfully commercialize any medicine that receives regulatory approval. Insurance coverage in this setting is increasingly expensive. We and/or the Pharmaceutical Companies may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise. In addition, if one of our or the Pharmaceutical Companies' collaboration partners were to become subject to product liability claims or were unable to successfully defend themselves against such claims, any such collaboration partner could be more likely to terminate such relationships and could potentially seek indemnification from us and/or the Pharmaceutical Companies, and therefore substantially limit the commercial potential of our and/or the Pharmaceutical Companies' products.

If we or the Pharmaceutical Companies fail to comply with environmental, health and safety laws and regulations, we or they could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our or their businesses.

We and the Pharmaceutical Companies are subject to numerous environmental, health, and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment, and disposal of hazardous materials and wastes. The Pharmaceutical Companies' operations involve the use of hazardous and flammable materials, including chemicals and biological and radioactive materials. The Pharmaceutical Companies' operations also produce hazardous waste products. The Pharmaceutical Companies generally contract with third parties for the disposal of these materials and wastes. The Pharmaceutical Companies cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from their use of hazardous materials, the Pharmaceutical Companies could be held liable for any resulting damages, and any liability could exceed their resources. The Pharmaceutical Companies also could incur significant costs associated with civil or criminal fines and penalties.

Although the Pharmaceutical Companies maintain workers' compensation insurance to cover them for costs and expenses they may incur due to injuries to their employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. The Pharmaceutical Companies may not maintain adequate insurance for environmental liability or toxic tort claims that may be asserted against them in connection with their storage or disposal of biological, hazardous or radioactive materials.

In addition, the Pharmaceutical Companies may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair the Pharmaceutical Companies' research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Current and future legislation may increase the difficulty and cost for us and the Pharmaceutical Companies and any future collaborators to obtain regulatory approval of the Pharmaceutical Companies' product candidates and affect the prices obtained.

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could, among other things, prevent or delay development and/or regulatory approval of the Pharmaceutical Companies' product candidates, restrict or regulate post-approval

activities and affect the Pharmaceutical Companies' ability, or the ability of any future collaborators, to profitably sell any products for which the Pharmaceutical Companies, or they, obtain regulatory approval. We and the Pharmaceutical Companies expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and additional downward pressure on the price that the Pharmaceutical Companies, or any future collaborators, may receive for any approved products.

For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively the ACA, was signed into law. Among the provisions of the ACA of potential importance to the Pharmaceutical Companies' business and the Pharmaceutical Companies' product candidates are the following:

- an annual, non-deductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program, or MDRP;
- a new methodology by which rebates owed by manufacturers under the MDRP are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- expansion of healthcare fraud and abuse laws, including the civil False Claims Act and the federal Anti-Kickback Statute, new government investigative powers and enhanced penalties for noncompliance;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to now offer 70% 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;
- extension of manufacturers' Medicaid rebate liability to individuals enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new requirements to report certain financial arrangements with physicians and teaching hospitals for eventual publication;
- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians for eventual publication;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and
- a Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models.

Since enactment of the ACA, there have been numerous executive and legal challenges and Congressional actions to repeal and replace provisions of the law. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Prior to the Supreme Court's decision, President Biden issued an Executive Order to initiate a special enrollment period from February 15, 2021 through August 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The Executive Order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including, among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. It is unclear how other healthcare reform measures of the Biden Administrations or other efforts, if any, to challenge, repeal or replace the ACA, will impact the Pharmaceutical Companies' businesses.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. On August 2, 2011, the U.S. Budget Control Act of 2011, among other things, included aggregate reductions of Medicare payments to providers of 2% per fiscal year. These reductions went into effect on April 1, 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 December 31, 2021, unless additional Congressional action is taken. Additionally, there has been increasing legislative and enforcement interest in the United States with respect to drug pricing practices. Specifically, there has been heightened governmental scrutiny of pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient assistance programs, and reform government program reimbursement methodologies for drug products. Among other things, such scrutiny has led to enactment of a budget reconciliation measure known as the Inflation Reduction Act of 2022, or IRA, signed into law by President Biden on August 16, 2022, which makes wide-reaching changes to Medicare prescription drug coverage and more targeted changes to Medicaid, the State Children's Health Insurance Coverage Program, or CHIP, and private health insurance, and which includes several provisions to lower prescription drug costs for people with Medicare and reduce drug spending by the federal government. The prescription drug provisions included in the IRA will, among other things:

- require the federal government to negotiate prices for certain drugs covered under Medicare Part B (physician-administered drugs) and Part D (retail prescription drugs), starting with 10 high-spending, single-source drugs for 2026 and increasing to 20 by 2029;
- require manufacturers that sell drugs used by Medicare beneficiaries through Parts B and D to pay rebates to Medicare if they increase drug prices faster than consumer inflation, beginning in 2023;
- cap out-of-pocket spending for Medicare Part D enrollees and make other Part D benefit design changes, beginning in 2024;
- expand eligibility for full benefits under the Medicare Part D Low-Income Subsidy Program, beginning in 2024; and
- further delay implementation of the Trump Administration's drug rebate rule, beginning in 2027.

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical, medical device, and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access, marketing cost disclosure and transparency measures, and, in some cases, encouraging importation of drugs from other countries and bulk purchasing. 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. These measures could reduce the ultimate demand for the Pharmaceutical Companies' products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand or lower pricing for the Pharmaceutical Companies' product candidates, or additional pricing pressures.

We expect that healthcare reform measures that may be adopted in the future could have a material adverse effect on our and the Pharmaceutical Companies' industry generally and on our ability to maintain or increase sales of any of the Pharmaceutical Companies' product candidates that we successfully develop, secure regulatory approval for, and commercialize.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We and the Pharmaceutical Companies cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the regulatory approvals of our product candidates, if any, may be. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent regulatory approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

Additional Risks Related to our Medical Device Business

Rafael Medical Devices' device candidates may cause significant adverse events, toxicities or other undesirable side effects when used alone or in combination with other approved or cleared devices or investigational or approved drugs that may result in a safety profile that could prevent regulatory approval, prevent market acceptance, limit their commercial potential, result in significant negative consequences, or potential product liability claims.

If Rafael Medical Devices' device candidates are associated with undesirable side effects or have unexpected characteristics in clinical trials when used alone or in combination with other approved or cleared devices or in combination with investigational or approved drugs, Rafael Medical Devices may need to interrupt, delay or abandon their development or limit development to more narrow uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Treatment-related side effects could also affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may prevent us from achieving or maintaining market acceptance of the affected device candidate and may adversely affect our business, financial condition, and prospects significantly.

In addition, many device candidates that initially showed promise in early-stage testing have later been found to cause side effects that prevented further development of the device candidates. If significant adverse events or other side effects are observed in any of Rafael Medical Devices' current or future clinical trials, Rafael Medical Devices may have difficulty recruiting patients to the clinical trials, patients may drop out of such trials, or they may be required to abandon the trials or our development efforts of a device candidate altogether. Rafael Medical Devices, the FDA, other comparable regulatory authorities or an IRB may suspend clinical trials of a device candidate at any time for various reasons, including a belief that subjects in such trials are being exposed to inadequate clinical benefit and/or unacceptable health risks or adverse side effects.

Further, if any of Rafael Medical Devices' device candidates obtains regulatory approval or clearance, toxicities or other serious adverse events associated with such device candidates previously not seen during clinical testing may also develop after such approval and lead to a number of potentially significant negative consequences, including, but not limited to:

- Regulatory authorities may suspend, limit or withdraw approvals or clearances of such device, if any, 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;
- Rafael Medical Devices may be required to change the way the device is implanted or conduct additional clinical trials or post-approval studies;
- Rafael Medical Devices may be subject to fines, injunctions or the imposition of criminal penalties;
- we or Rafael Medical Devices could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent Rafael Medical Devices from achieving or maintaining market acceptance of the particular device candidate, if approved or cleared, and could seriously harm our business.

Interim, “top-line” and preliminary data from preclinical studies and clinical trials that Rafael Medical Devices announce or publish from time to time may change as more patient 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 and/or Rafael Medical Devices may publicly disclose preliminary or top-line data from preclinical studies and clinical trials, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We and/or Rafael Medical Devices may also make assumptions, estimations, calculations, and conclusions as part of our analyses of data, and we or they may not have received or had the opportunity to fully and

carefully evaluate all data. As a result, the top-line or preliminary results reported may differ significantly from future results of the same studies, or different conclusions or considerations may qualify such results and/or limit the clinical conclusions that can be drawn from them, once additional data have been received and fully evaluated. 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. In addition, the full study results from all clinical trials are subject to FDA review, and the FDA may draw materially different conclusions than those reached by us or Rafael Medical Devices. As a result, top-line data should be viewed with caution until the final data are available, and then, until the full study results have been completely evaluated by the FDA.

From time to time, we and/or Rafael Medical Devices may also disclose interim data from preclinical studies or clinical trials. Interim data from preclinical studies and clinical trials are subject to the risk that one or more of the preclinical or clinical outcomes may materially change as patient enrollment continues and more patient data become available or as patients from such clinical trials continue other treatments for their condition. Adverse differences between preliminary or interim data and final data could materially adversely affect our business prospects.

Further, others, including regulatory agencies, may not accept or agree with our or Rafael Medical Devices' assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular device development program, the approvability or commercialization of the particular device candidate or device, and our company in general. In addition, the information we or they 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 material or otherwise appropriate information to include in our disclosure. If the interim, top-line, or preliminary data that we or Rafael Medical Devices report differs from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, Rafael Medical Devices' ability to obtain approval or clearance for, and commercialize, their device candidates may be adversely affected, which could materially adversely affect our business, financial condition, and results of operations.

Results of preclinical studies and early clinical trials may not be predictive of results of future preclinical studies and clinical trials.

The outcome of preclinical studies and early clinical trials may not be predictive of the success or failure of later preclinical studies and clinical trials, and interim results of preclinical studies and clinical trials do not necessarily predict success in future preclinical studies and clinical trials. Many companies in the medical device industry have suffered significant setbacks in late-stage clinical trials after achieving positive results in earlier development, and Rafael Medical Devices could face similar setbacks. The design of a clinical trial can determine whether its results will support approval or clearance of a device candidate, and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced or even completed. Rafael Medical Devices has limited experience in designing clinical trials and may be unable to design and execute a clinical trial to support regulatory approval or clearance. In addition, clinical data are often susceptible to varying interpretations and analyses. Many medical device companies that believed their device candidates performed satisfactorily in clinical trials have nonetheless failed to obtain regulatory approval for the device candidates. Even if Rafael Medical Devices, or future collaborators, believe that the results of clinical trials for Rafael Medical Devices' device candidates warrant regulatory approval or clearance, the FDA or comparable foreign regulatory authorities may disagree and may not grant regulatory approval or clearance of Rafael Medical Devices' device candidates.

In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same device candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the treatment regimen and other elements of the clinical trial protocol, and the rate of dropout among clinical trial participants. If Rafael Medical Devices fails to receive positive results in clinical trials of Rafael Medical Devices' device candidates, the development timeline and regulatory approval or clearance and commercialization prospects for Rafael Medical Devices' most advanced device candidates, and, correspondingly, Rafael Medical Devices' business and financial prospects, would be negatively impacted.

The regulatory approval and clearance processes of the FDA and comparable foreign regulatory authorities are lengthy, time consuming, and inherently unpredictable, and if Rafael Medical Devices is ultimately unable to obtain regulatory approval or clearance for their device candidates, their business will be substantially harmed.

Before Rafael Medical Devices can market or sell a new medical device or a new use of or a claim for or significant modification to any medical device that has received approval or clearance, if any, in the United States, Rafael Medical Devices must obtain either clearance from the FDA under the 510(k) pathway, marketing authorization in response to a De Novo request, or approval of a PMA, unless an exemption applies. In the 510(k) clearance process, the FDA must determine that a proposed device is “substantially equivalent” to a legally-marketed predicate device. To be “substantially equivalent,” the proposed device must have the same intended use as the predicate device, and either have the same technological characteristics as the predicate device or have different technological characteristics and not raise different questions of safety or effectiveness than the predicate device. If FDA determines that the device is “not substantially equivalent,” the device is automatically designated as a Class III device. The device sponsor then must either fulfill the more rigorous PMA requirements, or the sponsor can submit a De Novo request seeking a risk-based classification determination for the device in accordance with the FDA’s De Novo classification process, which is a route to market for novel medical devices that are low to moderate risk and are not substantially equivalent to a predicate device. A sponsor also can submit a De Novo classification request directly, without first submitting a 510(k), if the sponsor determines that there is no legally marketed predicate device upon which to base a determination of substantial equivalence. In the PMA process, the FDA must determine that a proposed device is safe and effective for its intended use based, in part, on extensive data, including, but not limited to, technical, preclinical, clinical trial, manufacturing, and labeling data. The PMA process is typically required for products that are deemed to pose the greatest risk, such as life-sustaining, life-supporting or implantable devices.

The PMA approval, the De Novo classification, and the 510(k) clearance process can be expensive, lengthy, and uncertain. The FDA’s 510(k) clearance process usually takes from three to twelve months, but can last longer, and the De Novo classification generally can be comparable. The process of obtaining a PMA is much more costly and uncertain than the 510(k) clearance and De Novo classification processes and generally takes from six to eighteen months, or even longer, from the time the application is filed with the FDA. In addition, a PMA generally requires the performance of one or more clinical trials. Despite the time, effort, and cost, we cannot assure you that any particular device candidate will be approved or cleared by the FDA. Any delay or failure to obtain necessary regulatory approvals, marketing authorizations, or clearances could harm Rafael Medical Devices’ business.

Any modification to any 510(k)-cleared product, if any, that would constitute a major change in its intended use, or any change that could significantly affect the safety or effectiveness of any such device, would require Rafael Medical Devices to obtain a new 510(k) marketing clearance and may even, in some circumstances, require the submission of a De Novo request or a PMA application, if the change raises complex or novel scientific issues or the product has a new intended use. The FDA requires every manufacturer to make the determination regarding the need for a new 510(k) submission in the first instance, but the FDA may review any manufacturer’s decision. Rafael Medical Devices may make changes to a 510(k)-cleared product, if any, in the future that Rafael Medical Devices may determine does not require a new 510(k) clearance, De Novo marketing authorization, or PMA approval. If the FDA disagrees with Rafael Medical Devices’ decision not to seek a new 510(k) clearance, De Novo marketing authorization, or PMA approval for changes or modifications to any existing devices and requires new clearances, marketing authorizations, or approvals, Rafael Medical Devices may be required to recall and stop marketing any products as modified, if any, which could require Rafael Medical Devices to redesign its products, conduct clinical trials to support any modifications, and pay significant regulatory fines or penalties. If there is any delay or failure in obtaining required clearances or approvals or if the FDA requires Rafael Medical Devices to go through a lengthier, more rigorous examination for future device candidates or modifications to existing devices, if any, than Rafael Medical Devices had expected, Rafael Medical Devices’ ability to introduce new or enhanced devices in a timely manner would be adversely affected, which in turn would result in delayed or no realization of revenue from such device enhancements or new devices and could also result in substantial additional costs which could decrease our profitability.

The FDA can delay, limit or deny approval or clearance of a device for many reasons, including:

- Rafael Medical Devices may not be able to demonstrate to the FDA’s satisfaction that the device or modification is substantially equivalent to the proposed predicate device or safe and effective for its intended use;

- The data from Rafael Medical Devices' preclinical studies and clinical trials may be insufficient to support approval or clearance, where required; and;
- The manufacturing process or facilities that Rafael Medical Devices use may not meet applicable requirements.

In addition, the FDA may change its approval and clearance policies, adopt additional regulations or revise existing regulations, or take other actions, which may prevent or delay approval, marketing authorization, or clearance of Rafael Medical Devices' future device candidates or impact Rafael Medical Devices' ability to modify approved, marketing authorized, or cleared devices, if any, on a timely basis. Even after approval, marketing authorization, or clearance for Rafael Medical Devices' products is obtained, they and the products are subject to extensive postmarket regulation by the FDA, including with respect to advertising, marketing, labeling, manufacturing, distribution, import, export, and clinical evaluation.

Rafael Medical Devices is also required to timely file various reports with regulatory agencies for any device that has received approval, marketing authorization, or clearance. If these reports are not timely filed, regulators may impose sanctions, and sales of Rafael Medical Devices' products may suffer, and they and we may be subject to product liability or regulatory enforcement actions, all of which could harm our business. In addition, if Rafael Medical Devices initiates a correction or removal for a device that receives approval, marketing authorization, or clearance, if any, issues a safety alert, or undertakes a field action or recall to reduce a risk to health posed by any such device, Rafael Medical Devices may be required to submit a report to the FDA, and in many cases, to other regulatory agencies. Such reports could lead to increased scrutiny by the FDA, other comparable regulatory agencies, and Rafael Medical Devices' customers regarding the quality and safety of their devices, and to negative publicity, including FDA alerts, press releases, or administrative or judicial actions. Furthermore, the submission of these reports has been and could be used by competitors against Rafael Medical Devices in competitive situations and cause customers to delay purchase decisions or cancel orders, which would harm our reputation and business.

The FDA, state, and foreign regulatory authorities have broad enforcement powers. Rafael Medical Devices' failure to comply with applicable regulatory requirements could result in enforcement action by the FDA, state or foreign regulatory agencies, which may include any of the following sanctions:

- adverse publicity, warning letters, untitled letters, fines, injunctions, consent decrees, and civil penalties;
- repair, replacement, refunds, recalls, termination of distribution, administrative detention or seizures of a device(s) that receives approval or clearance, if any;
- operating restrictions, partial suspension or total shutdown of production;
- customer notifications or repair, replacement or refunds;
- refusing Rafael Medical Devices' requests for 510(k) clearance or PMA approvals or foreign regulatory approvals of new device candidates, new intended uses or modifications to existing devices, if any;
- withdrawals of current 510(k) clearances or PMAs or foreign regulatory approvals, resulting in prohibitions on sales of any Rafael Medical Devices' device(s) that receives approval or clearance, if any;
- FDA refusal to issue certificates to foreign governments needed to export products for sale in other countries; and
- criminal prosecution.

Any of these sanctions could also result in higher than anticipated costs or lower than anticipated sales of any Rafael Medical Devices' device(s) that receives approval, marketing authorization, or clearance and adversely affect our business, results of operations, and financial condition.

Even if Rafael Medical Devices receives regulatory approval, marketing authorization, or clearance for any device candidate, they will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense.

Any regulatory approvals, marketing authorizations, or clearances that Rafael Medical Devices may receive for their device candidates will require the regular submission of reports to regulatory authorities and surveillance to monitor the safety and effectiveness of the medical device, may contain significant limitations related to use restrictions for specified age groups, warnings, precautions or contraindications, and may include burdensome post-approval study requirements. If the FDA or a comparable foreign regulatory authority approves, issues a marketing authorization for, or clears a device candidate, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, import, export, and recordkeeping for Rafael Medical Devices' devices, if any, will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMP and GCP requirements for any clinical trials that are conducted post-approval. Manufacturers of approved devices and their facilities are subject to continual review and periodic, unannounced inspections by the FDA and other regulatory authorities for compliance with cGMP regulations and standards. Later discovery of previously unknown problems with marketed devices, including adverse events of unanticipated severity or frequency, or with third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing or manufacturing of any Rafael Medical Devices' device that receives approval or clearance, withdrawal of the device from the market or voluntary or mandatory device recalls;
- requirements to conduct post-marketing studies or clinical trials;
- fines, restitutions, disgorgement of profits or revenue, warning letters, untitled letters or holds on clinical trials;
- refusal by the FDA to approve or clear pending applications or supplements to approved applications filed by Rafael Medical Devices or suspension or revocation of approvals, if any;
- product seizure or detention, or refusal to permit the import or export of Rafael Medical Devices' devices; and
- injunctions or the imposition of civil or criminal penalties.

The occurrence of any event or penalty described above may inhibit Rafael Medical Devices' ability to commercialize their device candidates and generate revenue and could require Rafael Medical Devices to expend significant time and resources in response and could generate negative publicity.

In addition, the FDA's and other regulatory authorities' policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval, marketing authorization, or clearance of Rafael Medical Devices' device candidates. We also 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 United States Presidential Election impacted our business and industry. Namely, the Trump Administration took several Executive Actions, including the issuance of a number of Executive Orders, that imposed significant burdens on, or otherwise materially delayed, the FDA's ability to engage in routine oversight activities, such as implementing statutes through rulemaking, issuance of guidance, and review and approval of applications seeking approval, marketing authorization, or clearance of device candidates. It is difficult to predict whether or how these orders will be rescinded and replaced under the Biden Administration. The policies and priorities of any administration are unknown and could materially impact the regulations governing our device candidates. If we or Rafael Medical Devices are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or they are not able to maintain regulatory compliance as a result of a changing regulatory landscape or otherwise, we or they may be subject to enforcement action, may lose any regulatory approval(s), marketing authorization(s), or clearance(s) that they obtain, if any, or fail to obtain new regulatory approvals, marketing authorizations, or clearances, and they may not be able to achieve or sustain profitability, which would adversely affect our business, prospects, financial condition, and results of operations.

Rafael Medical Devices is dependent upon third parties for a variety of functions. These arrangements may not provide Rafael Medical Devices with the benefits they expect.

Rafael Medical Devices relies on third parties to perform a variety of functions. Rafael Medical Devices is party to numerous agreements that place substantial responsibility on clinical research organizations, contract manufacturing organizations, consultants, and other service providers for the development of Rafael Medical Devices' device candidates. Rafael Medical Devices also relies on medical and academic institutions to perform aspects of its clinical trials of device candidates. In addition, an element of Rafael Medical Devices' research and development strategy has been to in-license technology and device candidates from academic and government institutions in order to minimize or eliminate investments in early research. Rafael Medical Devices may not be able to enter new arrangements without undue delays or expenditures or on favorable terms, and these arrangements may not allow Rafael Medical Devices to compete successfully. Moreover, if third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct clinical trials in accordance with regulatory requirements or applicable protocols, Rafael Medical Devices' device candidates may not be approved, receive marketing authorization, or be cleared for marketing and commercialization or such approval, marketing authorization, or clearance may be delayed. If that occurs, Rafael Medical Devices or its collaborators will not be able, or may be delayed in their efforts, to commercialize Rafael Medical Devices' device candidates.

Product liability lawsuits against Rafael Medical Devices or their collaborators or us could cause substantial liabilities and could limit commercialization of any medical devices that Rafael Medical Devices or their collaborators may develop.

Rafael Medical Devices and their collaborators and we face an inherent risk of product liability exposure related to the testing and manufacturing of Rafael Medical Devices' device candidates in human clinical trials and will face an even greater risk if Rafael Medical Devices or they commercially sell any medical devices that Rafael Medical Devices or they may develop that secure regulatory approval, marketing authorization, or clearance. Rafael Medical Devices' device candidates are designed to affect, and any future devices will be designed to affect, important bodily functions and processes. Any side effects, manufacturing defects, misuse or abuse associated with Rafael Medical Devices' device candidates or devices could result in patient injury or death. The medical device industry has historically been subject to extensive litigation over product liability claims, and we cannot assure you that we will not face product liability claims. We may be subject to product liability claims if Rafael Medical Devices' device candidates or devices cause, or merely appear to have caused, patient injury or death, even if such injury or death was as a result of supplies or components that are produced by third-party suppliers. Product liability claims may be brought against us by consumers, healthcare providers or others selling or otherwise coming into contact with our products, among others. If Rafael Medical Devices or their collaborators, or we, cannot successfully defend themselves or ourselves against product liability claims that Rafael Medical Devices' device candidates or devices caused injuries, Rafael Medical Devices and we could incur substantial liabilities and reputational harm. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any device candidates or devices that Rafael Medical Devices may develop;
- injury to Rafael Medical Devices' reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue;
- product recalls or withdrawals from the market;
- reduced resources of Rafael Medical Devices' management to pursue Rafael Medical Devices' business strategy, and diverted time and attention from executing on that strategy; and
- the inability to commercialize any devices that Rafael Medical Devices may successfully develop, if any.

Although Rafael Medical Devices and we maintain product liability and/or clinical study liability insurance coverage that they and we believe is appropriate, this insurance is subject to deductibles and coverage limitations, and it may not be adequate to cover all liabilities that Rafael Medical Devices may incur. Rafael Medical Devices' and our

current product liability insurance may not continue to be available to them or us on acceptable terms, if at all. If Rafael Medical Devices or we are unable to obtain insurance at an acceptable cost or on acceptable terms or otherwise protect against potential product liability claims, they or we could be exposed to significant liabilities. We anticipate that Rafael Medical Devices will need to increase their insurance coverage as they continue to run clinical trials and if they successfully commercialize any device that receives regulatory approval, marketing authorization, or clearance. Insurance coverage in this setting is increasingly expensive. Rafael Medical Devices or we may not be able to maintain insurance coverage at a reasonable cost, if at all, or in an amount adequate to protect them or us against any product liability claim that may arise. In addition, if one of Rafael Medical Devices' collaboration partners were to become subject to product liability claims or were unable to successfully defend themselves against such claims, any such collaboration partner could be more likely to terminate such relationships and could potentially seek indemnification from Rafael Medical Devices, and therefore substantially limit the commercial potential of Rafael Medical Devices' device candidates. A product liability claim, recall or other claim with respect to uninsured liabilities or for amounts in excess of insured liabilities could adversely affect our business, results of operations, and financial condition.

If Rafael Medical Devices fails to comply with environmental, health and safety laws and regulations, they could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of their businesses.

Rafael Medical Devices is subject to numerous environmental, health, and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Rafael Medical Devices' operations involve the use of hazardous materials, including chemical materials. Rafael Medical Devices' operations also produce hazardous waste products. Rafael Medical Devices generally contracts with third parties for the disposal of these materials and wastes. Rafael Medical Devices cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from their use of hazardous materials, Rafael Medical Devices could be held liable for any resulting damages, and any liability could exceed their resources. Rafael Medical Devices also could incur significant costs associated with civil or criminal fines and penalties.

Although Rafael Medical Devices maintains workers' compensation insurance to cover them for costs and expenses they may incur due to injuries to their employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. Rafael Medical Devices may not maintain adequate insurance for environmental liability or toxic tort claims that may be asserted against them in connection with their storage or disposal of hazardous materials.

In addition, Rafael Medical Devices may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair Rafael Medical Devices' research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Risks Related to Reliance on Third Parties

The Investment Companies currently rely on, and plan to rely on in the future, third parties to conduct and support their preclinical studies and clinical trials. If these third parties do not properly and successfully carry out their contractual duties or meet expected deadlines, the Investment Companies and may not be able to obtain regulatory approval of or commercialize their product candidates.

The Investment Companies have utilized and plan to continue to utilize and depend upon independent investigators and collaborators, such as medical institutions, CROs, CMOs, and strategic partners to conduct and support their preclinical studies and clinical trials under written agreements. The Investment Companies will generally have to negotiate budgets and contracts with CROs, trial sites, and CMOs, and they may not be able to do so on favorable terms, if at all, which may result in delays to anticipated development timelines and increased costs.

We expect that the Investment Companies will rely heavily on these third parties over the course of their preclinical studies and clinical trials, and they will control only certain aspects of their activities. As a result, the Investment Companies will have less direct control over the conduct, timing, and completion of these preclinical studies and clinical trials and the management of data developed through preclinical studies and clinical trials than would be the case if they were relying entirely upon their own staff. Nevertheless, the Investment Companies are responsible for ensuring

that each of their studies is conducted in accordance with the applicable protocol, legal and regulatory requirements, and scientific standards, and our reliance on third parties does not relieve us of our regulatory responsibilities. The Investment Companies and these third parties are required to comply with GLP and GCP requirements, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for product candidates in clinical development. Regulatory authorities enforce these GLP and GCP requirements through periodic inspections, both announced and unannounced, of trial sponsors, principal investigators, and trial sites, and the corresponding books and records of such parties.

If the Pharmaceutical Companies or Rafael Medical Devices or any of these third parties fail to comply with applicable GLP or GCP regulations, the preclinical data generated in their preclinical studies and/or the clinical data generated in their clinical trials may be deemed unreliable, and the FDA or comparable foreign regulatory authorities may require them to repeat clinical trials and/or to perform additional preclinical studies and/or clinical trials before approving any marketing applications. We cannot assure you that, upon inspection, such regulatory authorities will determine that any of the Pharmaceutical Companies' or Rafael Medical Devices' preclinical studies and/or clinical trials comply with the GLP or GCP regulations. In addition, such clinical trials must be conducted with pharmaceutical product or a medical device produced under cGMP regulations and will require a large number of test patients. The Pharmaceutical Companies' or Rafael Medical Devices' failure or any failure by these third parties to comply with these regulations or to recruit a sufficient number of patients may require them to repeat clinical trials and/or to perform additional clinical studies, which would delay the regulatory approval process. Moreover, our business may be implicated if any of these third parties violates federal or state fraud and abuse or false claims laws and regulations or healthcare privacy and security laws.

Any third parties conducting the Pharmaceutical Companies' or Rafael Medical Devices' preclinical studies and clinical trials will not be their employees and, except for remedies available to them under our agreements with such third parties, the Investment Companies cannot control whether or not any third-party personnel will devote sufficient time and resources to the Pharmaceutical Companies' product candidates or Rafael Medical Devices' device candidates. These third parties may also have relationships with other commercial entities, including competitors, for whom they may also be conducting clinical trials or other product development activities, which could affect their performance on our behalf. If these third parties do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced, or if the quality or accuracy of the preclinical and/or clinical data they obtain is compromised due to the failure to adhere to preclinical or clinical protocols or regulatory requirements or for other reasons, the Pharmaceutical Companies' and Rafael Medical Devices' preclinical studies and clinical trials may be extended, delayed or terminated, and they may not be able to complete development of, obtain regulatory approval of, or successfully commercialize their product candidates or device candidates. As a result, our financial results and commercial prospects would be adversely affected, our costs could increase, and our ability to generate revenue could be delayed.

The Investment Companies currently rely and expect to rely in the future on the use of manufacturing suites in third-party facilities or on third parties to manufacture our product candidates and device candidates, and we may rely on third parties to produce and process our products, if approved. Our business could be adversely affected if we are unable to use third-party manufacturing suites or if the third-party manufacturers fail to provide us with sufficient quantities of our product candidates or device candidates or fail to do so in a cGMP-compliant manner, at acceptable quality levels or at acceptable prices.

We do not currently own any facility that may be used as a clinical-scale manufacturing and processing facility and must currently rely on outside vendors to manufacture the Pharmaceutical Companies' product candidates and Rafael Medical Devices' device candidates. The Investment Companies have not yet caused their product candidates or device candidates to be manufactured on a commercial scale and may not be able to do so. We expect that the Investment Companies will need to negotiate and maintain contractual arrangements with these outside vendors for the supply of our product candidates and device candidates, and they may not be able to do so on favorable terms.

The facilities used by contract manufacturers to manufacture approved products must also be approved by the FDA or other comparable foreign regulatory authorities following inspections for any such approved products that generally will be conducted after the Pharmaceutical Companies or Rafael Medical Devices submit an application to the FDA or other comparable foreign regulatory authorities. Such inspections also could occur, for other products being manufactured by contract manufacturers, before the Pharmaceutical Companies or Rafael Medical Devices submit an application to the FDA or other comparable foreign regulatory authorities, and any adverse regulatory findings

from such inspections could adversely impact a contract manufacturer's ability to be a contract manufacturer for the Investment Companies. The Investment Companies may not control the manufacturing process of, and may be completely dependent on, contract manufacturing partners for compliance with cGMP requirements and any other regulatory requirements of the FDA or other regulatory authorities for the manufacture of product candidates and device candidates and of any products that receive regulatory approval or clearance. Beyond periodic audits, the Investment Companies have no control over the ability of their contract manufacturers to maintain adequate quality control, quality assurance, and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of any approved or cleared products or if they withdraw any approval in the future, the Investment Companies may need to find alternative manufacturing facilities, which would require the incurrence of significant additional costs and materially adversely affect the ability to develop, obtain regulatory approval or clearance for or market any product candidates or device candidates, if approved or cleared. Similarly, if any third-party manufacturers on which the Pharmaceutical Companies or Rafael Medical Devices will rely fail to manufacture quantities of their product candidates or device candidates at quality levels necessary to meet regulatory requirements and at a scale sufficient to meet anticipated demand at a cost that allows them to achieve profitability, our business, financial condition, and prospects could be materially and adversely affected.

The anticipated reliance on a limited number of third-party manufacturers exposes us to a number of risks, including the following:

- the Pharmaceutical Companies may be unable to identify manufacturers on acceptable terms or at all because the number of potential manufacturers is limited, and the FDA must inspect any manufacturers for cGMP compliance as part of our marketing applications;
- a new manufacturer would have to be educated in, or develop substantially equivalent processes for, the production of the Pharmaceutical Companies' product candidates and Rafael Medical Devices' device candidates;
- third-party manufacturers might be unable to timely manufacture Pharmaceutical Companies' product candidates and Rafael Medical Devices' device candidates or produce the quantity and quality required to meet their clinical and commercial needs, if any;
- contract manufacturers may not be able to execute the Pharmaceutical Companies' and Rafael Medical Devices' manufacturing procedures and other logistical support requirements appropriately;
- future contract manufacturers may not perform as agreed, may not devote sufficient resources to the Pharmaceutical Companies product candidates or Rafael Medical Devices' device candidates, or may not remain in the contract manufacturing business for the time required to supply clinical trials or to successfully produce, store, and distribute approved or cleared products, if any;
- manufacturers are subject to ongoing periodic unannounced inspection by the FDA and corresponding state agencies and foreign regulatory authorities to ensure strict compliance with cGMP and other government regulations and corresponding foreign standards, and the Healthcare Companies have no control over third-party manufacturers' compliance with these regulations and standards;
- the Healthcare Companies may not own, or may have to share, the intellectual property rights to any improvements made by any third-party manufacturers in the manufacturing process for the Pharmaceutical Companies' product candidates and Rafael Medical Devices' device candidates;
- third-party manufacturers could breach or terminate their agreements with us, the Pharmaceutical Companies or Rafael Medical Devices;
- raw materials and components used in the manufacturing process, particularly those for which the Healthcare Companies have no other source or supplier, may not be available or may not be suitable or acceptable for use due to material or component defects;
- contract manufacturers and critical reagent suppliers may be subject to inclement weather, as well as natural or man-made disasters; and

- contract manufacturers may have unacceptable or inconsistent product quality success rates and yields, and the Pharmaceutical Companies will have no direct control over contract manufacturers' ability to maintain adequate quality control, quality assurance, and qualified personnel.

Our business could be materially adversely affected by business disruptions caused by third-party providers that could materially adversely affect our potential future revenue and financial condition and increase our costs and expenses. Each of these risks could delay or prevent the completion of the Pharmaceutical Companies' and Rafael Medical Devices' clinical trials or the approval of any of the Pharmaceutical Companies' product candidates or Rafael Medical Devices' device candidates by the FDA, result in higher costs, or adversely impact commercialization of any product candidates in the event that they were to receive regulatory approval or clearance.

We may, in the future, form or seek collaborations or strategic alliances or enter into licensing arrangements, and we may not realize the benefits of such collaborations, alliances or licensing arrangements.

We may, in the future, form or seek strategic alliances, create joint ventures or collaborations, or enter into licensing arrangements with third parties that we believe will complement or augment our development and commercialization efforts with respect to the Pharmaceutical Companies' product candidates, any future product candidates that we or they may develop, Rafael Medical Devices' device candidates, and any future device candidates that we or they may develop. Any of these relationships may require us to incur non-recurring and other charges, increase our near and long-term expenditures, issue securities that dilute our existing stockholders or disrupt our management and business.

In addition, we face significant competition in seeking appropriate strategic partners, and the negotiation process is time-consuming and complex. Moreover, we may not be successful in our efforts to establish a strategic partnership or other alternative arrangements for any product candidates because they may be deemed to be at too early of a stage of development for collaborative effort, and third parties may not view such product candidates as having the requisite potential to demonstrate safety and efficacy and obtain regulatory approval.

Further, collaborations involving our product candidates and device candidates are subject to numerous risks, which may include the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to a collaboration;
- collaborators may not pursue development and commercialization of our product candidates or device candidates or may elect not to continue or renew development or commercialization of our product candidates or device candidates based on clinical trial results, changes in their strategic focus due to the acquisition of competitive products, availability of funding or other external factors, such as a business combination that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial, stop a clinical trial, abandon a product candidate or device candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate or device candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with the Pharmaceutical Companies' product candidates and Rafael Medical Devices' device candidates;
- a collaborator with marketing and distribution rights to one or more product candidates or device candidates may not commit sufficient resources to their marketing and distribution in the event that they were to receive regulatory approval or clearance;
- collaborators may not properly maintain or defend our intellectual property rights or may use our intellectual property or proprietary information in a way that gives rise to actual or threatened litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential liability;
- disputes may arise between us and a collaborator that cause the delay or termination of the research, development or commercialization of a product candidate or device candidate, or that result in costly litigation or arbitration that diverts management attention and resources;

- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates or device candidates; and
- collaborators may own or co-own intellectual property covering our products that results from our collaborating with them, and in such cases, we would not have the exclusive right to commercialize such intellectual property.

As a result, if we enter into future collaboration agreements and strategic partnerships or out-license the Pharmaceutical Companies' product candidates or Rafael Medical Devices' device candidates, we may not be able to realize the benefit of such transactions if we are unable to successfully integrate them with our existing operations and company culture, which could delay our timelines or otherwise adversely affect our business. We also cannot be certain that, following a strategic transaction or license, we will achieve the revenue or specific net income that justifies such transaction. Furthermore, if conflicts arise between our future corporate or academic collaborators or strategic partners and us, the other party may act in a manner adverse to us and could limit our ability to implement our strategies. Any delays in entering into future collaborations or strategic partnership agreements related to our product candidates or device candidates could delay the development and commercialization of our product candidates and device candidates in certain geographies for certain indications, which would harm our business prospects, financial condition and results of operations.

The Pharmaceutical Companies' and Rafael Medical Devices' relationships with customers, physicians and third-party payors may be subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, health information privacy and security laws, and other healthcare laws and regulations. If the Pharmaceutical Companies or Rafael Medical Devices or their respective employees, independent contractors, consultants, commercial partners, or vendors violate these laws, they could face substantial penalties.

The Pharmaceutical Companies' and Rafael Medical Devices' relationships with customers, physicians, and third-party payors may be subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, health information privacy and security laws, and other healthcare laws and regulations. These laws may impact, among other things, our clinical research program, as well as our proposed and future sales, marketing, and education programs. In particular, the promotion, sales, and marketing of healthcare items and services is subject to extensive laws and regulations designed to prevent fraud, kickbacks, self-dealing, and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive, and other business arrangements. The Investment Companies may also be subject to federal, state, and foreign laws governing the privacy and security of identifiable patient information. The U.S. healthcare laws and regulations that may affect their ability to operate include, but are not limited to:

- the federal Anti-Kickback Statute, which prohibits, among other things, any person or entity from knowingly and willfully, offering, paying, soliciting or receiving any remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, the purchasing, leasing, ordering or arranging for the purchase, lease, or order of any item or service reimbursable under Medicare, Medicaid or other federal healthcare programs. The term "remuneration" has been broadly interpreted to include anything of value. Although there are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution, the exceptions and safe harbors are drawn narrowly. Practices that may be alleged to be intended to induce prescribing, purchases or recommendations, include any payments of more than fair market value, and may be subject to scrutiny if they do not qualify for an exception or safe harbor. In addition, a person or entity does not need to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation;
- federal civil and criminal false claims laws, including the federal civil False Claims Act, and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment or approval from Medicare, Medicaid, or other federal government programs that are false or fraudulent or knowingly making a false statement to improperly avoid, decrease or conceal an obligation to pay money to the federal government, including federal healthcare programs. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act and the civil monetary penalties statute;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created new federal civil and criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, including private third-party payors, and knowingly and willfully falsifying, concealing or covering up by any trick, scheme or device, a material fact or making any materially false, fictitious or fraudulent statements in connection with the delivery of, or payment for, healthcare benefits, items or services. Similar to the 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, and their respective implementing regulations, which impose requirements on certain healthcare providers, health plans, and healthcare clearinghouses, known as covered entities, and their respective business associates that perform services for them that involve the use, or disclosure of, individually identifiable protected health information as well as their covered subcontractors, including breach notification regulations;
- analogous state data privacy and security laws and regulations that govern the collection, use, disclosure, transfer, storage, disposal, and protection of personal information, such as social security numbers, medical and financial information, and other information, including data breach laws that require timely notification to individuals, and at times regulators, the media or credit reporting agencies, if a company has experienced the unauthorized access or acquisition of personal information, as well as the California Consumer Privacy Act or CCPA, which, among other things, contains new disclosure obligations for businesses that collect personal information about California residents and affords those individuals numerous rights relating to their personal information that may affect companies' ability to use personal information or share it with business partners, and the California Privacy Rights Act, or CPRA, which expands the scope of the CCPA, imposes new restrictions on behavioral advertising and establishes a new California Privacy Protection Agency that will enforce the law and issue regulations, and is scheduled to become "operative" on January 1, 2023, with a 12-month "lookback provision," and the various state laws and regulations may be more restrictive and not preempted by United States federal laws;
- analogous foreign data protection laws, including among others the EU General Data Protection Regulation, or the GDPR, and EU member states' implementing legislation, which imposes data protection requirements that include strict obligations and restrictions on the ability to collect, analyze, and transfer EU personal data, a requirement for prompt notice of data breaches to data subjects and supervisory authorities in certain circumstances, and possible substantial fines for any violations (including possible fines for certain violations of up to the greater of 20 million Euros or 4% of total worldwide annual turnover of the preceding financial year), with legal requirements in foreign countries relating to the collection, storage, processing, and transfer of personal data continuing to evolve; and
- the federal Physician Payments Sunshine Act, which requires certain manufacturers of drugs, devices, biologicals and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to CMS information related to payments or other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists, and chiropractors) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Beginning in 2022, such reporting obligations will include payments and other transfers of value provided during the previous year to physician assistants, nurse practitioners, clinical nurse specialists, anesthesiologist assistants, certified registered nurse anesthetists, and certified nurse-midwives.

The Investment Companies may also be subject to state and foreign equivalents of each of the healthcare laws described above, among others, some of which may be broader in scope. For example, we may be subject to the following: state anti-kickback and false claims laws that may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third party payors, including private insurers, or that apply regardless of payor; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's

voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government; state laws that require drug and device manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers, marketing expenditures, or drug pricing; state and local laws requiring the registration of pharmaceutical and device sales and medical representatives; and state and foreign laws, such as the GDPR governing the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts. Additionally, we may be subject to federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers.

Because of the breadth of these laws and the narrowness of the statutory exceptions and regulatory safe harbors available, it is possible that some of our business activities, or our arrangements with physicians, could be subject to challenge under one or more of such laws. It is not always possible to identify and deter employee misconduct or business noncompliance, and the precautions we take to detect and prevent inappropriate conduct may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. Efforts to ensure that our business arrangements will comply with applicable healthcare laws may involve substantial costs. It is possible that governmental and enforcement authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. If the Pharmaceutical Companies or Rafael Medical Devices or their respective employees, independent contractors, consultants, commercial partners, and vendors violate these laws, we may be subject to investigations, enforcement actions and/or significant penalties, including the imposition of significant civil, criminal, and administrative penalties, damages, disgorgement, monetary fines, imprisonment, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, additional reporting requirements and/or oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, and curtailment of the Pharmaceutical Companies' and Rafael Medical Devices' operations, any of which could adversely affect their ability to operate their business and their results of operations. In addition, the approval or clearance and commercialization of any of the Pharmaceutical Companies' product candidates or Rafael Medical Devices' device candidates outside the United States will also likely subject us to foreign equivalents of the healthcare laws mentioned above, among other foreign laws.

Risks Related to our Commercial Real Estate Business

We may be unable to renew leases or relet space as leases expire.

If tenants decide not to renew their leases upon expiration, we may not be able to relet the space. Even if tenants do renew or we can relet the space, the terms of a renewal or new lease, taking into account among other things, the cost of improvements to the property and leasing commissions, may be less favorable than the terms in the expired leases. In addition, changes in space utilization by tenants may impact our ability to renew or relet space without the need to incur substantial costs in renovating or redesigning the internal configuration of the relevant property. If we are unable to promptly renew the leases or relet the space at similar rates or if we incur substantial costs in renewing or reletting the space, our cash flow and ability to service debt obligations and pay dividends and distributions to security holders could be adversely affected.

We face competition for tenants.

The leasing of real estate is highly competitive. The principal competitive factors are rent, location, services provided and the nature and condition of the property to be leased. We directly compete with all owners, developers and operators of similar space in the areas in which our properties are located. There are number of competitive office properties the areas in which our property is located, which may be newer or better located than our property and could have a material adverse effect on our ability to lease office space at our property, and on the effective rents we are able to charge.

Risks Related to Intellectual Property

If the companies in which we hold interests are unable to adequately maintain or protect their proprietary technology and product candidates, if the scope of the patent protection obtained is not sufficiently broad, or if the terms of patents are insufficient to protect product candidates for an adequate amount of time, competitors could develop and commercialize technology and products similar or identical to that technology or those product candidates and the ability to successfully commercialize technology or product candidates may be materially impaired.

We rely primarily upon a combination of patents, trademarks, trade secret protection, and other intellectual property rights as well as nondisclosure, confidentiality, and other contractual agreements to protect the intellectual property related to our brands, product candidates and device candidates, and other proprietary technologies. Our success depends on our ability to develop, manufacture, market, and sell our product candidates, if approved, and use our proprietary technologies without alleged or actual infringement, misappropriation or other violation of the patents and other intellectual property rights of third parties. There have been many lawsuits and other proceedings asserting patents and other intellectual property rights in the biopharmaceutical industries. We cannot assure you that our product candidates and device candidates will not infringe existing or future third-party patents. Because patent applications can take many years to issue and may be confidential for 18 months or more after filing, there may be applications now pending of which we are unaware and which may later result in issued patents that we may infringe by commercializing our product candidates or device candidates if they receive approval or clearance. There may also be issued patents or pending patent applications that we are aware of, but that we think are irrelevant to our product candidates or device candidates, which may ultimately be found to be infringed by the manufacture, sale, or use of our product candidates or device candidates. Moreover, we may face claims from non-practicing entities that have no relevant product revenue and against whom our own patent portfolio may thus have no deterrent effect. In addition, many of our product candidates have a complex structure that makes it difficult to conduct a thorough search and review of all potentially relevant third-party patents. Because we have not yet conducted a formal freedom to operate analysis for patents related to our product candidates or device candidates, we may not be aware of issued patents that a third party might assert are infringed by one of our current or future product candidates or device candidates, which could materially impair our ability to commercialize our product candidates or device candidates. Even if we diligently search third-party patents for potential infringement by our products or product candidates, or devices or device candidates, we may not successfully find patents that our products or product candidates devices or device candidates may infringe. If we are unable to secure and maintain freedom to operate, others could preclude us from commercializing our product candidates or device candidates.

The process of obtaining patent protection is expensive and time-consuming, and we may not be able to prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. We may choose not to seek patent protection for certain innovations or products and may choose not to pursue patent protection in certain jurisdictions, and, under the laws of certain jurisdictions, patents or other intellectual property rights may be unavailable or limited in scope and, in any event, any patent protection we obtain may be limited. As a result, in some jurisdictions, some of our products currently or in the future may not be protected by patents. We generally apply for patents in those countries where we intend to make, have made, use, offer for sale, or sell products and where we assess the risk of infringement to justify the cost of seeking patent protection. However, we may not accurately predict all the countries where patent protection would ultimately be desirable. If we fail to timely file a patent application in any such country or major market, we may be precluded from doing so at a later date. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories in which we have patent protection that may not be sufficient to terminate infringing activities. In addition, the actual protection afforded by a patent varies on a product-by-product basis, from country to country, and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country, and the validity and enforceability of the patent.

Furthermore, we cannot guarantee that any patents will be issued from any pending or future owned or licensed patent applications, or that any current or future patents will be valid or enforceable or provide us with any meaningful protection or competitive advantage. Even if issued, existing or future patents may be challenged, including with respect to ownership, narrowed, invalidated, held unenforceable or circumvented, any of which could limit our ability to prevent competitors and other third parties from developing and marketing similar products or limit the length of terms

of patent protection we may have for our product candidates or device candidates. Moreover, should we be unable to obtain meaningful patent coverage for clinically relevant infusion rates in jurisdictions with commercially significant markets, our ability to extend and reinforce patent protection for these product candidates in those jurisdictions may be adversely impacted, which could limit our ability to prevent competitors and other third parties from developing and marketing similar products or limit the length of terms of patent protection we may have for those product candidates. Other companies may also design around technologies we have patented, licensed or developed. In addition, the issuance of a patent does not give us the right to practice the patented invention. Third parties may have blocking patents that could prevent us from marketing our products or practicing our own patented technology.

The patent positions of biopharmaceutical companies can be highly uncertain and involve complex legal, scientific, and factual questions for which important legal principles remain unresolved. As a result, the issuance, scope, validity, enforceability, and commercial value of our patent rights may be uncertain. The standards that the United States Patent and Trademark Office, or the USPTO, and its foreign counterparts use to grant patents are not always applied predictably or uniformly. Changes in either the patent laws, implementing regulations or the interpretation of patent laws may diminish the value of our rights. The legal systems of certain countries do not protect intellectual property rights to the same extent as the laws of the United States, if at all, and many companies have encountered significant problems in protecting and defending such rights in foreign jurisdictions. For example, patent laws in various jurisdictions, including significant commercial markets such as Europe, restrict the patentability of methods of treatment of the human body more than United States law does. In addition, many countries, including certain countries in Europe, have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties (for example, the patent owner has failed to “work” the invention in that country, or the third party has patented improvements). In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of the patent. Moreover, the legal systems of certain countries, particularly certain developing countries, do not favor the aggressive enforcement of patent and other intellectual property protection, which makes it difficult to stop infringement.

Because patent applications in the United States, Europe, and many other jurisdictions are typically not published until 18 months after filing, or in some cases not at all, and because publications of discoveries in scientific literature lag behind actual discoveries, we cannot be certain that we were the first to conceive or reduce to practice the inventions claimed in our issued patents or pending patent applications, or that we were the first to file for protection of the inventions set forth in our patents or pending patent applications. We can give no assurance that all of the potentially relevant art relating to our patents and patent applications has been found; overlooked prior art could be used by a third party to challenge the validity, enforceability, and scope of our patents or prevent a patent from issuing from a pending patent application. As a result, we may not be able to obtain or maintain protection for certain inventions. Therefore, the validity, enforceability, and scope of our patents in the United States, Europe, and in other countries cannot be predicted with certainty and, as a result, any patents that we own or license may not provide sufficient protection against our competitors.

Third parties may challenge any existing patent or future patent we own or license through adversarial proceedings in the issuing offices or in court proceedings, including as a response to any assertion of our patents against them. In any of these proceedings, a court or agency with jurisdiction may find our patents invalid and/or unenforceable, or even if valid and enforceable, insufficient to provide protection against competing products and services sufficient to achieve our business objectives. We may be subject to a third-party pre-issuance submission of prior art to the USPTO, or reexamination by the USPTO if a third party asserts a substantial question of patentability against any claim of a U.S. patent we own or license. The adoption of the Leahy-Smith America Invents Act, or the Leahy-Smith Act, in September 2011 established additional opportunities for third parties to invalidate U.S. patent claims, including inter partes review and post-grant review proceedings. Outside of the United States, patents we own or license may become subject to patent opposition or similar proceedings, which may result in loss of scope of some claims or the entire patent. In addition, such proceedings are very complex and expensive, and may divert our management’s attention from our core business. If any of our patents are challenged, invalidated, circumvented by third parties or otherwise limited or expire prior to the commercialization of our products, and if we do not own or have exclusive rights to other enforceable patents protecting our products or other technologies, competitors and other third parties could market products and use processes that are substantially similar, or superior, to ours, and our business would suffer.

The entities in which we hold interests or in which we may invest may not make necessary payments or take other actions to protect intellectual property or other rights that they license or have acquired from third parties, which could result in the loss or impairment of those rights and the reduction of the value of our interests.

The degree of future protection for our proprietary rights is uncertain because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep a competitive advantage. For example:

- others may be able to develop products that are similar to, or better than, ours in a way that is not covered by the claims of our patents;
- might not have been the first to conceive or reduce to practice the inventions covered by our patents or pending patent applications;
- we might not have been the first to file patent applications for our inventions;
- any patents that we obtain may not provide us with any competitive advantages or may ultimately be found invalid or unenforceable; and/or
- we may not develop additional proprietary technologies that are patentable.

We are generally also subject to all of the same risks with respect to protection of intellectual property that we license as we are for intellectual property that we own. We currently in-license certain intellectual property from third parties to be able to use such intellectual property in our products and product candidates and to aid in our research activities. In the future, we may in-license intellectual property from additional licensors. We may rely on certain of these licensors to file and prosecute patent applications and maintain, or assist us in the maintenance of, patents and otherwise protect the intellectual property we license from them. We may have limited control over these activities or any other intellectual property that may be related to our in-licensed intellectual property. For example, we cannot be certain that such activities by these licensors have been or will be conducted diligently or in compliance with applicable laws and regulations or will result in valid and enforceable patents and other intellectual property rights. We may have limited control over the manner in which our licensors initiate, or support our efforts to initiate, an infringement proceeding against a third-party infringer of the intellectual property rights, or defend certain of the intellectual property that is licensed to us. If we or our licensors fail to adequately protect this intellectual property, our ability to commercialize products could suffer.

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

Competitors may infringe, misappropriate or otherwise violate our patents, trademarks, copyrights, trade secrets or other intellectual property, or those of our licensors. To counter infringement, misappropriation, unauthorized use or other violations, we may be required to file legal claims, which can be expensive and time consuming and divert the time and attention of our management and scientific personnel. In some cases, it may be difficult or impossible to detect third-party infringement or misappropriation of our intellectual property rights, even in relation to issued patent claims, and proving any such infringement may be even more difficult.

We may not be able to prevent, alone or with our licensees or any future licensors, infringement, misappropriation or other violations of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. The outcome following legal assertions of invalidity and unenforceability is unpredictable. We cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a third party or a defendant were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of any future patent protection on our current or future product candidates. Such a loss of patent protection could harm our business. In addition, in a patent infringement proceeding, there is a risk that a court will decide that a patent of ours is invalid or unenforceable, in whole or in part, and that we do not have the right to stop the other party from exploiting the claimed subject matter at issue. There is also a risk that, even if the validity of such patents is upheld, the court will construe the patent's claims narrowly or decide that we do not have the right to stop the other party from exploiting its technology on the grounds that our patents do not cover such technology. An adverse outcome in a litigation or proceeding involving our patents could limit our ability to assert our patents against those parties or other competitors, and may curtail

or preclude our ability to exclude third parties from making, using, importing, and selling similar or competitive products. Any of these occurrences could adversely affect our competitive business position, business prospects, and financial condition. Similarly, if we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the marks in question or has not infringed them. In this case, we could ultimately be forced to cease use of such trademarks.

In any infringement, misappropriation or other intellectual property litigation, any award of monetary damages we receive may not be commercially valuable. 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 litigation. Moreover, there can be no assurance that we will have sufficient financial or other resources to file and pursue such infringement claims, which typically last for years before they are concluded. Even if we ultimately prevail in such claims, the monetary cost of such litigation and the diversion of the attention of our management and scientific personnel could outweigh any benefit we receive as a result of the proceedings. We may not be able to detect or prevent misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States. Our business could be harmed if in litigation the prevailing party does not offer us a license on commercially reasonable terms. Any litigation or other proceedings to enforce our intellectual property rights may fail, and even if successful, may result in substantial costs and distract our management and other employees.

Our commercial success depends significantly on our ability to operate without infringing upon the intellectual property rights of third parties.

The biopharmaceutical industries are subject to rapid technological change and substantial litigation regarding patent and other intellectual property rights. Our competitors in both the United States and abroad, many of which have substantially greater resources and have made substantial investments in patent portfolios and competing technologies, may have applied for or obtained, or may in the future apply for or obtain, patents that will prevent, limit or otherwise interfere with our ability to make, use, and sell our product candidates, device candidates, services, and technologies. Numerous third-party patents exist in the fields relating to our products and services, and it is difficult for industry participants, including us, to identify all third-party patent rights relevant to our product candidates, device candidates, services, and technologies. As the biopharmaceutical industries expand and more patents are issued, the risk increases that our product candidates or device candidates may give rise to claims of infringement of the patent rights of others. Moreover, because some patent applications are maintained as confidential for a certain period of time, we cannot be certain that third parties have not filed patent applications that cover our product candidates, device candidates, services, and technologies. Therefore, it is uncertain whether the issuance of any third-party patent would require us to alter our development or commercial strategies for our product candidates, device candidates, or processes, or to obtain licenses or cease certain activities.

Patents could be issued to third parties that we may ultimately be found to infringe. Third parties may have or obtain valid and enforceable patents or proprietary rights that could block us from developing products using our technology. If any third-party patents were held by a court of competent jurisdiction to cover the manufacturing process of our product candidates, constructs or molecules used in or formed during the manufacturing process, any final product itself, or our device candidates, the holders of any such patents may be able to block our ability to commercialize the product candidate or device candidate unless we obtain a license under the applicable patents, or until such patents expire or they are determined to be held invalid or unenforceable. Our failure to obtain or maintain a license to any technology that we require to develop or commercialize our current and future product candidates and device candidates, may materially harm our business, financial condition, and results of operations. Furthermore, we would be exposed to a threat of litigation.

From time to time, we may be party to, or threatened with, litigation or other proceedings with third parties, including non-practicing entities, who allege that our product candidates, components of our product candidates, device candidates, components of our device candidates, services, and/or proprietary technologies infringe, misappropriate or otherwise violate their intellectual property rights. The types of situations in which we may become a party to such litigation or proceedings include:

- we or our collaborators may initiate litigation or other proceedings against third parties seeking to invalidate the patents held by those third parties or to obtain a judgment that our product candidates, device candidates, or processes do not infringe those third parties' patents;

- we or our collaborators may participate at substantial cost in International Trade Commission proceedings to abate importation of third-party products that would compete unfairly with our products;
- if our competitors file patent applications that claim technology also claimed by us or our licensors, we or our licensors may be required to participate in interference, derivation or opposition proceedings to determine the priority of invention, which could jeopardize our patent rights and potentially provide a third party with a dominant patent position;
- if third parties initiate litigation claiming that our processes or product candidates, infringe their patent or other intellectual property rights, we and our collaborators will need to defend against such proceedings;
- if third parties initiate litigation or other proceedings, including inter partes reviews, oppositions or other similar agency proceedings, seeking to invalidate patents owned by or licensed to us or to obtain a declaratory judgment that their products, services, or technologies do not infringe our patents or patents licensed to us, we will need to defend against such proceedings;
- we may be subject to ownership disputes relating to intellectual property, including disputes arising from conflicting obligations of consultants or others who are involved in developing our product candidate; and
- if a license to necessary technology is terminated, the licensor may initiate litigation claiming that our processes or product candidates infringe or misappropriate its patent or other intellectual property rights and/or that we breached our obligations under the license agreement, and we and our collaborators would need to defend against such proceedings.

These lawsuits and proceedings, regardless of merit, are time-consuming and expensive to initiate, maintain, defend or settle, and could divert the time and attention of managerial and technical personnel, which could materially adversely affect our business. Any such claim could also force use to do one or more of the following:

- incur substantial monetary liability for infringement or other violations of intellectual property rights, which we may have to pay if a court decides that the product candidate, service, or technology at issue infringes or violates the third party's rights, and if the court finds that the infringement was willful, we could be ordered to pay up to treble damages and the third party's attorneys' fees;
- pay substantial damages to our customers or end users to discontinue use or replace infringing technology with non-infringing technology;
- stop manufacturing, offering for sale, selling, using, importing, exporting or licensing the product or technology incorporating the allegedly infringing technology or stop incorporating the allegedly infringing technology into such product, service, or technology;
- obtain from the owner of the infringed intellectual property right a license, which may require us to pay substantial upfront fees or royalties to sell or use the relevant technology and which may not be available on commercially reasonable terms, or at all;
- redesign our product candidates, services, and technology so they do not infringe or violate the third party's intellectual property rights, which may not be possible or may require substantial monetary expenditures and time;
- enter into cross-licenses with our competitors, which could weaken our overall intellectual property position;
- lose the opportunity to license our technology to others or to collect royalty payments based upon successful protection and assertion of our intellectual property against others;
- find alternative suppliers for non-infringing products and technologies, which could be costly and create significant delay; or
- relinquish rights associated with one or more of our patent claims, if our claims are held invalid or otherwise unenforceable

Some of our competitors may be able to sustain the costs of complex intellectual property litigation more effectively than we can because they have substantially greater resources. In addition, intellectual property litigation, regardless of its outcome, may cause negative publicity, adversely impact prospective customers, cause product shipment delays, or prohibit us from manufacturing, marketing or otherwise commercializing our products, services, and technology. Any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise additional funds or otherwise have a material adverse effect on our business, results of operation, financial condition or cash flows.

In addition, we may indemnify our customers and distributors against claims relating to the infringement of intellectual property rights of third parties related to our product candidates or device candidates. Third parties may assert infringement claims against our customers or distributors. These claims may require us to initiate or defend protracted and costly litigation on behalf of our customers or distributors, regardless of the merits of these claims. If any of these claims succeed, we may be forced to pay damages on behalf of our customers, suppliers or distributors, or may be required to obtain licenses for the product candidates, or services they use. If we cannot obtain all necessary licenses on commercially reasonable terms, our customers may be forced to stop using our products or services.

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. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments, which could have a material adverse effect on the price of our common stock. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock. The occurrence of any of these events may have a material adverse effect on our business, results of operation, financial condition or cash flows.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position may be harmed.

In addition to patent and trademark protection, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. Because we expect to rely on third parties to manufacture our product candidates, and we expect to continue to collaborate with third parties on the development of our product candidates, we must, at times, share trade secrets with them. We seek to protect our trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them prior to disclosing our proprietary information, such as our consultants and vendors, or our former or current employees. These agreements typically limit the rights of third parties to use or disclose our confidential information, including our trade secrets. We also enter into confidentiality and invention assignment agreements with our employees and consultants. Despite these efforts, however, any of these parties may breach the agreements and disclose our trade secrets and other unpatented or unregistered proprietary information, and once disclosed, we are likely to lose trade secret protection. Monitoring unauthorized uses and disclosures of our intellectual property is difficult, and we do not know whether the steps we have taken to protect our intellectual property will be effective. In addition, we may not be able to obtain adequate remedies for any such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive, and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to enforce trade secret protection. A competitor's discovery of our trade secrets would impair our competitive position and have an adverse impact on our business, operating results, and financial condition. Additionally, we cannot be certain that competitors will not gain access to our trade secrets and other proprietary confidential information or independently develop substantially equivalent information and techniques.

Changes in patent law could diminish the value of patents in general, thereby impairing our ability to protect our existing and future product candidates and processes.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industries involves both technological and legal complexity, and is therefore costly, time consuming, and inherently uncertain. In addition, the United States has recently enacted and is currently implementing wide-ranging patent reform legislation. Recent patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. On September 16, 2011, the Leahy-Smith Act was signed into law. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that

affect the way patent applications are prosecuted, redefine prior art, may affect patent litigation, and switched the United States patent system from a “first-to-invent” system to a “first-to-file” system. Under a “first-to-file” system, assuming the other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to the patent on an invention regardless of whether another inventor had conceived or reduced to practice the invention earlier. The USPTO recently developed new regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, in particular, the first-to-file provisions, only became effective on March 16, 2013. Accordingly, it is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. The Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

In addition, patent reform legislation may pass in the future that could lead to additional uncertainties and increased costs surrounding the prosecution, enforcement and defense of our patents and pending patent applications. Recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. Furthermore, the U.S. Supreme Court and the U.S. Court of Appeals for the Federal Circuit have made, and will likely continue to make, changes in how the patent laws of the United States are interpreted. Similarly, foreign courts have made, and will likely continue to make, changes in how the patent laws in their respective jurisdictions are interpreted. We cannot predict future changes in the interpretation of patent laws or changes to patent laws that might be enacted into law by United States and foreign legislative bodies. Those changes may materially affect our patents or patent applications and our ability to obtain additional patent protection in the future.

The United States federal government retains certain rights in inventions produced with its financial assistance under the Patent and Trademark Law Amendments Act, or the Bayh-Dole Act. The federal government retains a “nonexclusive, nontransferable, irrevocable, paid-up license” for its own benefit. The Bayh-Dole Act also provides federal agencies with “march-in rights.” March-in rights allow the government, in specified circumstances, to require the contractor or successors in title to the patent to grant a “nonexclusive, partially exclusive, or exclusive license” to a “responsible applicant or applicants.” If the patent owner refuses to do so, the government may grant the license itself. We partner with a number of universities, including the University of Iowa and the University of Texas Southwestern Medical Center, with respect to certain of our research, development, and manufacturing. While it is our policy to avoid engaging our university partners in projects in which there is a risk that federal funds may be commingled, we cannot be sure that any co-developed intellectual property will be free from government rights pursuant to the Bayh-Dole Act. If, in the future, we co-own or license in technology which is critical to our business that is developed in whole or in part with federal funds subject to the Bayh-Dole Act, our ability to enforce or otherwise exploit patents covering such technology may be adversely affected.

If we do not obtain patent term extensions in the United States under the Hatch-Waxman Act and in foreign countries under similar legislation with respect to our product candidates, thereby potentially extending the term of marketing exclusivity for such product candidates, our business may be harmed.

In the United States, a patent that covers an FDA-approved drug or biologic may be eligible for a term extension designed to restore the period of the patent term that is lost during the premarket regulatory review process conducted by the FDA. Depending upon the timing, duration, and conditions of FDA regulatory approval of our product candidates, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, which permits a patent term extension of up to a maximum of five years beyond the normal expiration of the patent if the patent is eligible for such an extension under the Hatch-Waxman Act as compensation for patent term lost during development and the FDA regulatory review process, which is limited to the approved indication (and potentially additional indications approved during the period of extension) covered by the patent. This extension is limited to only one patent that covers the approved product, the approved use of the product, or a method of manufacturing the product. However, the applicable authorities, including the FDA and the USPTO in the United States, and any equivalent regulatory authority in other countries, may not agree with our assessment of whether such extensions are available, and may refuse to grant extensions to our patents, or may grant more limited extensions than we request.

We may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Even if we are granted such extension, the duration of such extension may be less than our request, and the patent term may still expire before or shortly after we

receive FDA marketing approval. If we are unable to extend the expiration date of our existing patents or obtain new patents with longer expiry dates, our competitors may be able to take advantage of our investment in development and clinical trials by referencing our clinical and preclinical data to obtain approval of competing products following our patent expiration and launch their product earlier than might otherwise be the case.

Obtaining and maintaining patent protection depends on compliance with various procedural, document submission, fee payment, and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment, and other similar provisions during the patent application process. In addition, periodic maintenance fees on issued patents often must be paid to the USPTO and foreign patent agencies over the lifetime of the patent. While an unintentional lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees, and failure to properly legalize and submit formal documents. If we fail to maintain the patents and patent applications covering our product candidates, device candidates, or procedures, we may not be able to stop a competitor from marketing products that are the same as or similar to our own, which would have a material adverse effect on our business.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

We have not yet registered trademarks for a commercial trade name for all of our product candidate(s) or device candidates, including in the United States or elsewhere. During trademark registration proceedings, our trademark application(s) may be rejected. Although we are given an opportunity to respond to those rejections, we may be unable to overcome such rejections. In addition, in the USPTO and in comparable agencies in many foreign jurisdictions, third parties can oppose pending trademark applications and seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings. Moreover, any name we propose to use with our product candidate(s) in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. The FDA typically conducts a review of proposed product names, including an evaluation of potential for confusion with other product names. If the FDA objects to any of our proposed proprietary product names, we may be required to expend significant additional resources in an effort to identify a suitable substitute name that would qualify under applicable trademark laws, not infringe the existing rights of third parties, and be acceptable to the FDA.

Our registered or unregistered trademarks or trade names may be challenged, infringed, circumvented, declared generic or determined to be infringing on other marks. We may not be able to protect our rights in these trademarks and trade names, which we need in order to build name recognition with potential partners or customers in our markets of interest. In addition, third parties have used trademarks similar and identical to our trademarks in foreign jurisdictions, and have filed or may in the future file for registration of such trademarks. If they succeed in registering or developing common law rights in such trademarks, and if we are not successful in challenging such third-party rights, we may not be able to use these trademarks to market our products in those countries. In any case, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected.

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

Certain of our key patent families have been filed in the United States, as well as in numerous jurisdictions outside the United States. However, our intellectual property rights in certain jurisdictions outside the United States may be less robust. The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the United States. For example, the requirements for patentability may differ in certain countries, particularly developing countries, and we may be unable to obtain issued patents that contain claims that adequately cover or protect our current or future product candidates or device candidates. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, particularly developing countries, do not favor the enforcement of patents and other intellectual property

protection, especially those relating to life sciences. This could make it difficult for us to stop the infringement of our patents or the misappropriation of our other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. In addition, many countries limit the enforceability of patents against third parties, including government agencies or government contractors. In these countries, patents may provide limited or no benefit.

Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and attention from other aspects of our business. Furthermore, while we intend to protect our intellectual property rights in our expected significant markets, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market current or future product candidates or device candidates. Consequently, we may not be able to prevent third parties from practicing our technology in all countries outside the United States, or from selling or importing products made using our technology in and into those other jurisdictions where we do not have intellectual property rights. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and may also export infringing products to territories where we have patent protection, but where enforcement is not as strong as that in the United States. These products may compete with our product candidates or device candidates, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate. In addition, changes in the law and legal decisions by courts in the United States and foreign countries may affect our ability to obtain and enforce adequate intellectual property protection for our technology.

We may not identify relevant third-party patents or may incorrectly interpret the relevance, scope or expiration of a third-party patent, which might adversely affect our ability to develop and market our product candidates.

We cannot guarantee that any of our or our licensors' patent searches or analyses, including the identification of relevant patents, the scope of patent claims or the expiration of relevant patents, are complete or thorough, nor can we be certain that we have identified each and every third-party patent and pending application in the United States and abroad that is relevant to or necessary for the commercialization of our product candidates or device candidates. For example, U.S. patent applications filed before November 29, 2000 and certain U.S. patent applications filed after that date that will not be filed outside the United States remain confidential until patents issue. Patent applications in the United States and elsewhere are published approximately 18 months after the earliest filing for which priority is claimed, with such earliest filing date being commonly referred to as the priority date. Therefore, patent applications covering our product candidates or device candidates could have been filed by others without our knowledge. Additionally, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our product candidates, device candidates, or the use of our products. The scope of a patent claim is determined by an interpretation of the law, the written disclosure in a patent, and the patent's prosecution history. Our interpretation of the relevance or the scope of a patent or a pending application may be incorrect, which may negatively impact our ability to market our product candidates or device candidates. We may incorrectly determine that our product candidates or device candidates are not covered by a third-party patent or may incorrectly predict whether a third party's pending patent application will issue with claims of relevant scope. Our determination of the expiration date of any patent in the United States or abroad that we consider relevant may be incorrect, which may negatively impact our ability to develop and market our product candidates, device candidates, services, and technologies. Our failure to identify and correctly interpret relevant patents may negatively impact our ability to develop and market our product candidates, device candidates, services, and technologies.

If we fail to identify and correctly interpret relevant patents, we may be subject to infringement claims. We cannot guarantee that we will be able to successfully settle or otherwise resolve such infringement claims. If we fail in any such dispute, in addition to being forced to pay damages, we may be temporarily or permanently prohibited from commercializing any of our product candidates or device candidates that are held to be infringing. We might, if possible, also be forced to redesign products, product candidates, devices, device candidates, or services so that we no longer infringe the third-party intellectual property rights. Any of these events, even if we were ultimately to prevail, could require us to divert substantial financial and management resources that we would otherwise be able to devote to our business.

Patent terms may be inadequate to protect our competitive position on our product candidates or device candidates for an adequate amount of time.

Patents have a limited lifespan, and the protection patents afford is limited. In the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date. Even if patents covering our product candidates and device candidates are obtained, once the patent life has expired for patents covering a product or product candidate, a device or a device candidate, we may be subject to competition from competitive products and services. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

Intellectual property rights do not necessarily address all potential threats to our business.

While we seek broad coverage under our existing patent applications, there is always a risk that an alteration to products or processes may provide sufficient basis for a competitor to avoid infringing our patent claims. In addition, patents, if granted, expire and we cannot provide any assurance that any potentially issued patents will adequately protect our product candidates or device candidates. Once granted, patents may remain open to invalidity challenges including opposition, interference, re-examination, post-grant review, inter partes review, nullification or derivation action in court or before patent offices or similar proceedings for a given period after allowance or grant, during which time third parties can raise objections against such grant. In the course of such proceedings, which may continue for a protracted period of time, the patent owner may be compelled to limit the scope of the allowed or granted claims thus attacked, or may lose the allowed or granted claims altogether.

In addition, the degree of future protection afforded by our intellectual property rights is uncertain because even granted intellectual property rights have limitations, and may not adequately protect our business, provide a lawful barrier to entry against our competitors or potential competitors or permit us to maintain our competitive advantage. Moreover, if a third party has intellectual property rights that cover the practice of our technology, we may not be able to fully exercise or extract value from our intellectual property rights. The following examples are illustrative:

- others may be able to develop and/or practice technology that is similar to our technology or aspects of our technology, but that are not covered by the claims of the patents that we own or control, assuming such patents have issued or do issue;
- we or our licensors or any future strategic partners might not have been the first to conceive or reduce to practice the inventions covered by the issued patents or pending patent applications that we own or have exclusively licensed;
- we or our licensors or any future strategic partners might not have been the first to file patent applications covering certain of our inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible that our pending patent applications will not lead to issued patents;
- issued patents that we own or have exclusively licensed may not provide us with any competitive advantage, or may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- third parties performing manufacturing or testing for us using our product candidates, including technologies could use the intellectual property of others without obtaining a proper license;
- parties may assert an ownership interest in our intellectual property and, if successful, such disputes may preclude us from exercising exclusive rights over that intellectual property;
- we may not develop or in-license additional proprietary technologies that are patentable;

- we may not be able to obtain and maintain necessary licenses on commercially reasonable terms, or at all; and
- the patents of others may have an adverse effect on our business.

Should any of these events occur, they could have a material adverse effect on our business, financial condition, results of operations and prospects.

We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of their former employers or other third parties.

We do and may employ individuals who were previously employed at universities or other biopharmaceutical companies, including our licensors, competitors or potential competitors. Although we try to ensure that our employees, consultants, and independent contractors do not use the proprietary information or know-how of others in their work for us, and we are not currently subject to any claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties, we may in the future be subject to such claims.

Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Such intellectual property rights could be awarded to a third party, and we could be required to obtain a license from such third party to commercialize our technology or product candidates. Such a license may not be available on commercially reasonable terms or at all. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees, and could result in customers seeking other sources for the technology or ceasing from doing business with us.

Our intellectual property agreements with third parties may be subject to disagreements over contract interpretation, which could narrow the scope of our rights to the relevant intellectual property or technology.

Certain provisions in our intellectual property agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could affect the scope of our rights to the relevant intellectual property or technology, or affect financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

In addition, while we typically require our employees, consultants and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact conceives or develops intellectual property that we regard as our own. To the extent that we fail to obtain such assignments, such assignments do not contain a self-executing assignment of intellectual property rights or such assignment agreements are breached, we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property, and this may interfere with our ability to capture the commercial value of such intellectual property. If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Such intellectual property rights could be awarded to a third party, and we could be required to obtain a license from such third party to commercialize our technology or products. Such a license may not be available on commercially reasonable terms or at all. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to our management and scientific personnel. Disputes regarding ownership or inventorship of intellectual property can also arise in other contexts, such as collaborations and sponsored research. We may be subject to claims that former collaborators or other third parties have an ownership interest in our patents or other intellectual property. If we are subject to a dispute challenging our rights in or to patents or other intellectual property, such a dispute could be expensive and time-consuming. If we are unsuccessful, we could lose valuable rights in intellectual property that we regard as our own.

We may not be successful in obtaining necessary intellectual property rights to future products through acquisitions and in-licenses.

Although we intend to develop products and technology through our own internal research, we may also seek to acquire or in-license technologies to grow our product offerings and technology portfolio. However, we may be unable to acquire or in-license intellectual property rights relating to, or necessary for, any such products or technology from

third parties on commercially reasonable terms or at all. In that event, we may be unable to develop or commercialize such products or technology. We may also be unable to identify products or technology that we believe are an appropriate strategic fit for our Company and protect intellectual property relating to, or necessary for, such products and technology.

The in-licensing and acquisition of third-party intellectual property rights for product candidates and device candidates is a competitive area, and a number of more established companies are also pursuing strategies to in-license or acquire third-party intellectual property rights for products that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, cash resources, and greater clinical development and commercialization capabilities. Furthermore, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. If we are unable to successfully obtain rights to additional technologies or products, our business, financial condition, results of operations and prospects for growth could suffer.

In addition, we expect that competition for the in-licensing or acquisition of third-party intellectual property rights for products and technologies that are attractive to us may increase in the future, which may mean fewer suitable opportunities for us as well as higher acquisition or licensing costs. We may be unable to in-license or acquire the third-party intellectual property rights for products or technology on terms that would allow us to make an appropriate return on our investment.

Risks Related to Employee Matters, Managing Our Growth, and Other Risks Related to Our Business

Our success is highly dependent on our ability to attract and retain highly skilled executive officers and employees.

To succeed, we must recruit, retain, manage, and motivate qualified clinical, scientific, technical, and management personnel, and we face significant competition for experienced personnel. We are highly dependent on the principal members of our management and scientific and medical staff. If we do not succeed in attracting and retaining qualified personnel, particularly at the management level, it could adversely affect our ability to execute our business plan and harm our operating results. In particular, the loss of one or more of our executive officers could be detrimental to us if we cannot recruit suitable replacements in a timely manner. The competition for qualified personnel in the biopharmaceutical field is intense and, as a result, we may be unable to continue to attract and retain qualified personnel necessary for the future success of our business. We could in the future have difficulty attracting experienced personnel to our company and may be required to expend significant financial resources in our employee recruitment and retention efforts.

Many of the other biopharmaceutical companies that we compete against for qualified personnel have greater financial and other resources, different risk profiles, and a longer history in the industry than we do. They also may provide more diverse opportunities and better prospects for career advancement. Some of these characteristics may be more appealing to high-quality candidates than what we have to offer. If we are unable to continue to attract and retain high-quality personnel, the rate and success at which we can discover, develop, and commercialize our product candidates and device candidates will be limited, and the potential for successfully growing our business will be harmed.

The requirements of being a public company may strain our resources, result in more litigation, and divert management's attention.

As a public company, we are and will continue to be subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, or the Exchange Act, the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, or the Dodd-Frank Act, the listing requirements of Nasdaq, and other applicable securities rules and regulations. Complying with these rules and regulations has increased and will continue to increase our legal and financial compliance costs, make some activities more difficult, time consuming or costly, and increase demand on our systems and resources. The Exchange Act requires, among other things, that we file annual, quarterly, and current reports with respect to our business and operating results. The Sarbanes-Oxley Act requires, among other things, that we maintain effective disclosure controls and procedures and internal controls over financial reporting. We are required to disclose changes made in our internal controls over financial reporting on a quarterly basis. In order to maintain and, if required, improve our disclosure controls and procedures and internal controls over financial reporting to meet this standard, significant resources and management

oversight may be required. As a result, management's attention may be diverted from other business concerns, which could adversely affect our business and operating results. We may also need to hire additional employees or engage outside consultants to comply with these requirements, which will increase our costs and expenses.

In addition, changing laws, regulations and standards relating to corporate governance and public disclosure are creating uncertainty for public companies, increasing legal and financial compliance costs, and making some activities more time consuming. These laws, regulations, and standards are subject to varying interpretations, in many cases due to their lack of specificity and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices. We have invested and intend to continue to invest in resources to comply with evolving laws, regulations, and standards, and this investment may result in increased general and administrative expenses and a diversion of management's time and attention from revenue-generating activities to compliance activities. If our efforts to comply with new laws, regulations, and standards differ from the activities intended by regulatory or governing bodies due to ambiguities related to their application and practice, regulatory authorities may initiate legal proceedings against us and our business may be adversely affected.

These new rules and regulations may make it more expensive for us to obtain director and officer liability insurance and, during certain periods, including currently, we may utilize alternatives for such coverage, accept reduced coverage or incur substantially higher costs to obtain coverage. These factors could also make it more difficult for us to attract and retain qualified members of our board of directors, particularly to serve on our audit committee and compensation committee, and qualified executive officers. By disclosing information in filings required of us as a public company, our business and financial condition will continue to become more visible, which we believe may result in threatened or actual litigation, including by competitors and other third parties. If those claims are successful, our business could be seriously harmed. Even if the claims do not result in litigation or are resolved in our favor, the time and resources needed to resolve them could divert our management's resources and seriously harm our business.

Public health threats could have an adverse effect on the Company's operations and financial results.

In 2020, a strain of novel coronavirus disease, COVID-19, was declared a pandemic and spread across the world, including throughout the United States, Europe, and Asia. The pandemic and government measures taken in response have also had a significant impact, both direct and indirect, on businesses and commerce, as worker shortages have occurred, clinical trials have been suspended, supply chains have been disrupted, and facilities and production have been suspended.

The impacts on the operations and specifically the ongoing clinical trials of the Pharmaceutical Companies have been actively managed by respective pharmaceutical management teams who have worked closely with the appropriate regulatory agencies to continue clinical trial activities with as minimal impact as possible, including receiving waivers for certain clinical trial activities from the respective regulatory agencies to continue the studies.

In the earlier days of the pandemic's impact, Cornerstone experienced certain delays in enrollment in certain clinical trials. We believe, however, that those trials' enrollment goals were ultimately attained in a timely manner.

We have implemented a number of measures to protect the health and safety of our workforce, including a mandatory work-from-home policy for our workforce who can perform their jobs from home as well as restrictions on business travel and workplace and in-person meetings.

As a result of the COVID-19 pandemic, we may experience further disruptions that could severely impact our business, preclinical studies, and clinical trials, including:

- delays in receiving approval from local regulatory authorities to initiate our planned clinical trials;
- delays or difficulties in enrolling patients in our clinical trials;
- delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff;
- diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials;

- risk that participants enrolled in our clinical trials or related staff will acquire COVID-19 while the clinical trial is ongoing, which could impact the results of the clinical trial, including by increasing the number of observed adverse events;
- interruption of key clinical trial activities, such as clinical trial site data monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others or interruption of clinical trial subject visits and study procedures (such as endoscopies that are deemed non-essential), which may impact the integrity of subject data and clinical study endpoints;
- interruption or delays in the operations of the FDA, which may impact approval timelines;
- interruption of, or delays in receiving, supplies of our product candidates from our contract manufacturing organizations due to staffing or supply shortages, production slowdowns, global shipping delays or stoppages and disruptions in delivery systems;
- limitations on employee resources that would otherwise be focused on the conduct of our preclinical studies and clinical trials, including because of sickness of employees or their families or the desire of employees to avoid contact with large groups of people;
- refusal of the FDA to accept data from clinical trials in affected geographies;
- impacts from prolonged remote work arrangements, such as increased cybersecurity risks and strains on our business continuity plans; and
- delays or difficulties with equity offerings due to disruptions and uncertainties in the securities market.

The COVID-19 pandemic could also negatively impact our real estate business in a number of ways, including:

- the financial condition of our tenants and their ability or willingness to pay rent in full on a timely basis;
- the impact on rents and demand for office and retail space;
- a complete or partial closure of operations resulting from government action;
- the impact of new regulations or norms on physical space needs and expectations;
- the effectiveness of governmental measures aimed at slowing and containing the spread;
- the extent and terms associated with governmental relief programs;
- the ability of debt and equity markets to function and provide liquidity;
- the ability to avoid delays or cost increases associated with building materials or construction services necessary for development, redevelopment and tenant improvements; and
- our tenants' ability to ensure business continuity in the event a continuity of operations plan is not effective or improperly implemented.

Due to both known and unknown risks, including quarantines, closures, and other restrictions resulting from the outbreak, our operations and those of our holdings may be adversely impacted. Additionally, as there is an evolving nature to the COVID-19 situation, we cannot reasonably assess or predict at this time the full extent of the negative impact that the COVID-19 pandemic or a subsequent variant may have on our business, financial condition, results of operations, and cash flows. The impact will depend on future developments, such as the ultimate duration and the severity of the spread of the COVID-19 pandemic and any subsequent variant in the U.S. and globally, the effectiveness of federal, state, local, and foreign government actions on mitigation and spread of COVID-19 and any subsequent variant, the pandemic's impact on the U.S. and global economies, changes in our customers' behavior emanating from the pandemic and how quickly we can resume our normal operations, among others. For all these reasons, we may incur expenses or delays relating to such events outside of our control, which could have a material adverse impact on our business.

If we fail to implement and maintain an effective system of internal controls, we may be unable to accurately report our results of operations, meet our reporting obligations or prevent fraud. As a result, stockholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our common stock.

Effective internal controls over financial reporting are necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation, could cause us to fail to meet our reporting obligations. In addition, any testing by us conducted in connection with Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, or any subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our stock.

We are required to disclose changes made in our internal controls and procedures on a quarterly basis and to disclose any changes and material weaknesses in those internal controls. A material weakness is a deficiency, or a combination of deficiencies, in internal controls over financial reporting, such that there is a reasonable possibility that a material misstatement of the company's annual or interim financial statements will not be prevented or detected on a timely basis.

We cannot be certain that we will continue to maintain an effective system of internal controls over our financial reporting in future periods. Any failure to maintain such internal controls could adversely impact our ability to report our financial results on a timely and accurate basis. If our financial statements are not accurate, investors may not have a complete understanding of our operations. Likewise, if our financial statements are not filed on a timely basis as required by the Securities and Exchange Commission and The New York Stock Exchange, we could face severe consequences from those authorities. In either case, there could result a material adverse effect on our business. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our stock.

We have identified material weaknesses in our internal controls over financial reporting.

Maintaining effective internal controls over financial reporting is necessary for us to produce reliable financial statements.

In the past, we have identified material weaknesses in our internal controls over financial reporting which have since been remediated.

If additional material weaknesses in our internal controls over financial reporting are discovered or occur in the future, our consolidated financial statements may contain material misstatements and we could be required to restate our financial results.

Conditions in Israel, including the recent terrorist attack by Hamas and other terrorist organizations from the Gaza Strip and Israel's war against them, may adversely affect our real estate holding and operations of our Investment Companies, which would lead to a decrease in revenues.

On October 7, 2023, Hamas terrorists and members of other terrorist organizations infiltrated Israel's southern border from the Gaza Strip and conducted a series of terror attacks on civilian and military targets. Thereafter, these terrorists launched extensive rocket attacks on Israeli population and industrial centers located along the Israeli border with the Gaza Strip.

It is possible that other terrorist organizations will join the hostilities as well, including Hezbollah in Lebanon, and Palestinian military organizations in the West Bank. Our real estate holding in Jerusalem and operations of Lipomedix and Day Three in Jerusalem and Rosh Haayin, respectively, are not only within the range of rockets from the Gaza Strip, but also within the range of rockets that can be fired from Lebanon, Syria or elsewhere in the Middle East. Our lone real estate holding can be damaged as a result of hostile action or hostilities or the ongoing operations of Lipomedix and Day Three may be disrupted.

Our commercial insurance does not cover losses that may occur as a result of events associated with war and terrorism. Although the Israeli government currently covers the reinstatement value of direct damages that are caused by terrorist attacks or acts of war, we cannot assure you that this government coverage will be maintained or that it will sufficiently cover our potential damages. Any losses or damages incurred by us could have a material adverse effect on our business.

As a result of the Israeli security cabinet's decision to declare war against Hamas, several hundred thousand Israeli reservists were drafted to perform immediate military service. Certain of our employees and consultants in Israel, in addition to employees of our service providers located in Israel, have been called for service in the current war with Hamas as of the date of this registration statement, and such persons are expected may be absent for an extended period of time. As a result, operations of Lipomedix and Day Three may be disrupted by such absences, which may materially and adversely affect their business and results of operations.

The relationships between Howard S. Jonas and IDT Corporation, Genie Energy, and Cornerstone Pharmaceuticals could conflict with our stockholders' interests.

Howard S. Jonas, Chairman of our Board of Directors and Executive Chairman and former Chief Executive Officer, is also the chairman of IDT Corporation and Chairman of the Board of Genie and holds certain direct and indirect interests in Cornerstone and serves as Chairman of its Board in addition to his interests through ownership of our common stock. These relationships may cause a conflict of interest with our stockholders.

Insurance policies are expensive and protect us only from some business risks, which leaves us exposed to uninsured liabilities.

Some of the insurance policies we currently maintain, or which we have maintained in the past, include general liability, employment practices liability, property, product liability, workers' compensation, umbrella, and directors' and officers' insurance. These policies may not adequately cover all categories of risk that our business may encounter.

Any additional product liability insurance coverage we acquire in the future may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive and, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. If we obtain regulatory approval or clearance for any of the Investment Companies' product candidates or device candidates, we intend to acquire insurance coverage to include the sale of commercial products; however, we may be unable to obtain product liability insurance on commercially reasonable terms or in adequate amounts. A successful product liability claim or series of claims brought against us could cause our share price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operations and business, including preventing or limiting the development and commercialization of any product candidates or device candidates we develop. We may not carry adequate specific biological or hazardous waste insurance coverage, and our property, casualty, and general liability insurance policies specifically exclude coverage for damages and fines arising from biological or hazardous waste exposure or contamination. Accordingly, in the event of contamination or injury, we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended.

We also expect that operating as a public company will make it more difficult and more expensive for us to obtain director and officer liability insurance, and, during certain periods, including currently, we may utilize alternatives for such coverage, accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. As a result, it may be more difficult for us to attract and retain qualified people to serve on our board of directors, our board committees or as executive officers. We do not know, however, if we will be able to maintain existing insurance with adequate levels of coverage. Any significant uninsured liability may require us to pay substantial amounts, which would adversely affect our cash position and results of operations.

We rely significantly on information technology and any failure, inadequacy, interruption or security lapse of that technology, including any cyber security incidents, could harm our ability to operate our business and that of the companies in which we hold interests effectively.

Despite the implementation of security measures, our and the Investment Companies' internal computer systems and those of third parties with which we and the Investment Companies contract are vulnerable to damage from cyber-attacks, computer viruses, unauthorized access, natural disasters, terrorism, war, and telecommunication and

electrical failures. System failures, accidents or security breaches could cause interruptions in our and the Investment Companies' operations, and could result in a material disruption of their clinical and commercialization activities and business operations, in addition to possibly requiring substantial expenditures of resources to remedy. The loss of clinical trial data could result in delays in the Investment Companies' regulatory approval efforts and significantly increase their costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of, or damage to, our or the Investment Companies' data or applications, or inappropriate disclosure of confidential or proprietary information, we and the Investment Companies could incur liability and their product research, development, and commercialization efforts could be delayed.

Furthermore, we and our third-party providers rely on electronic communications and information systems to conduct our operations. We and our third-party providers have been, and may continue to be, targeted by parties using fraudulent e-mails and other communications in attempts to misappropriate bank accounting information, passwords, or other personal information or to introduce viruses or other malware to our information systems. In October 2021, we experienced a cybersecurity incident where a related party's email was hacked which led to payment of two invoices. As of the date of this filing, one of the invoice payments had been recovered by the Company. We continue to explore a range of steps to enhance our security protections and prevent future unauthorized activity.

Although we endeavor to mitigate these threats, such cyber-attacks against us or our third-party providers and business partners remain a serious issue. The pervasiveness of cybersecurity incidents in general and the risks of cyber-crime are complex and continue to evolve. Although we are making significant efforts to maintain the security and integrity of our information systems and are exploring various measures to manage the risk of a security breach or disruption, there can be no assurance that our security efforts and measures will be effective or that attempted security breaches or disruptions would not be successful or damaging.

Our insurance policies may not be adequate to compensate us for the potential losses arising from any such disruption, failure or security breach. In addition, such insurance may not be available to us in the future on economically reasonable terms, or at all. Further, our insurance may not cover all claims made against us and could have high deductibles in any event, and defending a suit, regardless of its merit, could be costly and divert management attention.

Failure to complete the merger could subject us to litigation.

We could be subject to litigation related to any failure to complete the proposed merger with Cornerstone or related to any proceeding to specifically enforce our obligations under the merger agreement. If any of these risks materialize, they may materially and adversely affect our business, financial condition, financial results, and stock prices.

Risks Related to Ownership of our Common Stock

We do not currently intend to pay dividends on our common stock and, consequently, your ability to achieve a return on your investment will depend on appreciation of the value of our common stock.

We have never declared or paid any cash dividends on our equity securities. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Any return to stockholders will therefore be limited to any appreciation in the value of our common stock, which is not certain.

We are controlled by our principal stockholder, which limits the ability of other stockholders to affect the management of the Company.

Howard S. Jonas, our Chairman of our Board of Directors and our Executive Chairman, controls a majority of the voting power of our capital stock. As of October 27, 2023, Mr. Jonas has voting power over 787,163 shares of our Class A common stock (which are convertible into shares of our Class B common stock on a 1-for-1 basis) and 665,247 shares of our Class B common stock, representing approximately 51% of the combined voting power of our outstanding capital stock. Mr. Jonas will be able to control matters requiring approval by our stockholders, including the election of all of the directors and the approval of significant corporate matters, including any merger, consolidation or sale of all or substantially all of our assets. As a result, the ability of any of our other stockholders to influence our management is limited.

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

Sales of a substantial number of shares of our common stock in the public market, or the perception in the market that the holders of a large number of shares of common stock intend to sell shares, could reduce the market price of our common stock. Outstanding shares of our common stock may be freely sold in the public market at any time to the extent permitted by Rules 144 and 701 under the Securities Act, or to the extent that such shares have already been registered under the Securities Act and are held by non-affiliates of ours. Moreover, holders of a substantial number of shares of our common stock have rights, subject to certain conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. We also have registered all shares of common stock that we may issue under our equity compensation plans or that are issuable upon exercise of outstanding options. These shares can be freely sold in the public market upon issuance, and once vested, subject to volume limitations applicable to affiliates. If any of these additional shares are sold, or if it is perceived that they will be sold, in the public market, the market price of our common stock could decline.

We are a “smaller reporting company,” and the reduced disclosure requirements applicable to smaller reporting companies may make our common stock less attractive to investors.

We are considered a “smaller reporting company.” We are therefore entitled to rely on certain reduced disclosure requirements, such as an exemption from providing selected financial data and executive compensation information. These exemptions and reduced disclosures in our SEC filings due to our status as a smaller reporting company may make it harder for investors to analyze our results of operations and financial prospects. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock prices may be more volatile.

General Risk Factors

If we engage in future acquisitions or strategic collaborations, this may increase our capital requirements, dilute our stockholders, cause us to incur debt or assume contingent liabilities, and subject us to other risks.

From time to time, we may evaluate various acquisition opportunities and strategic collaborations, including licensing or acquiring complementary products, intellectual property rights, technologies or businesses. Any potential acquisition or strategic partnership may entail numerous risks, including:

- increased operating expenses and cash requirements;
- the assumption of additional indebtedness or contingent liabilities;
- the issuance of our equity securities;
- assimilation of operations, intellectual property and products of an acquired company, including difficulties associated with integrating new personnel;
- the diversion of our management’s attention from our existing programs and initiatives in pursuing such a strategic merger or acquisition;
- retention of key employees, the loss of key personnel and uncertainties in our ability to maintain key business relationships;
- risks and uncertainties associated with the other party to such a transaction, including the prospects of that party and their existing products or product candidates and regulatory approvals; and
- our inability to generate revenue from acquired technology and/or products sufficient to meet our objectives in undertaking the acquisition or even to offset the associated acquisition and maintenance costs. In addition, if we undertake acquisitions or pursue collaborations in the future, we may issue dilutive securities, assume or incur debt obligations, incur large one-time expenses and acquire intangible assets that could result in significant future amortization expense. Moreover, we may not be able to locate suitable acquisition opportunities, and this inability could impair our ability to grow or obtain access to technology or products that may be important to the development of our business.

Investors may suffer dilution.

We may engage in equity financing to fund our future operations and growth or issue equity securities in commercial or other transactions. If we raise additional funds by issuing equity securities, or issue equity securities for other purposes, stockholders may experience significant dilution of their ownership interest (both with respect to the percentage of total securities held, and with respect to the book value of their securities) and such securities may have rights senior to those of the holders of our common stock. In addition, if we do not provide our Investment Companies with the capital they require, they may seek capital from other sources, which would result in dilution and possible subordination or other diminution in value of our interests in those companies.

The trading price of the shares of our Class B common stock is likely to remain volatile, and purchasers of our Class B common stock could incur substantial losses.

Our stock price is likely to remain volatile. The stock market in general and the market for Investment Companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, investors may not be able to sell their Class B common stock at or above the price paid for the shares. The market price for our Class B common stock may be influenced by many factors, including:

- actual or anticipated variations in quarterly operating results;
- changes in financial estimates by us or by any securities analysts who might cover our stock;
- conditions or trends in our industry;
- stock market price and volume fluctuations of other publicly traded companies and, in particular, those that operate in the real estate or healthcare industries;
- announcements by us or our competitors of the results of clinical trials, new product or service offerings, or significant acquisitions;
- strategic collaborations or divestitures;
- announcements of investigations or regulatory scrutiny of our operations or lawsuits filed against us;
- capital commitments;
- additions or departures of key personnel; and
- sales of our common stock, including sales by our directors and officers or specific stockholders. In addition, in the past, stockholders have initiated class action lawsuits against companies following periods of volatility in the market prices of these companies' stock. Such litigation, if instituted against us, could cause us to incur substantial costs and divert management's attention and resources.

The realization of any of the above risks or any of a broad range of other risks, including those described in this "Risk Factors" section, could have a dramatic and adverse impact on the market price of our common stock.

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

The trading market for our common stock will rely in part on the research and reports that equity research analysts may publish about us and our business. We do not currently have analyst coverage and may never obtain research coverage by equity research analysts. Equity research analysts may elect not to provide research coverage of our common stock and such lack of research coverage may adversely affect the market price of our common stock. In the event we do have equity research analyst coverage, we will not have any control over the analysts or the content and opinions included in their reports. The price of our stock could decline if one or more equity research analysts or others downgrade our stock or issue other unfavorable commentary or research. If one or more equity research analysts ceases coverage of our company or fails to publish reports on us regularly, demand for our stock could decrease, which in turn could cause our stock price or trading volume to decline.

We may be subject to securities litigation, which is expensive and could divert management attention.

The market price of our common stock may be volatile and, 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.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

Our principal executive office is located in 520 Broad Street, Newark, New Jersey.

LipoMedix has a Research and Services Agreement with Shaare Zedek Scientific Ltd. by which laboratory space at Shaare Zedek Medical Center is used for R&D activities. This agreement is conditioned to grant support for the Shaare Zedek Nano-Oncology research center either directly from LipoMedix or indirectly through the Israel Innovation Authority Fund (Israel Chief Scientist Office). This arrangement has been in place since 2012, and the grant support is negotiable and renewed on an annual basis. However, there can be no guarantees that Shaare Zedek will continue this agreement in the future.

LipoMedix leased an administrative office in Giv'at Ram Hi-Tech Park from the Hebrew University. Rent was \$3,600 annually, and the lease agreement ran through September 30, 2022.

See Item 1 — "Real Estate" for a discussion of properties held by the Company for investment purposes and Item 8 — "Financial Statements and Supplemental Data," for a detailed listing of such facilities.

Item 3. Legal Proceedings

Legal proceedings disclosure is presented in Note 19 to our Consolidated Financial Statements and in Item 8 to Part II of this Annual Report.

The Company may from time to time be subject to legal proceedings that may arise in the ordinary course of business. Although there can be no assurance in this regard, other than noted above, the Company does not expect any of those legal proceedings to have a material adverse effect on the Company's results of operations, cash flows or financial condition.

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

PRICE RANGE OF COMMON STOCK

Our Class B common stock trades on the New York Stock Exchange under the symbol “RFL.” Trading commenced on the NYSE American on March 27, 2018 and the Company uplisted and commenced trading on the New York Stock Exchange on November 21, 2019.

On October 27, 2023, there were 262 holders of record of our Class B common stock and one holder of record of our Class A common stock. Howard Jonas has voting and dispositive power over all shares of Class A common stock. The number of holders of record of our Class B common stock does not include the number of persons whose shares are in nominee or in “street name” accounts through brokers. On October 27, 2023, the last sales price reported on the NYSE for the Class B common stock was \$1.55 per share.

We do not anticipate paying dividends on our common stock until we achieve sustainable profitability (after satisfying all of our operational needs) and retain certain minimum cash reserves. Distributions will be subject to the need to retain earnings for investment in growth opportunities or the acquisition of complementary assets. The payment of dividends in any specific period will be at the sole discretion of our Board of Directors.

The information required by Item 201(d) of Regulation S-K will be contained in our Proxy Statement for our Annual Stockholders Meeting, which we will file with the Securities and Exchange Commission within 120 days after July 31, 2023, and which is incorporated by reference herein.

Performance Graph of Stock

We are a smaller reporting company as defined by Rule 12b-2 of the Securities and Exchange Act of 1934 and are not required to provide the information under this item.

Issuer Repurchases of Equity Securities

None.

Item 6. [Reserved].

Item 7. Management’s Discussion and Analysis of Financial Condition and Results of Operations

This Annual Report contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934, including statements that contain the words “believes,” “anticipates,” “expects,” “plans,” “intends” and similar words and phrases. These forward-looking statements are subject to risks and uncertainties that could cause actual results to differ materially from the results projected in any forward-looking statement. In addition to the factors specifically noted in the forward-looking statements, other important factors, risks and uncertainties that could result in those differences include, but are not limited to, those discussed under Item 1A to Part I “Risk Factors” in this Annual Report. The forward-looking statements are made as of the date of this Annual Report, and we assume no obligation to update the forward-looking statements, or to update the reasons why actual results could differ from those projected in the forward-looking statements. Investors should consult all of the information set forth in this report and the other information set forth from time to time in our reports filed with the Securities and Exchange Commission pursuant to the Securities Act of 1933 and the Securities Exchange Act of 1934, including our reports on Forms 10-Q and 8-K.

The following discussion should be read in conjunction with the Consolidated Financial Statements and Notes thereto included in Item 8 of this Annual Report.

Overview

Rafael Holdings, Inc. (NYSE:RFL), (“Rafael Holdings”, “we” or the “Company”), a Delaware corporation, is a holding company with interests in clinical and early-stage pharmaceutical companies (the “Pharmaceutical Companies”), including an investment in Cornerstone Pharmaceuticals, Inc., formerly known as Rafael Pharmaceuticals Inc., a cancer metabolism-based therapeutics company, a majority equity interest in LipoMedix Pharmaceuticals Ltd. (“LipoMedix”), a clinical stage pharmaceutical company, the Barer Institute Inc. (“Barer”), a wholly-owned preclinical cancer metabolism research operation, an investment in Cyclo Therapeutics, Inc. (Nasdaq: CYTH) (“Cyclo Therapeutics” or “Cyclo”), a clinical-stage biotechnology company dedicated to developing life-changing medicines for patients and families living with challenging diseases through its lead therapeutic asset, Trappsol® Cyclo™, an investment in Day Three Labs, Inc. (“Day Three”), a company which reimagines existing cannabis offerings with pharmaceutical-grade technology and innovation like Unlokt™ to bring to market better, cleaner, more precise and predictable products in the cannabis industry, and a majority interest in Rafael Medical Devices, LLC, an orthopedic-focused medical device company developing instruments to advance minimally invasive surgeries (“Rafael Medical Devices” and Day Three Labs together with the Pharmaceutical Companies, represent our “Investment Companies”). In November 2022, the Company resolved to curtail its early-stage development efforts, including pre-clinical research at Barer. The decision was taken to reduce spending as the Company focuses on exploring strategic opportunities. The Company’s primary focus is to expand our investment portfolio through opportunistic and strategic investments including therapeutics which address high unmet medical needs.

The Company holds debt and equity investments in Cornerstone, that include preferred and common equity interests and a warrant to purchase additional equity. On June 17, 2021, the Company entered into a merger agreement to acquire full ownership of Cornerstone in exchange for issuing Company Class B common stock to the other stockholders of Cornerstone (“Merger Agreement” or “Merger”). On October 28, 2021, the Company announced that the AVENGER 500 Phase 3 clinical trial for CPI-613® (devimistat), Cornerstone’s lead product candidate, did not meet its primary endpoint of significant improvement in overall survival in patients with metastatic adenocarcinoma of the pancreas. In addition, following a pre-specified interim analysis, the independent data monitoring committee for the ARMADA 2000 Phase 3 study for devimistat recommended the trial to be stopped due to a determination that it was unlikely to achieve the primary endpoint (the “Data Events”). In light of the Data Events, the Company concluded that the prospects for CPI-613 were uncertain and fully impaired in its financial statements for the year ended July 31, 2022, the value of its loans, receivables, and investment in Cornerstone based upon its valuation of Cornerstone.

On September 24, 2021, the Company entered into a Line of Credit Loan Agreement (the “Line of Credit Agreement”) with Cornerstone under which Cornerstone borrowed \$25 million from the Company. Due to the Data Events, the Company recorded a full reserve on the \$25 million due the Company from Cornerstone.

On February 2, 2022, the Company terminated the Merger Agreement with Cornerstone Pharmaceuticals, effective immediately, in accordance with its terms. Subsequently, on February 2, 2022, the Company withdrew its Registration Statement on Form S-4 related to the proposed Merger.

On March 21, 2023, the Company loaned \$2.0 million to Cornerstone which debt is represented by a Promissory Note made by Cornerstone (the “Promissory Note” or “Note”). The Note, which bears interest at a rate of seven and one-half percent (7.5%) per annum, was originally due and payable on May 22, 2023. On May 22, 2023, the Promissory Note was amended to extend the maturity date to November 30, 2023 and to waive any increase in the interest rate provided for in the Note, provided that the entire principal amount and all accrued interest thereon is repaid in cash or converted into equity securities of Cornerstone no later than November 30, 2023.

Cornerstone is in the process of a comprehensive restructuring transaction including, an equity investment by the Company of \$1.5 million with other stockholders having the right to invest amounts on the same terms to avoid dilution, the conversion and modification of other Cornerstone debt obligations, the extension of the Cornerstone debt held by RP Finance, a reverse stock split, the conversion of all outstanding preferred stock of Cornerstone into common stock and the adoption of certain governance measures. This transaction is subject to a number of conditions which are beyond the Company’s control.

In 2019, the Company established the Barer Institute Inc., an early-stage small molecule research operation focused on developing a pipeline of novel therapeutic compounds, including compounds to regulate cancer metabolism with potentially broader application in other indications beyond cancer. Barer was led by a team of scientists and academic advisors considered to be among the leading experts in cancer metabolism, chemistry, and drug development.

In addition to its own internal discovery efforts, Barer pursued collaborative research agreements and in-licensing opportunities with leading scientists from top academic institutions. Farber Partners, LLC (“Farber”) was formed to support agreements with Princeton University’s Office of Technology Licensing for technology from the laboratory of Professor Joshua Rabinowitz, in the Department of Chemistry, Princeton University, including an exclusive worldwide license to its SHMT (serine hydroxymethyltransferase) inhibitor program. The Company also holds a majority equity interest in LipoMedix, a clinical stage oncological pharmaceutical company based in Israel. In addition, the Company has invested in other early-stage pharmaceutical ventures.

In 2016, the Company first invested in LipoMedix Pharmaceuticals Ltd. (“LipoMedix”), a clinical stage pharmaceutical company. On February 9, 2023, the Company entered into a Share Purchase Agreement with LipoMedix in which LipoMedix sold 70,000,000 ordinary shares to the Company at a price per share of \$0.03 and an aggregate sale price of approximately \$2.1 million. Subsequent to this transaction, the Company owns 95% of LipoMedix.

On April 7, 2023, the Company entered into a Common Stock Purchase Agreement (the “Day Three Purchase Agreement”) with Day Three. Day Three is a cannabinoid ingredient manufacturer specializing in the development and commercialization of novel cannabis product solutions. Pursuant to the Day Three Purchase Agreement, the Company purchased 4,302,224 shares of common stock representing 38% of the outstanding shares of common stock of Day Three (33.333% on a fully diluted basis), for a purchase price of \$3.0 million. The Company also received a warrant exercisable for 7,528,893 shares of common stock at an aggregate purchase price of \$3.0 million, which expires five years from the date of issuance or earlier based on the occurrence of certain events as defined in the Day Three Purchase Agreement. As of July 31, 2023, the Company had not exercised the warrant. Refer to Note 8 to our accompanying consolidated financial statements for further detail.

On May 2, 2023, the Company entered into a Securities Purchase Agreement (the “Cyclo SPA”) with Cyclo. Cyclo is a clinical stage biotechnology company, whose common stock is listed on the Nasdaq Capital Market under the symbol CYTH, that develops cyclodextrin-based products for the treatment of neurodegenerative diseases. The Company purchased from Cyclo (i) 2,514,970 common shares (the “Purchased Shares”) and (ii) a warrant to purchase 2,514,970 common shares with an exercise price of \$0.71 per share (the “Cyclo Warrant”), at a combined purchase price equal to \$0.835 per Purchased Share and Cyclo Warrant to purchase one share, for an aggregate purchase price of \$2.1 million. The Cyclo Warrant is exercisable for a period of seven years from the date of issuance.

On August 1, 2023, the Company purchased an additional 4,000,000 shares of common stock (the “Cyclo II Shares”), and a warrant to purchase an additional 4,000,000 Shares (the “Cyclo II Warrant”), for an aggregate purchase price of \$5,000,000. The Cyclo II Warrant has an exercise price of \$1.25 per share and is exercisable until July 31, 2030. The August 1, 2023 investment increased the Company’s percentage ownership of Cyclo common stock to 34%.

On October 20, 2023, the Company exercised the Cyclo Warrant to purchase 2,514,970 common shares at an exercise price of \$0.71 per share, pursuant to a Securities Purchase Agreement dated October 20, 2023, and in consideration received a new warrant to purchase an additional 2,766,467 common shares at an exercise price of \$0.95 per share which are exercisable for a period of four years following the issuance date (the “Cyclo III Warrant”), for an aggregate purchase price of \$1,785,629.

During the fourth quarter of fiscal 2023, Rafael Medical Devices received \$825 thousand as a deposit from outside third party investors for the purchase of membership units. On August 1, 2023, the Company received an additional \$100 thousand. Following these investments, the Company holds 53.4% (on a fully diluted basis) of the ownership interests in Rafael Medical Devices. As of July 31, 2023, the Company recorded the funds received within prepaid expenses and other current assets and other current liabilities within the consolidated balance sheets.

Historically, the Company owned real estate assets. In 2020, the Company sold an office building located in Piscataway, New Jersey and on August 22, 2022, the Company sold the building at 520 Broad Street in Newark, New Jersey and an associated public garage. Currently, the Company holds a portion of a commercial building in Jerusalem, Israel as its remaining real estate asset.

On July 1, 2022, the Company determined that the 520 Property met the held-for-sale criteria and the Company has therefore classified the 520 Property as held-for-sale in the consolidated balance sheet at July 31, 2022. The sale of the 520 Property also represents a significant strategic shift that will have a major effect on the Company’s operations and financial results. Therefore, the Company has classified the results of operations related to the 520 Property as

discontinued operations in the consolidated statements of operations and comprehensive loss. Depreciation on the 520 Property ceased effective July 1, 2022, as a result of the 520 Property being classified as held-for-sale. See Note 3 to our accompanying consolidated financial statements for further information regarding discontinued operations.

As of July 31, 2023, the Company's commercial real estate holdings consisted of a portion of a commercial building in Israel. On August 22, 2022, the Company completed the sale of the building at 520 Broad Street in Newark, New Jersey that serves as headquarters for the Company for a purchase price of approximately \$49.4 million and realized net proceeds of approximately \$33 million.

Results of Operations

Our business consists of two reportable segments — Healthcare and Real Estate. We evaluate the performance of our Healthcare segment based primarily on research and development efforts and results of clinical trials, and our Real Estate segment based primarily on results of operations. Accordingly, the income and expense line items below loss from operations are only included in the discussion of consolidated results of operations.

Healthcare Segment

Our consolidated expenses for our Healthcare segment were as follows:

	Year Ended July 31,		Change	
	2023	2022	\$	%
	<i>(in thousands)</i>			
General and administrative	\$ (8,794)	\$ (16,818)	8,024	48%
Research and development	(6,312)	(8,742)	2,430	28%
Depreciation	(15)	(3)	(12)	—%
Provision for loss on receivable from Cornerstone Pharmaceuticals pursuant to line of credit	—	(25,000)	25,000	(100)%
Provision for losses on related party receivables.	—	(10,095)	10,095	(100)%
Loss from operations.	<u>\$ (15,121)</u>	<u>\$ (60,658)</u>	<u>45,537</u>	<u>75%</u>

To date, the Healthcare segment has not generated any revenues. The entirety of the expenses in the Healthcare segment relate to the activities of LipoMedix, Barer, Farber, and Rafael Medical Devices. As of July 31, 2023, we held a 100% interest in Barer, a 95% interest in LipoMedix, a 93% interest in Farber, and a 100% interest in Rafael Medical Devices. On August 1, 2023, the Rafael Medical Devices closed on the sale of membership units in exchange of \$925,000, and following that sale, the Company holds 53.4% (on a fully diluted basis) of the outstanding equity interests in Rafael Medical Devices, on a fully-diluted basis. As of July 31, 2023, the Company recorded the funds received within prepaid expenses and other current assets and other liabilities of \$825,000 within the consolidated balance sheets.

General and administrative expenses. General and administrative expenses consist mainly of payroll, stock-based compensation expense, benefits, facilities, consulting and professional fees. The decrease in general and administrative expenses during the year ended July 31, 2023 compared to the year ended July 31, 2022 is primarily due to a net decrease in severance expense of approximately \$5.0 million, a decrease in payroll expense of approximately \$3.4 million, a decrease in legal expense of approximately \$1.1 million, a decrease in professional fees of approximately \$1.2 million and a decrease in other general and administrative expenses of approximately \$0.7 million, partially offset by a net increase in stock-based compensation expense of approximately \$3.6 million due to a material forfeiture of granted equity interests in the year ended July 31, 2022.

Research and development expenses. Research and development expenses decreased for the year ended July 31, 2023 as compared to the corresponding period in fiscal 2022. Research and development expenses are derived from activity at Barer, LipoMedix, Farber, and Rafael Medical Devices. In November 2022, the Company resolved to curtail its early-stage development efforts, including pre-clinical research at the Barer Institute. The decision was taken to reduce spending as the Company focuses on exploring strategic opportunities.

Loss on line of credit. Due to the Data Events, in the year ended July 31, 2022, the Company recorded a full reserve on the \$25 million due to the Company from Cornerstone Pharmaceuticals related to the Line of Credit Agreement.

Loss on related party receivables. Due to the Data Events, in the year ended July 31, 2022, the Company recorded a loss of approximately \$10.1 million related to the full reserve recorded on the RP Finance receivable of \$9.375 million, an equity method investment (see Note 6), and a full reserve recorded on the Cornerstone Pharmaceuticals receivable, see (Note 4) of \$720 thousand.

Real Estate Segment

The revenue and expenses of the 520 Property have been excluded from the real estate segment in the figures below due to its classification of held-for-sale and discontinued operations, and the sale of the 520 Property on August 22, 2022. The Real Estate segment consists of a portion of a commercial building in Israel. Consolidated income and expenses for our Real Estate segment were as follows:

	<u>Year Ended July 31,</u>		<u>Change</u>	
	<u>2023</u>	<u>2022</u>	<u>\$</u>	<u>%</u>
	<i>(in thousands)</i>			
Rental – Third Party	\$ 171	\$ 179	(8)	(4)%
Rental – Related Party	108	111	(3)	(3)%
Other – Related Party	—	120	(120)	(100)%
General and administrative	(138)	(160)	22	14%
Depreciation and amortization	(63)	(69)	6	9%
Income from operations	<u>\$ 78</u>	<u>\$ 181</u>	<u>(103)</u>	<u>57%</u>

Other — Related Party. Other — related party revenues decreased by approximately \$120 thousand during the year ended July 31, 2023, compared to the year ended July 31, 2022. During the year ended July 31, 2022, the Company only billed Cornerstone Pharmaceuticals \$120 thousand for the first quarter of 2022 for administrative, finance, accounting, tax, and legal services. As of July 31, 2023 and 2022, Cornerstone Pharmaceuticals owed the Company \$720 thousand which relates to administrative and back-office services, for which a full allowance for uncollectibility has been recorded.

General and administrative expenses. General and administrative expenses consist mainly of payroll, benefits, facilities, consulting and professional fees. The decrease in general and administrative expenses of approximately \$22 thousand during the year ended July 31, 2023 compared to the year ended July 31, 2022 is primarily due to a decrease in professional fees.

Consolidated Operations

Our consolidated income and expense line items below loss from operations were as follows:

	Year Ended July 31,		Change	
	2023	2022	\$	%
	<i>(in thousands)</i>			
Loss from continuing operations	\$ (15,043)	\$ (60,477)	45,434	75%
Interest expense	—	(6)	6	100%
Interest income	3,253	201	3,052	(1518)%
Impairment of investments – Other Pharmaceuticals	(334)	—	(334)	(100)%
Impairment of cost method investment – Cornerstone Pharmaceuticals	—	(79,141)	79,141	(100)%
Realized gain (loss) on available-for-sale securities	154	(45)	199	(442)%
Realized gain on investment in equity securities	309	—	309	(100)%
Unrealized gain on investment in equity securities.	33	—	33	(100)%
Unrealized gain on investments – Cyclo Therapeutics Inc. . .	2,663	—	2,663	(100)%
Unrealized gain (loss) on investments – Hedge Funds	220	(504)	724	(144)%
Loss from continuing operations before income taxes	(8,745)	(139,972)	131,227	94%
Benefit from income taxes	255	—	255	(100)%
Equity in loss of Day Three Labs Inc.	(203)	—	(203)	100%
Equity in loss of RP Finance.	—	(575)	575	(100)%
Consolidated net loss from continuing operations	(8,693)	(140,547)	131,854	94%
Income (loss) from discontinued operations related to 520 Property	6,478	(1,830)	8,308	454%
Net loss attributable to noncontrolling interests	(339)	(17,719)	17,380	98%
Net loss attributable to Rafael Holdings, Inc.	<u>\$ (1,876)</u>	<u>\$ (124,658)</u>	<u>\$ 122,782</u>	<u>98%</u>

Interest income. Interest income was \$3.3 million and \$201 thousand for the years ended July 31, 2023 and 2022, respectively. The increase is primarily due to the interest income earned and accretion of the discount on the face value of our investments in available-for-sale securities whose balance increased to \$57.7 million at July 31, 2023 from \$36.7 million at July 31, 2022.

Impairment of investments — Other Pharmaceuticals. We recorded an impairment loss of \$334 thousand for the year ended July 31, 2023, related to an investment in securities in another entity using the measurement alternative.

Impairment of cost method investment — Cornerstone Pharmaceuticals. In connection with the Data Events, during the year ended July 31, 2022, we recorded a full impairment charge to our cost method investment in Cornerstone Pharmaceuticals in the amount of \$79 million.

Realized gain (loss) on available-for-sale securities. We recorded a realized gain of approximately \$154 thousand related to the sale of available-for-sale securities for the year ended July 31, 2023. We recorded a realized loss of approximately \$45 thousand related to the sale of available-for-sale securities for the year ended July 31, 2022.

Realized gain on investment in equity securities. We recorded a realized gain of approximately \$309 thousand related to the sale of equity securities for the year ended July 31, 2023.

Unrealized gain on investment — Cyclo. We recorded an unrealized gain of approximately \$2.7 million related to the change in fair value in our investment in Cyclo for the year ended July 31, 2023.

Unrealized gain (loss) on investments — Hedge Funds. We recorded unrealized gains of approximately \$220 thousand and losses of approximately \$504 thousand for the years ended July 31, 2023 and 2022, respectively.

Benefit from income taxes. Our benefit from income taxes was approximately \$255 thousand and \$0 for the years ended July 31, 2023 and 2022, respectively. The increase is primarily attributed to approximately \$274 thousand in proceeds for the sale of the Company's 2018 and 2019 New Jersey tax credits. These benefits were realized by utilizing the New Jersey Technology Business Tax Certificate Transfer Program whereby the State of New Jersey allows us to sell a portion of our state net operating loss carryforwards.

Equity in loss of Day Three Labs, Inc. We recognized a loss of approximately \$203 thousand from our ownership interest in Day Three due to operating results for the year ended July 31, 2023. As of July 31, 2023, the equity method investment in Day Three on our balance sheet is approximately \$2.8 million.

Equity in loss of RP Finance. We recognized a loss of \$575 thousand from our ownership interest in RP Finance due to operating results for the year ended July 31, 2022. As of July 31, 2022, the equity method investment in RP Finance on our balance sheet was \$0, and no additional equity loss of RP Finance was recorded subsequent to the year ended July 31, 2022.

Income (loss) from discontinued operations related to 520 Property. Discontinued operations include: (i) rental and parking revenues, (ii) payroll, benefits, facilities, consulting and professional fees dedicated to 520 Property, (iii) depreciation and amortization expenses, (iv) interest (including amortization of debt issuance costs) on the note payable that was secured by a mortgage on the 520 Property, and (v) gain on the disposal of the 520 Property. The operating results of these items are presented in our consolidated statements of operations and comprehensive loss as discontinued operations for all periods presented. The increase in the net income attributable to discontinued operations for the year ended July 31, 2023 as compared to the year ended July 31, 2022 was due to a gain on the sale of the 520 Property of \$6.8 million, an approximate \$1.4 million decrease in interest expense, partially offset by a \$3.3 million decrease in rental revenue, a \$2.2 million decrease in general and administrative expenses (which is primarily comprised of a decrease in real estate taxes, utilities other building related repairs, maintenance expenses, and other expenses totaling approximately \$2.4 million, slightly offset by a \$129 thousand increase in expense related to the write-off of deferred rental income), and a \$1.3 million decrease in depreciation and amortization expense due to no depreciation expense during the year ended July 31, 2023 as depreciation stopped as of July 1, 2022 when the 520 Property was classified as held-for-sale.

See Note 3 to our accompanying consolidated financial statements for further information regarding discontinued operations.

Net loss attributable to noncontrolling interests. The change in the net loss attributable to noncontrolling interests was due to an approximate \$17.3 million loss related to the Cornerstone Pharmaceuticals impairment loss (the total impairment loss was approximately \$79 million) which was applicable to noncontrolling interests in certain of the Company's subsidiaries and was allocated to the holders of interests in CS Pharma and Pharma Holdings in the approximate amounts of \$10.4 million and \$6.9 million, respectively, for the year ended July 31, 2022.

Liquidity and Capital Resources

	As of July 31,		Change	
	2023	2022	\$	%
	<i>(in thousands)</i>			
Balance Sheet Data:				
Cash and cash equivalents	\$ 21,498	\$ 26,537	(5,039)	(19)%
Convertible note receivable, related party . .	1,921	—	1,921	100%
Working capital	80,796	87,321	(6,525)	(7)%
Total assets	98,829	118,320	(19,491)	(16)%
Note payable, net of debt issuance costs, held-for-sale	—	15,000	(15,000)	(100)%
Total equity attributable to Rafael Holdings, Inc.	100,293	100,515	(222)	—%
Noncontrolling interests	(3,664)	(3,309)	(355)	11%
Total equity	96,629	97,206	(577)	(1)%

	For the Years Ended		Change	
	July 31,		\$	%
	2023	2022		
	<i>(in thousands)</i>			
Cash flows (used in) provided by				
Operating activities of continuing operations . . .	\$ (10,247)	\$ (26,038)	15,791	(61)%
Investing activities of continuing operations . . .	(26,960)	(63,683)	36,723	(58)%
Financing activities of continuing operations . . .	(218)	103,864	(104,082)	(100)%
Effect of exchange rates on cash and cash equivalents	(146)	(306)	160	(52)%
Operating, investing, and financing activities of discontinued operations	32,532	(154)	32,686	(21,224)%
(Decrease) increase in cash and cash equivalents	<u>\$ (5,039)</u>	<u>\$ 13,683</u>	<u>(18,722)</u>	<u>(137)%</u>

Capital Resources

As of July 31, 2023, we held cash and cash equivalents of approximately \$21.5 million, and available-for-sale securities valued at approximately \$57.7 million. On August 22, 2022, the Company received net proceeds of approximately \$33 million in connection with the sale of the 520 Property (see Note 3 to our accompanying consolidated financial statements for further details). The Company expects its balance of cash and cash equivalents, and available-for-sale securities, to be sufficient to meet our obligations for at least the 12 months from the filing of this Annual Report on Form 10-K.

Operating Activities

The decrease in cash used in operating activities for the year ended July 31, 2023 as compared to the year ended July 31, 2022 was primarily related to the lower loss from continuing operations of \$8.7 million in fiscal 2023 as compared to the corresponding period in fiscal 2022 due to an impairment of cost method investment in Cornerstone Pharmaceuticals of approximately \$79 million, a provision for loss on receivable from Cornerstone Pharmaceuticals of \$25 million, and a provision for losses on related party receivables of approximately \$10 million in fiscal 2022, coupled with the impact from non-cash items, primarily \$1.2 million in accretion of discount on available-for-sale securities, \$0.2 million in net unrealized (gain) loss on investments — Hedge Funds, \$0.2 million in realized (gain) loss on available-for-sale securities, offset by impairment of investments — other pharmaceuticals of \$0.3 million and stock-based compensation of \$2.2 million. The decrease was also impacted by a decrease in prepaid expenses and other current assets of \$0.4 million and a decrease in accounts payable and accrued expenses of \$0.8 million, as well as other changes in assets and liabilities.

Cash used in operating activities for the year ended July 31, 2022 was primarily related to the loss from continuing operations of \$140.5 million and an increase in prepaid expenses and other current assets of \$3.5 million, partially offset by the impact from noncash items included in the loss from operations, principally the impairment of the Company's cost method investment in Cornerstone Pharmaceuticals of \$79 million, the reserve on the amounts due the Company from Cornerstone Pharmaceuticals related to the Line of Credit Agreement of \$25 million, the reserve on receivables due from Cornerstone Pharmaceuticals totaling \$10.1 million, changes in other current liabilities of \$3.6 million, as well as other changes in assets and liabilities.

Investing Activities

Cash used in investing activities for the year ended July 31, 2023 was primarily due to purchases of available-for-sale securities of approximately \$204.8 million, the investment in Day Three of \$3.0 million, the purchase of investment in Cyclo of \$2.1 million, the loan of \$2.0 million to Cornerstone and the purchase of equity securities of \$1.6 million. This is partially offset by proceeds of \$185.1 million from the sale and maturities of available-for-sale securities and proceeds of \$1.3 million from the sale of equity securities.

Cash used in investing activities for the year ended July 31, 2022 was primarily related to purchases of available-for-sale securities of approximately \$65 million, amounts loaned to Cornerstone Pharmaceuticals of approximately \$25 million

pursuant to the Line of Credit Agreement and the payments to fund our portion of advances under the line of credit between RP Finance and Cornerstone Pharmaceuticals in the amount of approximately \$1.9 million, partially offset by proceeds of \$28.5 million from the maturities of available-for-sale securities.

Financing Activities

Cash used in financing activities for the year ended July 31, 2023 was primarily related to repayment of the \$15 million note payable in connection with the sale of 520 Property and for payment of taxes related to shares withheld for employee taxes on vesting of shares granted to employees.

Cash provided by financing activities for the year ended July 31, 2022 was primarily related to proceeds of approximately \$110 million related to the sale of our common stock to investors and a related party, partially offset by payment of transaction costs of \$6.2 million.

We do not anticipate paying dividends on our common stock until we achieve sustainable profitability and retain certain minimum cash reserves. The payment of dividends in any specific period will be at the sole discretion of our Board of Directors.

Operating, Financing, and Investing Activities of Discontinued Operations

The cash flows from discontinued operations — 520 Property represents the net income excluding non-cash depreciation and amortization, as well as the proceeds from the sale of the 520 Property. For the year ended July 31, 2023, net cash used in operating activities of discontinued operations totaled \$0.6 million. Net cash provided by investing activities of discontinued operations of \$48.2 million related to proceeds from sale of the 520 Property of \$49.4 million, slightly offset by payment of transaction costs of \$1.2 million. Net cash used in financing activities of discontinued operations of \$15.0 million related to the payment of the Note Payable in connection with sale of the 520 Property. For the year ended July 31, 2022, net cash used in operating activities of discontinued operations totaled \$41 thousand, and net cash used in investing activities of discontinued operations totaled \$113 thousand.

Critical Accounting Estimates

We have chosen accounting policies that we believe are appropriate to accurately and fairly report our operating results and financial condition in conformity with U.S. GAAP. We apply these accounting policies in a consistent manner. Our significant accounting policies are discussed in Note 2, “Summary of Significant Accounting Policies,” in our accompanying consolidated financial statements.

The application of critical accounting policies requires that we make estimates and assumptions that affect the reported amounts of assets, liabilities, revenues and expenses and related disclosures. These estimates and assumptions are based on historical and other factors believed to be reasonable under the circumstances. We evaluate these estimates and assumptions on an ongoing basis and may retain outside consultants to assist in our evaluation. If actual results ultimately differ from previous estimates, the revisions are included in results of operations in the period in which the actual amounts become known. The critical accounting policies that involve the most significant management judgments and estimates used in preparation of our consolidated financial statements, or are the most sensitive to change from outside factors, are discussed below.

Corporate Bonds

The Company’s marketable securities are considered to be available-for-sale as defined under ASC 320, *Investments — Debt and Equity Securities*, and are recorded at fair value based on the quoted price in active markets for similar assets and inputs that are observable for the asset. Unrealized gains or losses are included in accumulated other comprehensive income. Realized gains or losses are released from accumulated other comprehensive income and into earnings on the consolidated statements of operations and comprehensive loss.

Convertible Note Receivable, Related Party

The Convertible Note Receivable is classified as available-for-sale as defined under ASC 320, *Investments — Debt and Equity Securities*, and is recorded at fair value. Subsequent changes in fair value are recorded in accumulated other comprehensive loss.

The fair value of the Convertible Note Receivable is estimated using a scenario-based analysis based on the probability-weighted present value of future investment returns, considering each of the possible outcomes available to the Company, including cash repayment, equity conversion, and collateral transfer scenarios. Estimating the fair value of the Convertible Note Receivable requires the development of significant and subjective estimates that may, and are likely to, change over the duration of the instrument with related changes in internal and external market factors.

Stock-based Compensation

We record stock-based compensation for options granted and restricted stock units awarded to employees, non-employees, and to members of the board of directors for their services on the board of directors based on the grant date fair value of awards issued, and the expense is recorded on a straight-line basis over the requisite service period. Forfeitures are recognized when they occur.

The fair value of restricted stock units is determined by the grant date market price of our common shares. We use the Black-Scholes-Merton option pricing model to determine the fair value of stock options. The use of the Black-Scholes-Merton option pricing model requires management to make assumptions with respect to the expected term of the option, the expected volatility of the common stock consistent with the expected life of the option, risk-free interest rates and expected dividend yields of the common stock. We have concluded that its historical share option exercise experience does not provide a reasonable basis upon which to estimate expected term. Therefore, the expected term was determined according to the simplified method, which is the average of the vesting tranche dates and the contractual term. Due to the lack of Company-specific historical and implied volatility data, the estimate of expected volatility is primarily based on the historical volatility of a group of similar companies that are publicly traded. For these analyses, companies with comparable characteristics are selected, including enterprise value and position within the industry, and with historical share price information sufficient to meet the expected life of the stock-based awards. We compute the historical volatility data using the daily closing prices for the selected companies' shares during the equivalent period of the calculated expected term of its stock-based awards. The risk-free interest rate is determined by reference to U.S. Treasury zero-coupon issues with remaining maturities similar to the expected term of the options. We have not paid, and do not anticipate paying, cash dividends on shares of our common stock.

Investments — Hedge Funds

We account for our investments in hedge funds in accordance with ASC 321, *Investments — Equity Securities*. Unrealized gains and losses resulting from the change in fair value of these securities is included in unrealized (loss) gain on investments — Hedge Funds in the consolidated statements of operations and comprehensive loss. Hedge funds classified as Level 3 include investments and securities which may not be based on readily observable data inputs. The availability of observable inputs can vary from security to security and is affected by a wide variety of factors, including, for example, the type of security, whether the security is new and not yet established in the marketplace, the liquidity of markets, and other characteristics particular to the security. The fair value of these assets is estimated based on information provided by the fund managers or the general partners. Therefore, these assets are classified as Level 3.

Investments — Cost Method

We periodically evaluate our investments for impairment due to declines considered to be other than temporary. If we determine that a decline in fair value is other than temporary, then a charge to earnings is recorded in the accompanying consolidated statements of operations and comprehensive loss, and a new basis in the investment is established.

Investments — Fair Value Method

The method of accounting applied to long-term investments in equity securities involves an evaluation of the significant terms of each investment that explicitly grant or suggest evidence of control or influence over the operations of the investee and also include the identification of any variable interests in which the Company is the primary beneficiary. The consolidated financial statements include the Company's controlled affiliates. All significant intercompany accounts and transactions between the consolidated affiliates are eliminated.

Investments in equity securities may be accounted for using (i) the fair value option if elected, (ii) fair value through earnings if fair value is readily determinable or (iii) for equity investments without readily determinable fair values, the measurement alternative to measure at cost adjusted for any impairment and observable price changes, as applicable. The election to use the measurement alternative is made for each eligible investment.

The Company has elected the fair value option to account for its investment in Cyclo Therapeutics Inc. over which the Company has significant influence. The fair value option is irrevocable once elected. The Company measured its initial investment in Cyclo at fair value and shall record all subsequent changes in fair value in earnings in the consolidated statement of operations. The Company believes the fair value option best reflects the underlying economics of the investment. See Note 9, "Investments," in our accompanying consolidated financial statements for further details.

Off-Balance Sheet Arrangements

We do not have any "off-balance sheet arrangements," as defined in relevant SEC regulations, that are reasonably likely to have a current or future effect on our financial condition, results of operations, liquidity, capital expenditures or capital resources.

Discontinued Operations

In accordance with the Financial Accounting Standards Board, ASC 205-20, *Presentation of Financial Statements — Discontinued Operations*, the results of operations of a component of an entity or a group or component of an entity that represents a strategic shift that has, or will have, a major effect on the reporting company's operations that has either been disposed of or is classified as held-for-sale are required to be reported as discontinued operations in a company's consolidated financial statements. In order to be considered a discontinued operation, both the operations and cash flows of the discontinued component must have been (or will be) eliminated from the ongoing operations of the Company and the Company will not have any significant continuing involvement in the operations of the discontinued component after the disposal transaction. As a result of the agreement to sell the 520 Property, the accompanying consolidated financial statements reflect the activity related to the sale of the 520 Property as discontinued operations. See Note 3 to our consolidated financial statements for additional information regarding the results, major classes of assets and liabilities, significant non-cash operating items, and capital expenditures of discontinued operations.

Item 7A. Quantitative and Qualitative Disclosures about Market Risks

FOREIGN CURRENCY RISK

Revenue from tenants located in Israel represented 53% and 7% of our consolidated revenues, inclusive of revenue from discontinued operations, for the years ended July 31, 2023 and 2022, respectively. The entirety of these revenues is in currencies other than the U.S. Dollar. Our foreign currency exchange risk is somewhat mitigated by our ability to offset a portion of these non-U.S. Dollar-denominated revenues with operating expenses that are paid in the same currencies. While the impact from fluctuations in foreign exchange rates affects our revenues and expenses denominated in foreign currencies, the net amount of our exposure to foreign currency exchange rate changes at the end of each reporting period is generally not material.

INVESTMENT RISK

In addition to, but separate from our primary business, we will hold a portion of our assets in hedge funds and a passive investment in another entity. Investments in hedge funds carry a degree of risk and depend to a great extent on correct assessments of the future course of price movements of securities and other instruments. There can be no assurance that our investment managers will be able to accurately predict these price movements. The securities markets have in recent years been characterized by great volatility and unpredictability. Our passive interests in other entities are not currently liquid and we cannot assure that we will be able to liquidate them when we desire, or ever. Accordingly, the value of our investments may go down as well as up and we may not receive the amounts originally invested upon redemption.

Item 8. Financial Statements and Supplementary Data.

The Consolidated Financial Statements of the Company and the report of the independent registered public accounting firm thereon starting on page F-1 are included herein.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure.

None.

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

An evaluation was performed under the supervision and with the participation of the Company's management, including the Chief Executive Officer and Chief Financial Officer, of the effectiveness of the design and operation of the Company's disclosure controls and procedures (as defined in Rule 13a-15(e) promulgated under the Securities and Exchange Act of 1934, as amended) as of July 31, 2023. Based on that evaluation, the Company's management, including the President and Chief Executive Officer and Chief Financial Officer, concluded that the Company's disclosure controls and procedures were effective.

Management's Annual Report on Internal Control over Financial Reporting

The Company's management is responsible for establishing and maintaining adequate internal control over financial reporting. The internal control process has been designed under management's supervision to provide reasonable assurance regarding the reliability of financial reporting and the preparation of the Company's financial statements for external reporting purposes in accordance with U.S. GAAP.

Management conducted an assessment of the effectiveness of the Company's internal control over financial reporting as of July 31, 2023 utilizing the framework established in Internal Control — Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). Based on this assessment, management has determined that the Company's internal control over financial reporting as of July 31, 2023 is effective.

The Company's internal control over financial reporting includes policies and procedures that pertain to the maintenance of records that accurately and fairly reflect, in reasonable detail, transactions and dispositions of assets; and provide reasonable assurances that: (1) transactions are recorded as necessary to permit preparation of financial statements in accordance with U.S. GAAP; (2) receipts and expenditures are being made only in accordance with authorizations of management and the directors of the Company; and (3) unauthorized acquisition, use, or disposition of the Company's assets that could have a material effect on the Company's financial statements are prevented or timely detected.

All internal control systems, no matter how well designed, have inherent limitations. Therefore, even those systems determined to be effective can provide only reasonable assurance with respect to financial statement preparation and presentation. 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 significant changes made in the Company's internal control over financial reporting during the fourth quarter of the year ended July 31, 2023 that have materially affected, or are reasonably likely to materially affect, the Company's internal control over financial reporting.

Attestation Report of the Independent Registered Public Accounting Firm

This Annual Report on Form 10-K does not include an attestation report of our independent registered public accounting firm due to an exemption established by the JOBS Act for "emerging growth companies."

Item 9B. Other Information.

None.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections.

Not applicable.

Part III

Item 10. Directors, Executive Officers and Corporate Governance.

The following is a list of our directors and executive officers as of October 27, 2023, along with the specific information required by Rule 14a-3 of the Securities Exchange Act of 1934:

Executive Officers

Howard S. Jonas — Executive Chairman

William Conkling — Chief Executive Officer

David Polinsky — Chief Financial Officer

Directors

Howard S. Jonas — Chairman of the Board

Stephen Greenberg

Mark McCamish

Dr. Michael J. Weiss

The remaining information required by this Item will be contained in our Proxy Statement for our Annual Stockholders Meeting, which will be filed with the Securities and Exchange Commission within 120 days after July 31, 2023, and which is incorporated by reference herein.

Corporate Governance

We have included as exhibits to this Annual Report on Form 10-K certificates of our Chief Executive Officer and Chief Financial Officer certifying the quality of our public disclosure.

We make available free of charge through the investor relations page of our web site (<http://rafaelholdings.irpass.com/>) our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and all amendments to those reports, and all beneficial ownership reports on Forms 3, 4 and 5 filed by directors, officers and beneficial owners of more than 10% of our equity, as soon as reasonably practicable after such reports are electronically filed with the Securities and Exchange Commission. We have adopted codes of business conduct and ethics for all of our employees, including our principal executive officer, principal financial officer and principal accounting officer. Copies of the codes of business conduct and ethics are available on our web site.

Our web site and the information contained therein or incorporated therein are not intended to be incorporated into this Annual Report on Form 10-K or our other filings with the Securities and Exchange Commission.

Item 11. Executive Compensation.

The information required by this Item will be contained in our Proxy Statement for our Annual Stockholders Meeting, which will be filed with the Securities and Exchange Commission within 120 days after July 31, 2023, and which is incorporated by reference herein.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

The information required by this Item will be contained in our Proxy Statement for our Annual Stockholders Meeting, which will be filed with the Securities and Exchange Commission within 120 days after July 31, 2023, and which is incorporated by reference herein.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

The information required by this Item will be contained in our Proxy Statement for our Annual Stockholders Meeting, which will be filed with the Securities and Exchange Commission within 120 days after July 31, 2023, and which is incorporated by reference herein.

Item 14. Principal Accounting Fees and Services.

The information required by this Item will be contained in our Proxy Statement for our Annual Stockholders Meeting, which will be filed with the Securities and Exchange Commission within 120 days after July 31, 2023, and which is incorporated by reference herein.

Part IV

Item 15. Exhibits, Financial Statement Schedules.

(a) The following documents are filed as part of this Report:

1 Report of Independent Registered Public Accounting Firm on Consolidated Financial Statements.

Consolidated Financial Statements covered by Report of Independent Registered Public Accounting Firm.

2 Financial Statement Schedules.

All schedules have been omitted since they are either included in the Notes to Consolidated Financial Statements or not required or not applicable.

3 Exhibits. The exhibits listed in paragraph (b) of this item are filed, furnished, or incorporated by reference as part of this Form 10-K.

Certain of the agreements filed as exhibits to this Form 10-K contain representations and warranties by the parties to the agreements that have been made solely for the benefit of the parties to the agreement. These representations and warranties:

- may have been qualified by disclosures that were made to the other parties in connection with the negotiation of the agreements, which disclosures are not necessarily reflected in the agreements;
- may apply standards of materiality that differ from those of a reasonable investor; and
- were made only as of specified dates contained in the agreements and are subject to subsequent developments and changed circumstances.

Accordingly, these representations and warranties may not describe the actual state of affairs as of the date that these representations and warranties were made or at any other time. Investors should not rely on them as statements of fact.

(b) Exhibits.

Exhibit Number	Description
3.1 ⁽¹⁾	Amended and Restated Certificate of Incorporation of Rafael Holdings, Inc.
3.2 ⁽²⁾	Third Amended and Restated By-Laws of Rafael Holdings, Inc.
4.2*	Description of the Registrant's Securities Registered Pursuant to Section 12 of the Securities Exchange Act of 1934
10.1 ⁽³⁾	2021 Equity Incentive Plan, as amended and restated
10.2 ⁽²⁾	Employment Agreement dated as of June 13, 2022, between the Company and Howard S. Jonas.
10.3 ⁽⁴⁾	Letter Agreement dated January 20, 2022, between the Company and William Conkling.
10.6 ⁽⁵⁾	Securities Purchase Agreement, dated August 19, 2021, by and among Rafael Holdings, Inc. and the Investors named therein.
10.7 ⁽⁵⁾	Securities Purchase Agreement, dated August 19, 2021, by and among Rafael Holdings, Inc. and I9 Plus, LLC.
10.8 ⁽⁵⁾	Registration Rights Agreement, dated August 19, 2021, by and among Rafael Holdings, Inc. and the Investors named therein.
10.9 ⁽⁶⁾	Contract of Sale between Broad Atlantic Associates LLC and 520 Broad Street Propco LLC, dated February 18, 2022. (schedules, exhibits and similar attachments to the Contract of Sale that are not material have been omitted pursuant to Item 601(b)(2) of Regulation S-K. The Company will furnish supplementally a copy of any omitted schedule, exhibit or similar attachment to the Securities and Exchange Commission upon request).
21.01*	Subsidiaries of the Registrant
23.1*	Consent of CohnReznick LLP, Independent Registered Public Accounting Firm
31.01*	Certification of Chief Executive Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
31.02*	Certification of Chief Financial Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002

Exhibit Number	Description
32.01*	Certification of Chief Executive Officer pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
32.02*	Certification of Chief Financial Officer pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
101.INS*	Inline XBRL Instance Document
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*	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101).

* Filed or furnished herewith.

- (1) Incorporated by reference to Form 10-12G/A, filed March 26, 2018.
- (2) Incorporated by reference to Form 8-K, filed June 14, 2022.
- (3) Incorporated by reference to Exhibit A of the Company's Definitive Proxy Statement, filed with the Commission on November 28, 2022.
- (4) Incorporated by reference to Form 8-K, filed January 21, 2022.
- (5) Incorporated by reference to Form 8-K, filed August 24, 2021.
- (6) Incorporated by reference to Form 8-K, filed May 9, 2022.

Item 16. Form 10-K Summary

None.

Signatures

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this Annual Report on Form 10-K to be signed on its behalf by the undersigned, thereunto duly authorized.

Rafael Holdings, Inc.

By: /s/ William Conkling

William Conkling
Chief Executive Officer

Date: October 30, 2023

Pursuant to the requirements of the Securities Exchange Act of 1934, this Annual Report on Form 10-K has been signed by the following persons on behalf of the Registrant and in the capacities and on the dates indicated.

<u>Signature</u>	<u>Titles</u>	<u>Date</u>
<u>/s/ William Conkling</u> William Conkling	President and Chief Executive Officer (Principal Executive Officer)	October 30, 2023
<u>/s/ David Polinsky</u> David Polinsky	Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)	October 30, 2023
<u>/s/ Howard S. Jonas</u> Howard S. Jonas	Director, Chairman of the Board and Executive Chairman	October 30, 2023
<u>/s/ Stephen Greenberg</u> Stephen Greenberg	Director	October 30, 2023
<u>/s/ Mark McCamish</u> Mark McCamish	Director	October 30, 2023
<u>/s/ Michael J. Weiss</u> Dr. Michael J. Weiss	Director	October 30, 2023

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Rafael Holdings, Inc.

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Consolidated Balance Sheets as of July 31, 2023 and 2022	F-3
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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Stockholders
Rafael Holdings, Inc.

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of Rafael Holdings, Inc. as of July 31, 2023 and 2022, and the related consolidated statements of operations and comprehensive loss, equity and cash flows for the years then ended, 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 Rafael Holdings, Inc. as of July 31, 2023 and 2022, and the results of its operations and its cash flows for the years then ended, in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company’s management. Our responsibility is to express an opinion on these consolidated financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (“PCAOB”) and are required to be independent with respect to Rafael Holdings, Inc. 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. Rafael Holdings, Inc. is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company’s internal control over financial reporting. Accordingly, we express no such opinion.

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.

/s/ CohnReznick LLP

We have served as Company’s auditor since 2019.

New York, New York

October 30, 2023

PART I. FINANCIAL INFORMATION

**RAFAEL HOLDINGS, INC.
CONSOLIDATED BALANCE SHEETS
(in thousands, except share and per share data)**

	Year Ended July 31,	
	2023	2022
ASSETS		
CURRENT ASSETS		
Cash and cash equivalents	\$ 21,498	\$ 26,537
Available-for-sale securities	57,714	36,698
Interest receivable	387	140
Convertible note receivable, related party	1,921	—
Accounts receivable, net of allowance for doubtful accounts of \$245 and \$197 at July 31, 2023 and July 31, 2022, respectively	213	157
Prepaid expenses and other current assets	914	4,621
Assets held-for-sale	—	40,194
Investment in equity securities	294	—
Total current assets	<u>82,941</u>	<u>108,347</u>
Property and equipment, net.	1,695	1,770
Investments – Other Pharmaceuticals.	65	477
Investments – Hedge Funds	4,984	4,764
Investment – Day Three Labs Inc.	2,797	—
Investments – Cyclo Therapeutics Inc.	4,763	—
In-process research and development and patents	1,575	1,575
Other assets.	9	1,387
TOTAL ASSETS	<u>\$ 98,829</u>	<u>\$ 118,320</u>
LIABILITIES AND EQUITY		
CURRENT LIABILITIES		
Accounts payable	\$ 333	\$ 564
Accrued expenses	763	1,875
Other current liabilities.	1,023	3,518
Due to related parties	26	69
Note payable, net of debt issuance costs, held-for-sale	—	15,000
Total current liabilities	<u>2,145</u>	<u>21,026</u>
Other liabilities	55	88
TOTAL LIABILITIES	<u>2,200</u>	<u>21,114</u>
COMMITMENTS AND CONTINGENCIES		
EQUITY		
Class A common stock, \$0.01 par value; 35,000,000 shares authorized, 787,163 shares issued and outstanding as of July 31, 2023 and July 31, 2022, respectively.	8	8
Class B common stock, \$0.01 par value; 200,000,000 shares authorized, 23,635,709 issued and 23,490,527 outstanding as of July 31, 2023, and 23,712,449 shares issued and 23,687,964 shares outstanding as of July 31, 2022	236	237
Additional paid-in capital	264,010	262,023
Accumulated deficit	(167,333)	(165,457)
Accumulated other comprehensive loss related to unrealized loss on available-for-sale securities	(353)	(63)
Accumulated other comprehensive income related to foreign currency translation adjustment.	3,725	3,767
Total equity attributable to Rafael Holdings, Inc.	<u>100,293</u>	<u>100,515</u>
Noncontrolling interests	(3,664)	(3,309)
TOTAL EQUITY	<u>96,629</u>	<u>97,206</u>
TOTAL LIABILITIES AND EQUITY	<u>\$ 98,829</u>	<u>\$ 118,320</u>

See accompanying notes to the consolidated financial statements.

RAFAEL HOLDINGS, INC.
CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(in thousands, except share and per share data)

	Year Ended July 31,	
	2023	2022
REVENUE		
Rental – Third Party	\$ 171	\$ 179
Rental – Related Party	108	111
Other – Related Party	—	120
Total revenue	279	410
COSTS AND EXPENSES		
General and administrative	8,932	16,978
Research and development	6,312	8,742
Depreciation and amortization	78	72
Provision for loss on receivable from Cornerstone Pharmaceuticals pursuant to line of credit	—	25,000
Provision for losses on related party receivables	—	10,095
Loss from operations	(15,043)	(60,477)
Interest expense	—	(6)
Interest income	3,253	201
Impairment of investments – Other Pharmaceuticals	(334)	—
Impairment of cost method investment – Cornerstone Pharmaceuticals	—	(79,141)
Realized gain (loss) on available-for-sale securities	154	(45)
Realized gain on investment in equity securities	309	—
Unrealized gain on investment in equity securities	33	—
Unrealized gain on investments – Cyclo Therapeutics Inc.	2,663	—
Unrealized gain (loss) on investments – Hedge Funds	220	(504)
Loss from continuing operations before income taxes	(8,745)	(139,972)
Benefit from income taxes	255	—
Equity in loss of Day Three Labs Inc.	(203)	—
Equity in loss of RP Finance	—	(575)
Consolidated net loss from continuing operations	(8,693)	(140,547)
Discontinued Operations (Note 3)		
Loss from discontinued operations related to 520 Property	(306)	(1,830)
Gain on disposal of 520 Property	6,784	—
Income (loss) from discontinued operations	6,478	(1,830)
Consolidated net loss	(2,215)	(142,377)
Net loss attributable to noncontrolling interests	(339)	(17,719)
Net loss attributable to Rafael Holdings, Inc.	\$ (1,876)	\$ (124,658)
OTHER COMPREHENSIVE LOSS		
Consolidated net loss	\$ (2,215)	\$ (142,377)
Unrealized loss on available-for-sale securities	(290)	(63)
Foreign currency translation adjustment	(42)	(5)
Total comprehensive loss	(2,547)	(142,445)
Comprehensive loss attributable to noncontrolling interests	(336)	(17,746)
Total comprehensive loss attributable to Rafael Holdings, Inc.	\$ (2,211)	\$ (124,699)
Loss per share attributable to common stockholders		
Basic and diluted:		
Continuing operations	\$ (0.36)	\$ (6.22)
Discontinued operations	0.28	(0.09)
Total basic and diluted loss per share	\$ (0.08)	\$ (6.31)
Weighted average number of shares used in calculation of loss per share		
Basic and diluted	23,263,211	19,767,342

See accompanying notes to the consolidated financial statements.

RAFAEL HOLDINGS, INC.
CONSOLIDATED STATEMENTS OF EQUITY
(in thousands, except share data)

Year Ended July 31, 2023

	Common Stock, Series A		Common Stock, Series B		Additional paid-in- capital	Accumulated deficit	Accumulated other comprehensive income	Noncontrolling interests	Total Equity
	Shares	Amount	Shares	Amount					
Balance at August 1,									
2022	787,163	\$ 8	23,687,964	\$ 237	\$ 262,023	\$ (165,457)	\$ 3,704	\$ (3,309)	\$ 97,206
Net loss for the year ended July 31,									
2023	—	—	—	—	—	(1,876)	—	(339)	(2,215)
Stock-based compensation	—	—	220,019	2	3,089	—	—	—	3,091
Forfeiture of restricted stock	—	—	(296,759)	(2)	(901)	—	—	—	(903)
Shares withheld for payroll taxes	—	—	(120,697)	(1)	(217)	—	—	—	(218)
Unrealized loss on available-for-sale securities	—	—	—	—	—	—	(290)	—	(290)
Acquisition of additional ownership interest in LipoMedix	—	—	—	—	16	—	—	(16)	—
Foreign currency translation adjustment	—	—	—	—	—	—	(42)	—	(42)
Balance at July 31,									
2023	<u>787,163</u>	<u>\$ 8</u>	<u>23,490,527</u>	<u>\$ 236</u>	<u>\$ 264,010</u>	<u>\$ (167,333)</u>	<u>\$ 3,372</u>	<u>\$ (3,664)</u>	<u>\$ 96,629</u>

See accompanying notes to the consolidated financial statements.

RAFAEL HOLDINGS, INC.
CONSOLIDATED STATEMENTS OF EQUITY
(in thousands, except share data)

Year Ended July 31, 2022

	Common Stock, Series A		Common Stock, Series B		Additional paid-in- capital	Accumulated deficit	Accumulated other comprehensive income	Noncontrolling interests	Total Equity
	Shares	Amount	Shares	Amount					
Balance at August 1,									
2021	787,163	\$ 8	16,936,864	\$ 169	\$ 159,136	\$ (40,799)	\$ 3,772	\$ 14,418	\$ 136,704
Net loss for the year ended July 31,									
2022	—	—	—	—	—	(124,658)	—	(17,719)	(142,377)
Stock-based compensation	—	—	1,533,311	16	18,045	—	—	—	18,061
Forfeiture of restricted stock	—	—	(943,305)	(9)	(18,969)	—	—	—	(18,978)
Common stock sold to investors	—	—	2,833,425	28	99,142	—	—	—	99,170
Transaction costs incurred in connection with sale of common stock ...	—	—	—	—	(6,228)	—	—	—	(6,228)
Common stock sold to related party	—	—	3,338,307	33	10,964	—	—	—	10,997
Acquisition of additional ownership interest in LipoMedix	—	—	—	—	8	—	—	(8)	—
Shares withheld for payroll taxes	—	—	(10,638)	—	(75)	—	—	—	(75)
Unrealized loss on available-for-sale securities.	—	—	—	—	—	—	(63)	—	(63)
Foreign currency translation adjustment	—	—	—	—	—	—	(5)	—	(5)
Balance at July 31,									
2022	787,163	\$ 8	23,687,964	\$ 237	\$ 262,023	\$ (165,457)	\$ 3,704	\$ (3,309)	\$ 97,206

See accompanying notes to the consolidated financial statements.

RAFAEL HOLDINGS, INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(in thousands)

	<u>Year Ended July 31,</u>	
	<u>2023</u>	<u>2022</u>
Operating activities		
Consolidated net loss	\$ (2,215)	\$ (142,377)
Less: Income (loss) from discontinued operations	6,478	(1,830)
Loss from continuing operations	(8,693)	(140,547)
Adjustments to reconcile consolidated net loss to net cash used in operating activities		
Depreciation and amortization	78	72
Net unrealized (gain) loss on investments – Hedge Funds	(220)	504
Unrealized gain on equity securities	(33)	—
Unrealized gain in equity investments – Cyclo Therapeutics Inc.	(2,663)	—
Realized (gain) loss on available-for-sale securities	(154)	45
Amortization of discount on available-for-sale securities	(1,195)	—
Impairment of investments – Other Pharmaceuticals	334	—
Impairment of cost method investment – Cornerstone Pharmaceuticals	—	79,141
Provision for loss on receivable from Cornerstone Pharmaceuticals pursuant to line of credit	—	25,000
Equity in loss of RP Finance	—	575
Equity in loss of Day Three Labs Inc.	203	—
Provision for losses on related party receivables	—	10,095
Provision for doubtful accounts	—	4
Stock-based compensation, net	2,188	(917)
Change in assets and liabilities, net of effects from discontinued operations:		
Trade accounts receivable	(117)	74
Interest receivable	(247)	(140)
Prepaid expenses and other current assets	373	(3,545)
Other assets	(27)	130
Accounts payable and accrued expenses	(827)	52
Other current liabilities	781	3,566
Due to related parties	(43)	(67)
Due from Cornerstone Pharmaceuticals	—	(120)
Other liabilities	15	40
Net cash used in continuing operations	(10,247)	(26,038)
Net cash used in discontinued operations	(639)	(41)
Net cash used in operating activities	(10,886)	(26,079)
Investing activities		
Payment to Cornerstone Pharmaceuticals pursuant to Line of Credit	—	(25,000)
Purchases of property and equipment	—	(2)
Payment to fund RP Finance Line of Credit	—	(1,875)
Purchases of available-for-sale securities	(204,798)	(65,306)
Proceeds from the sale and maturities of available-for-sale securities	185,121	28,500
Issuance of convertible note receivable, related party	(2,000)	—
Proceeds from investments – Other Pharmaceuticals	78	—
Purchases of equity securities	(1,586)	—
Proceeds from sales of equity securities	1,325	—

RAFAEL HOLDINGS, INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS — (Continued)
(in thousands)

	Year Ended July 31,	
	2023	2022
Purchase of Investment in Day Three Labs Inc.	(3,000)	—
Purchase of Investment in Cyclo Therapeutics Inc.	(2,100)	—
Net cash used in investing activities of continuing operations	(26,960)	(63,683)
Net cash provided by (used in) investing activities of discontinued operations . . .	48,171	(113)
Net cash provided by (used in) investing activities.	<u>21,211</u>	<u>(63,796)</u>
Financing activities		
Proceeds from issuance of common stock	—	99,170
Proceeds from issuance of common stock from related party	—	10,997
Payment of transaction costs incurred in connection with sale of common stock.	—	(6,228)
Payments for taxes related to shares withheld for employee taxes	(218)	(75)
Net cash (used in) provided by continuing operations	(218)	103,864
Net cash used in financing activities of discontinued operations	(15,000)	—
Net cash (used in) provided by financing activities	<u>(15,218)</u>	<u>103,864</u>
Effect of exchange rate changes on cash and cash equivalents.	(146)	(306)
Net (decrease) increase in cash and cash equivalents.	(5,039)	13,683
Cash and cash equivalents, beginning of year.	26,537	12,854
Cash and cash equivalents, end of year.	<u>\$ 21,498</u>	<u>\$ 26,537</u>
Non-cash supplemental disclosure		
Acquisition of additional ownership interest in LipoMedix.	<u>\$ 16</u>	<u>\$ 8</u>

See accompanying notes to the consolidated financial statements.

RAFAEL HOLDINGS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

NOTE 1 — DESCRIPTION OF BUSINESS

Description of Business

Rafael Holdings, Inc. (NYSE:RFL), (“Rafael Holdings”, “we” or the “Company”), a Delaware corporation, is a holding company with interests in clinical and early-stage pharmaceutical companies (the “Pharmaceutical Companies”), including an investment in Cornerstone Pharmaceuticals, Inc. (“Cornerstone”), formerly known as Rafael Pharmaceuticals Inc., a cancer metabolism-based therapeutics company, a majority equity interest in LipoMedix Pharmaceuticals Ltd. (“LipoMedix”), a clinical stage pharmaceutical company, the Barer Institute Inc. (“Barer”), a wholly-owned preclinical cancer metabolism research operation, an investment in Cyclo Therapeutics Inc. (Nasdaq: CYTH), (“Cyclo Therapeutics” or “Cyclo”), a clinical-stage biotechnology company dedicated to developing life-changing medicines for patients and families living with challenging diseases through its lead therapeutic asset, Trappsol[®] Cyclo[™], an investment in Day Three Labs, Inc. (“Day Three”), a company which reimagines existing cannabis offerings with pharmaceutical-grade technology and innovation like Unlokt[™] to bring to market better, cleaner, more precise and predictable products in the cannabis industry, and a majority interest in Rafael Medical Devices, LLC, an orthopedic-focused medical device company developing instruments to advance minimally invasive surgeries (“Rafael Medical Devices” and Day Three Labs together with the Pharmaceutical Companies, represent our “Investment Companies”). In November 2022, the Company resolved to curtail its early-stage development efforts, including pre-clinical research at Barer. The decision was taken to reduce spending as the Company focuses on exploring strategic opportunities. The Company’s primary focus is to expand our investment portfolio through opportunistic and strategic investments including therapeutics which address high unmet medical needs.

Historically, the Company owned multiple real estate assets. In 2020, the Company sold an office building located in Piscataway, New Jersey and, on August 22, 2022, the Company sold the building at 520 Broad Street in Newark, New Jersey that serves as headquarters for the Company and several tenants and an associated public garage (the “520 Property”). See Note 3 for further details on the sale transaction. Currently, the Company holds a portion of a commercial building in Jerusalem, Israel as its remaining real estate asset.

The Company holds debt and equity investments in Cornerstone Pharmaceuticals that includes preferred and common equity interests and a warrant to purchase additional equity. On June 17, 2021, the Company entered into a merger agreement to acquire full ownership of Cornerstone Pharmaceuticals in exchange for issuing Company Class B common stock to the other stockholders of Cornerstone Pharmaceuticals (“Merger Agreement” or “Merger”). On October 28, 2021, the Company announced that the AVENGER 500 Phase 3 clinical trial for CPI-613[®] (devimistat), Cornerstone Pharmaceuticals’ lead product candidate, did not meet its primary endpoint of significant improvement in overall survival in patients with metastatic adenocarcinoma of the pancreas. In addition, following a pre-specified interim analysis, the independent data monitoring committee for the ARMADA 2000 Phase 3 study for devimistat recommended the trial to be stopped due to a determination that it was unlikely to achieve the primary endpoint (the “Data Events”). In connection with the preparation of the Company’s financial statements for the first quarter ended October 31, 2021, accounting principles generally accepted in the United States of America (“U.S. GAAP”) required that the Company assess the impact of the Data Events and determine whether the carrying values of the Company’s assets were impaired based upon the Company’s expectations to realize future value. In light of the Data Events, the Company concluded that the likelihood of further development of and prospects for CPI-613 is uncertain and fully impaired in the first quarter ended October 31, 2021 the value of its loans, receivables, and investment in Cornerstone Pharmaceuticals based upon its valuation of Cornerstone Pharmaceuticals. On February 2, 2022, the Company terminated the Merger Agreement with Cornerstone Pharmaceuticals, effective immediately, in accordance with its terms. Subsequently, on February 2, 2022, the Company withdrew its Registration Statement on Form S-4 related to the proposed Merger. On March 21, 2023, the Company loaned \$2.0 million to Cornerstone which debt is represented by a Promissory Note made by Cornerstone (the “Promissory Note” or “Note”).

RAFAEL HOLDINGS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

NOTE 1 — DESCRIPTION OF BUSINESS (cont.)

Cornerstone is in the process of a comprehensive restructuring transaction including, the conversion of the debt under the Line of Credit Agreement and the Promissory Note held by the Company, the conversion and modification of other Cornerstone debt obligations, the extension of the Cornerstone debt held by RP Finance, a reverse stock split, the conversion of all outstanding preferred stock of Cornerstone into common stock and the adoption of certain governance measures. This transaction is subject to a number of conditions which are beyond the Company's control.

In May 2023, the Company invested in Cyclo Therapeutics. Cyclo is a clinical stage biotechnology company that develops cyclodextrin-based products for the treatment of neurodegenerative diseases. Cyclo's lead drug candidate is Trappsol® Cyclo™ (hydroxypropyl beta cyclodextrin), a treatment for Niemann-Pick Type C disease ("NPC"). NPC is a rare and fatal autosomal recessive genetic disease resulting in disrupted cholesterol metabolism that impacts the brain, lungs, liver, spleen, and other organs. In January 2017, the FDA granted Fast Track designation to Trappsol® Cyclo™ for the treatment of NPC. Initial patient enrollment in the U.S. Phase I study commenced in September 2017, and in May 2020 Cyclo announced Top Line data showing a favorable safety and tolerability profile for Trappsol® Cyclo™ in this study. Cyclo is currently conducting a Phase 3 Clinical Trial Evaluating Trappsol® Cyclo™ in Pediatric and Adult Patients with Niemann-Pick Disease Type C1.

In 2019, the Company established Barer, a preclinical cancer metabolism research operation, to focus on developing a pipeline of novel therapeutic compounds, including compounds to regulate cancer metabolism with potentially broader application in other indications beyond cancer. Barer has been comprised of scientists and academic advisors that are experts in cancer metabolism, chemistry, and drug development. In addition to its own internal discovery efforts, Barer pursued collaborative research agreements and in-licensing opportunities with leading scientists from top academic institutions. Barer's subsidiary, Farber Partners, LLC ("Farber"), was formed around one such agreement with Princeton University's Office of Technology Licensing for technology from the laboratory of Professor Joshua Rabinowitz, in the Department of Chemistry, Princeton University, for an exclusive worldwide license to its SHMT (serine hydroxymethyltransferase) inhibitor program. In November 2022, the Company resolved to curtail its early-stage development efforts, including pre-clinical research at the Barer Institute.

In 2016, the Company first invested in LipoMedix, a clinical stage pharmaceutical company and holds a majority of the common stock.

In April 2023, the Company invested in Day Three Labs, the majority-owner of Day three Labs Manufacturing, a company which reimagines existing cannabis offerings with pharmaceutical-grade technology and innovation like Unlokt™ to bring to market better, cleaner, more precise and predictable products in the cannabis industry.

In May 2021, the Company formed Rafael Medical Devices, an orthopedic-focused medical device company developing instruments to advance minimally invasive surgeries. In August 2023, the Company raised \$925,000 from third parties in exchange for 31.62% ownership of Rafael Medical Devices.

The Company also holds a 95% investment in LipoMedix, a development-stage, privately held Israeli company focused on the development of an innovative, safe and effective cancer therapy based on liposome delivery.

The "Company" in these consolidated financial statements refers to Rafael Holdings and its subsidiaries on a consolidated basis.

RAFAEL HOLDINGS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

NOTE 1 — DESCRIPTION OF BUSINESS (cont.)

All majority-owned subsidiaries are consolidated with all intercompany transactions and balances eliminated in consolidation. In addition to Rafael Holdings, Inc., the subsidiaries included in these consolidated financial statements are as follows:

<u>Company</u>	<u>Country of Incorporation</u>	<u>Percentage Owned</u>
Broad Atlantic Associates, LLC	United States – Delaware	100%
IDT R.E. Holdings Ltd..	Israel	100%
Rafael Holdings Realty, Inc.	United States – Delaware	100%
Barer Institute, Inc.	United States – Delaware	100%*
The Barer Institute, LLC	United States – Delaware	100%*
Hillview Avenue Realty, JV	United States – Delaware	100%
Hillview Avenue Realty, LLC	United States – Delaware	100%
Rafael Medical Devices, Inc.	United States – Delaware	100%
Levco Pharmaceuticals Ltd.	Israel	95%***
Farber Partners, LLC.	United States – Delaware	93%
Pharma Holdings, LLC	United States – Delaware	90%
LipoMedix Pharmaceuticals Ltd.	Israel	95%****
Altira Capital & Consulting, LLC	United States – Delaware	67%
CS Pharma Holdings, LLC	United States – Delaware	45%**

* In November 2022, the Company resolved to curtail its early-stage development efforts, including pre-clinical research at Barer. The decision was taken to reduce spending as the Company focuses on exploring strategic opportunities.

** 50% of CS Pharma Holdings, LLC is owned by Pharma Holdings, LLC. We have a 90% ownership in Pharma Holdings, LLC and, therefore, an effective 45% interest in CS Pharma Holdings, LLC. The Company, along with CS Pharma and Pharma Holdings, collectively own securities representing 51% of the outstanding capital stock of Cornerstone Pharmaceuticals and 42% of the capital stock on a fully diluted basis (excluding the remainder of the Warrant). Refer to Note 4 for further details.

*** During Fiscal 2022, the Company discontinued further material investment in Levco.

**** On February 9, 2023, the Company increased its ownership interest in LipoMedix Pharmaceuticals Ltd. an additional 11% from 84% to 95%.

On March 15, 2022, the Company dissolved IDT 225 Old NB Road, LLC.

NOTE 2 — SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Basis of Presentation

The Company's fiscal year ends on July 31 of each calendar year. Each reference below to a fiscal year refers to the fiscal year ending in the calendar year indicated (e.g., fiscal year 2023 refers to the fiscal year ended July 31, 2023).

The accompanying consolidated financial statements of the Company and its subsidiaries have been prepared in accordance with U.S. GAAP. The accompanying consolidated financial statements reflect the activity related to the 520 Property as discontinued operations.

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the balance sheet and the reported amounts of revenue and expenses during the reporting periods. Actual results could differ significantly from those estimates.

RAFAEL HOLDINGS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

NOTE 2 — SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES (cont.)

Liquidity

As of July 31, 2023, the Company had cash and cash equivalents of approximately \$21.5 million, and available-for-sale securities valued at approximately \$57.7 million. On August 22, 2022, the Company received net proceeds of approximately \$33 million in connection with the sale of the 520 Property (see Note 3 for further details). The Company expects the balance of cash and cash equivalents, and available-for-sale securities to be sufficient to meet its obligations for at least the next 12 months from the issuance of these consolidated financial statements.

Concentration of Credit Risk and Significant Customers

The Company routinely assesses the financial strength of its customers. As a result, the Company believes that its accounts receivable credit risk exposure is limited. For the year ended July 31, 2023, including revenue from discontinued operations, related parties represented 42% of the Company's revenue. As of July 31, 2023, there were two customers which represented 27% and 47% of the Company's accounts receivable balance. For the year ended July 31, 2022, including revenue from discontinued operations, related parties represented 58% of the Company's revenue, and as of July 31, 2022, two customers, one of which is a related party, represented 24% and 47% of the Company's accounts receivable balance, respectively.

Cash and Cash Equivalents

The Company considers all liquid investments with an original maturity of three months or less when purchased to be cash equivalents.

Reserve for Receivables

The Company evaluates accounts receivable, loans, interest and fees receivable for impairment under Accounting Standards Codification ("ASC") 310, *Receivables*. The Company also evaluates the reserve for losses and estimates collectability of accounts receivable, loans, interest and fees receivable based on historical bad debt experience, management's assessment of the financial condition of individual companies with which the Company conducts business, current market conditions, and reasonable and supportable forecasts of future economic conditions.

The allowance for doubtful accounts reflects the Company's best estimate of probable losses inherent in the accounts receivable balance. The allowance is determined based on known troubled accounts, historical experience and other currently available evidence. Doubtful accounts are written off upon final determination that the trade accounts will not be collected. The computation of this allowance is based on the tenants' or parking customers' payment histories, as well as certain industry or geographic specific credit considerations. If the Company's estimates of collectability differ from the cash received, then the timing and amount of the Company's reported revenue could be impacted. The credit risk is mitigated by the high quality of the Company's existing tenant base, inclusive of related parties, which represented 42% and 58% of the Company's total revenue for the years ended July 31, 2023 and 2022, respectively. The Company recorded bad debt expense of approximately \$110 thousand and \$4 thousand for the years ended July 31, 2023 and 2022, respectively.

Convertible Note Receivable, Related Party

The Convertible Note Receivable is classified as available-for-sale as defined under ASC 320, *Investments — Debt and Equity Securities*, and is recorded at fair value. Subsequent changes in fair value are recorded in accumulated other comprehensive loss.

The fair value of the Convertible Note Receivable is estimated using a scenario-based analysis based on the probability-weighted present value of future investment returns, considering each of the possible outcomes available to the Company, including cash repayment, equity conversion, and collateral transfer scenarios. Estimating the fair value of the convertible note requires the development of significant and subjective estimates that may, and are likely to, change over the duration of the instrument with related changes in internal and external market factors.

RAFAEL HOLDINGS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

NOTE 2 — SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES (cont.)

Variable Interest Entities

In accordance with ASC 810, *Consolidation*, the Company assesses whether it has a variable interest in legal entities in which it has a financial relationship and, if so, whether or not those entities are variable interest entities (“VIEs”). For those entities that qualify as VIEs, ASC 810 requires the Company to determine if the Company is the primary beneficiary of the VIE, and if so, to consolidate the VIE.

If an entity is determined to be a VIE, the Company evaluates whether the Company is the primary beneficiary. The primary beneficiary analysis is a qualitative analysis based on power and economics. The Company consolidates a VIE if both power and benefits belong to the Company — that is, the Company (i) has the power to direct the activities of a VIE that most significantly influence the VIE’s economic performance (power), and (ii) has the obligation to absorb losses of, or the right to receive benefits from, the VIE that could potentially be significant to the VIE (benefits). The Company consolidates VIEs whenever it is determined that the Company is the primary beneficiary.

Investments

The method of accounting applied to long-term investments in equity securities involves an evaluation of the significant terms of each investment that explicitly grant or suggest evidence of control or influence over the operations of the investee and also include the identification of any variable interests in which the Company is the primary beneficiary. The consolidated financial statements include the Company’s controlled affiliates. All significant intercompany accounts and transactions between the consolidated affiliates are eliminated.

Investments in equity securities may be accounted for using (i) the fair value option if elected, (ii) fair value through earnings if fair value is readily determinable or (iii) for equity investments without readily determinable fair values, the measurement alternative to measure at cost adjusted for any impairment and observable price changes, as applicable. The election to use the measurement alternative is made for each eligible investment.

The Company has elected the fair value option to account for its investment in Cyclo Therapeutics Inc. over which the Company has significant influence. The fair value option is irrevocable once elected. The Company measured its initial investment in Cyclo at fair value and shall record all subsequent changes in fair value in earnings in the consolidated statement of operations. The Company believes the fair value option best reflects the underlying economics of the investment. See Note 9, “Investments.”

Investments in which the Company does not have the ability to exercise significant influence over operating and financial matters are accounted for in accordance with ASC 321, *Investments — Equity Securities*. Investments without readily determinable fair values are accounted for using the measurement alternative which is at cost minus impairment, if any, plus or minus changes resulting from observable price changes in orderly transactions for the identical or a similar investment of the same issuer. The Company periodically evaluates its investments for impairment due to declines considered to be other than temporary. If the Company determines that a decline in fair value is other than temporary, then a charge to earnings is recorded in the accompanying consolidated statements of operations and comprehensive loss, and a new basis in the investment is established.

Investments — Hedge Funds

The Company accounts for its investments in hedge funds in accordance with ASC 321, *Investments — Equity Securities*. Unrealized gains and losses resulting from the change in fair value of these securities is included in unrealized (loss) gain on investments — Hedge Funds in the consolidated statements of operations and comprehensive loss.

Corporate Bonds and US Treasury Bills

The Company’s marketable securities are considered to be available-for-sale as defined under ASC 320, *Investments — Debt and Equity Securities*, and are recorded at fair value. Unrealized gains or losses are included in accumulated other comprehensive loss. Realized gains or losses are released from accumulated other comprehensive loss and into earnings on the consolidated statements of operations and comprehensive loss.

RAFAEL HOLDINGS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

NOTE 2 — SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES (cont.)

Cost Method Investment

The Company has determined that Cornerstone Pharmaceuticals (see Note 4) is a VIE; however, the Company has determined that it is not the primary beneficiary as the Company does not have the power to direct the activities of Cornerstone Pharmaceuticals that most significantly impact Cornerstone Pharmaceuticals' economic performance.

Equity Method Investments

The Company has determined that each of RP Finance, LLC ("RP Finance") and Day Three Labs, Inc. ("Day Three", RP Finance and Day Three, collectively, the "Equity Method Investees" and the Company's investments in RP Finance and Day Three, collectively, the "Equity Method Investments"), (see Note 6 and Note 8), are each a VIE; however, the Company has determined that it is not the primary beneficiary as the Company does not have the power to direct the activities of the Equity Method Investees that most significantly impact the Equity Method Investees' economic performance and, therefore, is not required to consolidate the Equity Method Investees. The Company accounts for the Equity Method Investments using the equity method of accounting.

Long-Lived Assets

Equipment, buildings, leasehold improvements, and furniture and fixtures are recorded at cost and are depreciated on a straight-line basis over their estimated useful lives, which range as follows:

Classification	Years
Building and improvements	40
Tenant improvements	7 – 15
Other (primarily equipment and furniture and fixtures)	5

Properties

On August 22, 2022, Broad Atlantic Associates LLC, a wholly-owned subsidiary of the Company ("Broad Atlantic"), completed the sale of the 520 Property for a purchase price of \$49.4 million. The 520 Property served as the Company's headquarters and had several other tenants, and a related 800-car public parking garage. The Company determined that the 520 Property met the held-for-sale and discontinued operations criteria as of July 1, 2022. The 520 Property was disposed of on August 22, 2022.

The Company owns a portion of the 6th floor of a building located at 5 Shlomo Halevi Street, in Jerusalem, Israel.

Impairment of Long-Lived Assets

The Company assesses the recoverability of long-lived assets, which include property and equipment and in-process research and development and patents whenever significant events or changes in circumstances indicate that its carrying amount may not be recoverable. If indicators of impairment exist, projected future undiscounted cash flows associated with the asset are compared to its carrying amount to determine whether the asset's carrying value is recoverable. Any resulting impairment is recorded as a reduction in the carrying value of the related asset in excess of fair value and a change to operating results. For the years ended July 31, 2023 and 2022, the Company determined that there was no impairment of its long-lived assets.

Assets Held-for-Sale and Discontinued Operations

The Company classifies assets as held-for-sale if all held-for-sale criteria are met pursuant to ASC 360-10, *Property, Plant and Equipment*. Criteria include management commitment to sell the disposal group in its present condition and the sale being deemed probable of being completed within one year. Assets classified as held-for-sale are not depreciated and are measured at the lower of their carrying amount or fair value less cost to sell. The Company assesses

RAFAEL HOLDINGS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

NOTE 2 — SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES (cont.)

the fair value of a disposal group, less any costs to sell, each reporting period it remains classified as held-for-sale and reports any subsequent changes as an adjustment to the carrying value of the disposal group, as long as the new carrying value does not exceed the initial carrying value of the disposal group.

Strategic changes in the Company's operations can be considered a discontinued operation if both the operations and cash flows of the discontinued component have been (or will be) eliminated from the ongoing operations of the Company and the Company will not have any significant continuing involvement in the operations of the discontinued component after the disposal transaction. The results of the discontinued operations shall be reflected as a discontinued operation on the consolidated statements of operations and comprehensive loss and prior periods shall be recast to reflect the earnings from discontinued operations. As a result of the agreement to sell the 520 Property, the accompanying consolidated financial statements reflect the activity related to the sale of the 520 Property as discontinued operations. The Company determined that the 520 Property met the held-for-sale and discontinued operations criteria as of July 1, 2022. The 520 Property was disposed of on August 22, 2022. See Note 3 for additional information regarding the results, major classes of assets and liabilities, significant non-cash operating items, and capital expenditures of discontinued operations.

Debt Issuance Costs

Debt issuance costs are recorded net against the related debt and amortized to interest expense over the life of the related debt. During the years ended July 31, 2023 and 2022, amortized debt issuance costs of \$0 and \$472 thousand, respectively, were recorded as a component of interest expense which is included in Discontinued Operations.

Revenue Recognition

The Company applies the five-step approach as described in ASC 606, *Revenue from Contracts with Customers*, which consists of the following: (i) identifying the contract with a customer, (ii) identifying the performance obligations in the contract, (iii) determining the transaction price, (iv) allocating the transaction price to the performance obligations in the contract and (v) recognizing revenue when (or as) the entity satisfies a performance obligation.

The Company disaggregates its revenue by source within its consolidated statements of operations and comprehensive loss. As an owner and operator of real estate, the Company derives the majority of its revenue from leasing office and parking space to tenants at its properties. In addition, the Company earns revenue from recoveries from tenants, consisting of amounts due from tenants for common area maintenance, real estate taxes and other recoverable costs. Revenue from recoveries from tenants is recorded together with rental income on the consolidated statements of operations and comprehensive loss which is also consistent with the guidance under ASC 842, *Leases*.

The revenue derived from the 520 Property, which included leasing office and parking space to the tenants, is presented within discontinued operations in the consolidated statements of operations and comprehensive loss.

Contractual rental revenue is reported on a straight-line basis over the terms of the respective leases. Accrued rental income, included within other assets on the consolidated balance sheets, represents cumulative rental income earned in excess of rent payments received pursuant to the terms of the individual lease agreements.

The Company also earned revenue from parking which was derived primarily from monthly and transient daily parking. The monthly and transient daily parking revenue falls within the scope of ASC 606 and was accounted for at the point in time when control of the goods or services transfers to the customer and the Company's performance obligation is satisfied, consistent with the Company's previous accounting.

The Company maintains an allowance for doubtful accounts for estimated losses resulting from the inability of tenants to make required rent payments or parking customers to pay amounts due.

RAFAEL HOLDINGS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

NOTE 2 — SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES (cont.)

Research and Development Costs

Research and development costs and expenses incurred by consolidated entities consist primarily of salaries and related personnel expenses, stock-based compensation, fees paid to external service providers, laboratory supplies, costs for facilities and equipment, license costs, and other costs for research and development activities. Research and development expenses are recorded in operating expenses in the period in which they are incurred. Estimates have been used in determining the liability for certain costs where services have been performed but not yet invoiced. The Company monitors levels of performance under each significant contract for external service providers, including the extent of patient enrollment and other activities through communications with the service providers to reflect the actual amount expended.

Contingent milestone payments associated with acquiring rights to intellectual property are recognized when probable and estimable. These amounts are expensed to research and development when there is no alternative future use associated with the intellectual property.

Repairs and Maintenance

The Company charges the cost of repairs and maintenance, including the cost of replacing minor items not constituting substantial betterment, to selling, general and administrative expenses as these costs are incurred.

Stock-Based Compensation

The Company accounts for stock-based compensation using the provisions of ASC 718, *Stock-Based Compensation*, which requires the recognition of the fair value of stock-based compensation. Stock-based compensation is estimated at the grant date based on the fair value of the awards. The Company accounts for forfeitures of grants as they occur. Compensation cost for awards is recognized using the straight-line method over the vesting period. Stock-based compensation is included in general and administrative expense and research and development expense in the consolidated statements of operations and comprehensive loss.

Income Taxes

The Company recognizes deferred tax assets and liabilities for the future tax consequences attributable to temporary differences between the financial statements carrying amounts of existing assets and liabilities and their respective tax bases. A valuation allowance is provided when it is more likely than not that some portion or all of a deferred tax asset will not be realized. The ultimate realization of deferred tax assets depends on the generation of future taxable income during the period in which related temporary differences become deductible. The Company considers the scheduled reversal of deferred tax liabilities, projected future taxable income and tax planning strategies in its assessment of a valuation allowance. Deferred tax assets and liabilities are measured using the enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in income in the period that includes the enactment date of such change.

The Company uses a two-step approach for recognizing and measuring tax benefits taken or expected to be taken in a tax return. The Company determines whether it is more-likely-than-not that a tax position will be sustained upon examination, including resolution of any related appeals or litigation processes, based on the technical merits of the position. In evaluating whether a tax position has met the more-likely-than-not recognition threshold, the Company presumes that the position will be examined by the appropriate taxing authority that has full knowledge of all relevant information. Tax positions that meet the more-likely-than-not recognition threshold are measured to determine the amount of tax benefit to recognize in the financial statements. The tax position is measured at the largest amount of benefit that is greater than 50% likely of being realized upon ultimate settlement. Differences between tax positions taken in a tax return and amounts recognized in the financial statements will generally result in one or more of the following: an increase in a liability for income taxes payable, a reduction of an income tax refund receivable, a reduction in a deferred tax asset, or an increase in a deferred tax liability.

The Company classifies interest and penalties on income taxes as a component of income tax expense, if any.

RAFAEL HOLDINGS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

NOTE 2 — SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES (cont.)

Contingencies

The Company accrues for loss contingencies when both (a) information available prior to issuance of the financial statements indicates that it is probable that a liability had been incurred at the date of the financial statements and (b) the amount of loss can reasonably be estimated. When the Company accrues for loss contingencies and the reasonable estimate of the loss is within a range, the Company records its best estimate within the range. When no amount within the range is a better estimate than any other amount, the Company accrues the minimum amount in the range. The Company discloses an estimated possible loss or a range of loss when it is at least reasonably possible that a loss may have been incurred.

Leases

The Company categorizes leases at their inception as either operating or finance leases. On certain lease agreements, the Company may receive rent holidays and other incentives. The Company recognizes lease costs on a straight-line basis without regard to deferred payment terms, such as rent holidays, that defer the commencement date of required payments. As of July 31, 2023 and 2022, the Company was not a lessee under any leasing arrangements.

Fair Value Measurements

Fair value of financial and non-financial assets and liabilities is defined as an exit price, which is 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. The three-tier hierarchy for inputs used to measure fair value, which prioritizes the inputs to valuation techniques used to measure fair value, is as follows:

- Level 1 — quoted prices in active markets for identical assets or liabilities;
- Level 2 — quoted prices in active markets for similar assets and liabilities and inputs that are observable for the asset or liability; or
- Level 3 — unobservable inputs for the asset or liability, such as discounted cash flow models or valuations.

A financial asset's or liability's classification within the hierarchy is determined based on the lowest level input that is significant to the fair value measurement. The assessment of the significance of a particular input to the fair value measurement requires judgment and may affect the valuation of the assets and liabilities being measured and their placement within the fair value hierarchy.

Functional Currency

The U.S. Dollar is the functional currency of our entities operating in the United States. The functional currency for our subsidiaries operating outside of the United States is the New Israeli Shekel, the currency of the primary economic environment in which such subsidiaries primarily expend cash. The Company translates those subsidiaries' financial statements into U.S. Dollars. The Company translates assets and liabilities at the exchange rate in effect as of the consolidated financial statement date, and translates accounts from the consolidated statements of operations and comprehensive loss using the weighted average exchange rate for the period. The Company reports gains and losses from currency exchange rate changes related to intercompany receivables and payables, currently in non-operating expenses.

Loss Per Share

Basic loss per share is computed by dividing net loss attributable to all classes of common stockholders of the Company by the weighted average number of shares of all classes of common stock outstanding during the applicable period. Diluted loss per share is determined in the same manner as basic loss per share, except that the number of shares is increased to include restricted stock still subject to risk of forfeiture and to assume exercise of potentially dilutive stock options using the treasury stock method, unless the effect of such increase would be anti-dilutive.

RAFAEL HOLDINGS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

NOTE 2 — SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES (cont.)

The Company uses income from continuing operations as the “control number” or benchmark to determine whether potential common shares are dilutive or anti-dilutive for purposes of reporting earnings (loss) per share for discontinued operations.

Recently Issued Accounting Standards Not Yet Adopted

From time to time, new accounting pronouncements are issued by the Financial Accounting Standards Board (“FASB”) or other standard setting bodies and are adopted by the Company as of the specified effective date. The Company believes that the impact of recently issued standards that are not yet effective will not have a material impact on its financial position or results of operations upon adoption.

In June 2016, the FASB issued Accounting Standards Update (“ASU”) 2016-13, *Financial Instruments — Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments*, which changes the impairment model for most financial assets and certain other instruments. For receivables, loans and other instruments, entities will be required to use a new forward-looking “expected loss” model that generally will result in the earlier recognition of allowance for losses. For available-for-sale debt securities with unrealized losses, entities will measure credit losses in a manner similar to current practice, except the losses will be recognized as allowances instead of reductions in the amortized cost of the securities. In addition, an entity will have to disclose significantly more information about allowances, credit quality indicators and past due securities. The new standard is effective for fiscal years beginning after December 15, 2022, including interim periods within those fiscal years, and will be applied as a cumulative-effect adjustment to retained earnings. The Company intends to adopt the standard on August 1, 2023 and does not believe the adoption will have a material impact on its consolidated financial statements.

In August 2020, the FASB issued ASU No. 2020-06, *Accounting for Convertible Instruments and Contracts in an Entity’s Own Equity* (“ASU 2020-06”), which simplifies an issuer’s accounting for convertible instruments by reducing the number of accounting models that require separate accounting for embedded conversion features. ASU 2020-06 also simplifies the settlement assessment that entities are required to perform to determine whether a contract qualifies for equity classification and makes targeted improvements to the disclosures for convertible instruments and earnings-per-share (“EPS”) guidance. This update will be effective for the Company’s fiscal years beginning after December 15, 2023, and interim periods within those fiscal years. Early adoption is permitted, but no earlier than fiscal years beginning after December 15, 2020, and interim periods within those fiscal years. Entities can elect to adopt the new guidance through either a modified retrospective method of transition or a fully retrospective method of transition. The Company is currently evaluating the impact of the pending adoption of the new standard on its consolidated financial statements and intends to adopt the standard as of August 1, 2024.

NOTE 3 — DISCONTINUED OPERATIONS

On July 1, 2022, the Company determined that the 520 Property met the held-for-sale criteria and the Company therefore classified the 520 Property as held-for-sale in the consolidated balance sheets at July 31, 2022. The sale of the 520 Property also represented a significant strategic shift that will have a major effect on the Company’s operations and financial results. Therefore, the Company has classified the results of operations related to the 520 Property as discontinued operations in the consolidated statements of operations and comprehensive loss. Depreciation on the 520 Property ceased on July 1, 2022, as a result of the 520 Property being classified as held-for-sale.

On August 22, 2022, Broad Atlantic completed the sale of the 520 Property for an aggregate gross purchase price of \$49.4 million.

The 520 Property was encumbered by a mortgage securing a \$15 million note payable which was paid off in this transaction. Refer to Note 15 for further information on the note payable. After repaying the note payable, commissions, taxes, and other related costs, the Company received a net cash amount of approximately \$33 million at closing.

RAFAEL HOLDINGS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

NOTE 3 — DISCONTINUED OPERATIONS (cont.)

The carrying value of major classes of assets and liabilities related to discontinued operations at July 31, 2022 was as follows:

	<u>As of July 31, 2022</u>
	<i>(in thousands)</i>
Current assets held-for-sale	
Building and Improvements	\$ 45,437
Land	10,412
Furniture and Fixtures	1,145
Other	205
Property and equipment	57,199
Less Accumulated Depreciation	(17,005)
Property and equipment, net	40,194
Total current assets held-for-sale	40,194
Total assets held-for-sale	<u>\$ 40,194</u>
Current liabilities held-for-sale	
Total current liabilities	<u>\$ 15,000</u>

The current portion of deferred rental income included in Prepaid Expenses and Other Current Assets was \$0 and approximately \$150 thousand as of July 31, 2023 and 2022, respectively. The noncurrent portion of deferred rental income included in Other Assets was \$0 and approximately \$1.3 million as of July 31, 2023 and 2022, respectively. The deferred rental income pertains to the 520 Property and was settled at the date of the sale of the 520 Property with the other working capital accounts of the 520 Property.

Discontinued operations include (i) rental and parking revenues, (ii) payroll, benefits, facility costs, real estate taxes, consulting and professional fees dedicated to the 520 Property, (iii) depreciation and amortization expenses and (iv) interest (including amortization of debt issuance costs) on the note payable on the 520 Property. The operating results of these items are presented in our consolidated statements of operations and comprehensive loss as discontinued operations for all periods presented.

The following table details the components comprising net loss from our discontinued operations:

	<u>Year Ended July 31,</u>	
	<u>2023</u>	<u>2022</u>
	<i>(in thousands)</i>	
Revenue from discontinued operations:		
Rental – Third Party	\$ 68	\$ 644
Rental – Related Party	115	2,161
Parking	66	694
Total revenue from discontinued operations	249	3,499
Costs and expenses from discontinued operations:		
General and administrative	468	2,683
Depreciation and amortization	—	1,317
Loss from discontinued operations	(219)	(501)
Other income	—	157
Interest expense	(87)	(1,486)
Loss from discontinued operations	<u>(306)</u>	<u>(1,830)</u>
Gain on disposal of discontinued operations	6,784	—
Gain (loss) from discontinued operations	<u>\$ 6,478</u>	<u>\$ (1,830)</u>

RAFAEL HOLDINGS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

NOTE 3 — DISCONTINUED OPERATIONS (cont.)

The gain on disposal of discontinued operations of approximately \$6.8 million was derived from the gross proceeds of approximately \$49.4 million from the sale of the 520 Property, less the carrying value of the 520 Property of approximately \$40.2 million, net of approximately \$1.2 million in transaction costs and the write off of approximately \$1.2 million of deferred rental income.

NOTE 4 — INVESTMENT IN CORNERSTONE PHARMACEUTICALS

Equity Investment in Cornerstone Pharmaceuticals and Impairment of Cost Method Investment

Cornerstone Pharmaceuticals is a clinical stage, cancer metabolism-based therapeutics company focused on the development and commercialization of therapies that exploit the metabolic differences between normal cells and cancer cells.

The Company owns debt and equity interests and rights in Cornerstone Pharmaceuticals through a 90%-owned non-operating subsidiary, Pharma Holdings, LLC, or Pharma Holdings.

Pharma Holdings owns 50% of CS Pharma Holdings, LLC, or CS Pharma, a non-operating entity that owns equity interests in Cornerstone Pharmaceuticals. Accordingly, the Company holds an effective 45% indirect interest in the assets held by CS Pharma.

A trust for the benefit of the children of Howard Jonas (Chairman of the Board and Executive Chairman and former Chief Executive Officer of the Company and Member of the Board of Cornerstone Pharmaceuticals) holds a financial instrument (the “Instrument”) that owns 10% of Pharma Holdings.

Pharma Holdings holds 44.0 million shares of Cornerstone Pharmaceuticals’ Series D Convertible Preferred Stock and a warrant to increase the combined ownership of Pharma Holdings and CS Pharma to up to 56% of the fully diluted equity interests in Cornerstone Pharmaceuticals (the “Warrant”). The exercise price of the Warrant is the lower of 70% of the price sold in an equity financing, or \$1.25 per share, subject to certain adjustments.

On March 25, 2020, the Board of Directors of Cornerstone Pharmaceuticals extended the expiration date of the Warrant held by Pharma Holdings to purchase shares of the Warrant from December 31, 2020 to June 30, 2021, and on August 31, 2020 the Board of Directors of Cornerstone Pharmaceuticals further extended the expiration date of the Warrant held by Pharma Holdings, LLC to purchase shares of the Warrant to August 15, 2021. In connection with the Merger Agreement, the Warrant expiration was extended to April 1, 2022. The Company has asserted that it may be entitled to a further extension of the Warrant. At this time, the Company does not intend to exercise the Warrant.

Pharma Holdings also holds certain governance rights in Cornerstone Pharmaceuticals including appointment of directors. Pharma Holdings is not the primary beneficiary of Cornerstone Pharmaceuticals as it does not control or direct the activities of Cornerstone Pharmaceuticals that most significantly impact Cornerstone Pharmaceuticals’ economic performance.

CS Pharma holds 16.7 million shares of Cornerstone Pharmaceuticals Series D Convertible Preferred Stock. CS Pharma owned a \$10 million Series D Convertible Note, with 3.5% interest, in Cornerstone Pharmaceuticals which was converted to shares of Series D Preferred Stock in January 2019.

The Company and its subsidiaries collectively own securities representing 51% of the outstanding capital stock of Cornerstone Pharmaceuticals and 42% of the capital stock on a fully diluted basis (excluding the remainder of the Warrant).

The Series D Convertible Preferred Stock has a stated value of \$1.25 per share (subject to appropriate adjustment to reflect any stock split, combination, reclassification or reorganization of the Series D Preferred Stock or any dilutive issuances, as described below). Holders of Series D Stock are entitled to receive non-cumulative dividends when, as and if declared by the Board of Cornerstone Pharmaceuticals, prior to any dividends to any other class of capital stock of Cornerstone Pharmaceuticals. In the event of any liquidation, dissolution or winding up of Cornerstone

RAFAEL HOLDINGS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

NOTE 4 — INVESTMENT IN CORNERSTONE PHARMACEUTICALS (cont.)

Pharmaceuticals, or in the event of any deemed liquidation, proceeds from such liquidation, dissolution or winding up shall be distributed first to the holders of Series D Stock. Except with respect to certain major decisions, or as required by law, holders of Series D Stock vote together with the holders of the other preferred stock and common stock and not as a separate class.

The Company serves as the managing member of Pharma Holdings, and Pharma Holdings serves as the managing member of CS Pharma, with broad authority to make all key decisions regarding their respective holdings. Any distributions that are made to CS Pharma from Cornerstone Pharmaceuticals that are in turn distributed by CS Pharma, will need to be made pro rata to all members, which would entitle Pharma Holdings to 50% (based on current ownership) of such distributions. Similarly, if Pharma Holdings were to distribute proceeds it receives from CS Pharma, it would do so on a pro rata basis, entitling the Company to 90% (based on current ownership) of such distributions.

The Company evaluated its investments in Cornerstone Pharmaceuticals in accordance with ASC 323, *Investments — Equity Method and Joint Ventures*, to establish the appropriate accounting treatment for its investment and has concluded that its investment did not meet the criteria for the equity method of accounting or consolidation and is carried at cost.

The Company has determined that Cornerstone Pharmaceuticals is a VIE; however, the Company has determined that it is not the primary beneficiary as it does not have the power to direct the activities of Cornerstone Pharmaceuticals that most significantly impact Cornerstone Pharmaceuticals' economic performance. In addition, the interests held in Cornerstone Pharmaceuticals are Series D Convertible Preferred Stock and do not represent in-substance common stock.

The Instrument holds a contractual right to receive additional shares of Cornerstone Pharmaceuticals capital stock equal to 10% of the fully diluted capital stock of Cornerstone Pharmaceuticals (the "Bonus Shares") upon the achievement of certain milestones. The additional 10% is based on the fully diluted capital stock of Cornerstone Pharmaceuticals, excluding the remainder for the Warrant, at the time of issuance. If any of the milestones are met, the Bonus Shares are to be issued without any additional payment.

Pharma Holdings holds the Warrant as well as other equity and governance rights in Cornerstone Pharmaceuticals. The Company currently owns 51% of the issued and outstanding equity in Cornerstone Pharmaceuticals. Approximately 8% of the issued and outstanding equity is owned by the Company's subsidiary CS Pharma and 43% is held by the Company's subsidiary Pharma Holdings. The Company's subsidiary Pharma Holdings holds the Warrant. The Instrument holds 10% of the interest in Pharma Holdings and would need to contribute 10% of any cash necessary to exercise any portion of the Warrant. Following any exercise, a portion of the Company's interest in Cornerstone Pharmaceuticals would continue to be held for the benefit of the other equity holders in Pharma Holdings and CS Pharma. Cornerstone Pharmaceuticals may also issue additional equity interests, such as employee stock options, which will require the Company to pay additional cash to maintain the Company's ownership percentage or exercise the Warrant in full. The terms of the Warrant provide that it expired on April 1, 2022; however, the Company has asserted that it may be entitled to a further extension of the Warrant. At this time, the Company does not intend to exercise the Warrant.

Due to the Data Events, on October 28, 2021, the Company recorded an impairment charge of approximately \$79.1 million related to the cost method investment in Cornerstone Pharmaceuticals representing the total amount of the Company's cost method investment. The impairment loss was included in "Impairment of cost method investment — Cornerstone Pharmaceuticals" in the consolidated statements of operations and comprehensive loss for the year ended July 31, 2022.

Approximately \$17.3 million of the total impairment loss of \$79.1 million was applicable to noncontrolling interests in certain of the Company's subsidiaries and was allocated to the holders of interests in CS Pharma and Pharma Holdings in the approximate amounts of \$10.4 million and \$6.9 million, respectively.

RAFAEL HOLDINGS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

NOTE 4 — INVESTMENT IN CORNERSTONE PHARMACEUTICALS (cont.)

Line of Credit to Cornerstone Pharmaceuticals and Impairment of Related Receivable

On September 24, 2021, the Company entered into a Line of Credit Loan Agreement (the “Line of Credit Agreement”) with Cornerstone Pharmaceuticals under which Cornerstone Pharmaceuticals borrowed \$25 million from the Company. The first advance was in the amount of \$1.9 million on September 24, 2021. On October 1, 2021, a second advance was made in the amount of \$23.1 million. The Line of Credit Agreement accrues interest at 9% per annum. The maturity date of the Line of Credit Agreement was June 17, 2022, and the amounts due on that date were not paid. The Company is in discussions with Cornerstone Pharmaceuticals and is evaluating its rights and plan of action with respect to the Line of Credit Agreement (in the contexts of all of its interests in Cornerstone Pharmaceuticals).

Due to the Data Events, the Company recorded a full reserve on the amounts due the Company from Cornerstone Pharmaceuticals related to the Line of Credit Agreement for \$25 million during the year ended July 31, 2022.

The Company also recorded a loss on related party receivables of approximately \$2.6 million related to other amounts owed by Cornerstone Pharmaceuticals during the year ended July 31, 2022. The Company recorded a reserve on related party interest receivable of \$1.9 million in Interest income, net, on the consolidated statements of operations and comprehensive loss during the year ended July 31, 2022. There were no amounts recorded during the year ended July 31, 2023.

Planned Restructuring

Cornerstone is in the process of a comprehensive restructuring transaction including, the conversion of the debt under the Line of Credit Agreement and the Promissory Note held by the Company, the conversion and modification of other Cornerstone debt obligations, the extension of the Cornerstone debt held by RP Finance, a reverse stock split, the conversion of all outstanding preferred stock of Cornerstone into common stock and the adoption of certain governance measures. This transaction is subject to a number of conditions which are beyond the Company’s control.

NOTE 5 — CONVERTIBLE NOTE RECEIVABLE, RELATED PARTY

On March 21, 2023, the Company loaned \$2.0 million to Cornerstone which is represented by a Promissory Note (the “Promissory Note” or “Note”) made by Cornerstone. The Note, which bears interest at a rate of seven and one-half percent (7.5%) per annum, was originally due and payable on May 22, 2023. On May 22, 2023, the Promissory Note was amended to extend the maturity date to November 30, 2023 and to waive any increase in the interest rate provided for in the Note, provided that the entire principal amount and all accrued interest thereon is repaid in cash or converted into equity securities of Cornerstone no later than November 30, 2023.

The Promissory Note is secured by a first priority security interest in all of Cornerstone’s right, title and interest in and to all of the tangible and intangible assets purchased by Cornerstone pursuant to the Purchase Agreement between Cornerstone and Calithera Biosciences, Inc. (“Calithera”), a clinical-stage, precision oncology biopharmaceutical company developing targeted therapies to redefine treatment for biomarker-specific patient populations, and all proceeds therefrom and all rights to the data related to CB-839 (the “Collateral”).

The interest on the Promissory Note accrues from the issuance date until the Note is paid in full or converted, which shall accrue on a quarterly basis. Subject to the amendment described above, in the event the total outstanding amount under the Promissory Note is not repaid by the amended maturity date, the rate of interest shall be eleven percent (11%), retroactive from and after the maturity date. Subject to the amendment described above, following the occurrence of and during the continuation of an uncured Event of Default (as defined below), the outstanding principal amount shall bear interest at the rate of fourteen percent (14%) per annum (the “Default Interest Rate”) until the earliest of (i) cure of such Event of Default, (ii) repayment of all outstanding amounts due under the Note, (iii) conversion of all then outstanding obligations under the Note, or (iv) transfer of all its rights related to the Collateral.

The entire (and not less than the entire) outstanding principal amount due under the Promissory Note together with all accrued unpaid interest thereon and other amounts owing thereunder (together, the “Owed Amount”), may, at Cornerstone’s election at any time prior to the maturity date, be converted into a number of shares (the “Conversion Shares”) calculated

RAFAEL HOLDINGS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

NOTE 5 — CONVERTIBLE NOTE RECEIVABLE, RELATED PARTY (cont.)

by dividing the entire Owed Amount by the conversion price used by Cornerstone in a Qualified Offering/Conversion (as defined in the Note), and if no such Qualified Offering/Conversion has been consummated, the fair market value for the Conversion as determined by an independent third party valuation firm (the “Conversion Price”).

The Promissory Note contains certain trigger events (as defined in the Note) that generally, if uncured within five (5) trading days, may result in an event of default in accordance with the terms of the Notes (such event, an “Event of Default”). Upon an Event of a Default, the Company may consider the Promissory Note immediately due and payable. Upon an Event of Default, the interest rate may also be increased to the lesser of 18% per annum or the maximum rate permitted under applicable law.

The Company recorded the Promissory Note at fair value as the security is classified as available-for-sale. Subsequent changes in fair value are recorded in unrealized gain or loss on available-for-sale securities as a component of other comprehensive income (loss) in the consolidated statements of operations and comprehensive loss.

For the year ended July 31, 2023, the Company recorded a change in fair value of approximately \$79 thousand related to the decrease in fair value of the Promissory Note which was recognized in other comprehensive income (loss) on the consolidated statements of operations and comprehensive loss.

Interest income on the Promissory Note totaled approximately \$54 thousand for the year ended July 31, 2023 and is recorded in interest receivable on the consolidated balance sheets.

NOTE 6 — INVESTMENT IN RP FINANCE, LLC

On February 3, 2020, Cornerstone Pharmaceuticals entered into a Line of Credit with RP Finance (“RPF Line of Credit”) which provides a revolving commitment of up to \$50,000,000 to fund clinical trials and other capital needs.

The Company owns 37.5% of the equity interests in RP Finance and is required to fund 37.5% of funding requests from Cornerstone Pharmaceuticals under the RPF Line of Credit. The Instrument owns 37.5% of the equity interests in RP Finance, and is required to fund 37.5% of funding requests from Cornerstone Pharmaceuticals under the RPF Line of Credit. The remaining 25% equity interests in RP Finance are owned by other stockholders of Cornerstone Pharmaceuticals.

Under the RPF Line of Credit, all funds borrowed will bear interest at the mid-term Applicable Federal Rate published by the U.S. Internal Revenue Service. The maturity date is the earliest of February 3, 2025, upon a change of control of Cornerstone Pharmaceuticals or a sale of Cornerstone Pharmaceuticals or its assets. Cornerstone Pharmaceuticals can draw on the facility on 60 days’ notice. The funds borrowed under the RPF Line of Credit must be repaid out of certain proceeds from equity sales by Cornerstone Pharmaceuticals.

In connection with entering into the RPF Line of Credit, Cornerstone Pharmaceuticals agreed to issue to RP Finance shares of its common stock representing 12% of the issued and outstanding shares of Cornerstone Pharmaceuticals common stock, with such interest subject to anti-dilution protection as set forth in the RPF Line of Credit.

The Company has determined that RP Finance is a VIE; however, the Company has determined that it is not the primary beneficiary as the Company does not have the power to direct the activities of RP Finance that most significantly impact RP Finance’s economic performance and, therefore, is not required to consolidate RP Finance. Therefore, the Company will use the equity method of accounting to record its investment in RP Finance. The Company has recognized \$0 in earnings from its ownership interests of 37.5% in RP Finance for the years ended July 31, 2023 and 2022, respectively, and a loss of \$0 and \$575 thousand from its ownership interests of 37.5% in RP Finance for the years ended July 31, 2023 and 2022, respectively. The assets and operations of RP Finance are not significant and the Company has identified the equity investment in RP Finance as a related party transaction (see Note 16).

In August 2020, Cornerstone Pharmaceuticals called for a \$5 million draw on the RPF Line of Credit and the facility was funded by RP Finance in the amount of \$5 million. In November 2020, Cornerstone Pharmaceuticals called for a second \$5 million draw on the RPF Line of Credit and the facility was funded by RP Finance in the amount of

RAFAEL HOLDINGS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

NOTE 6 — INVESTMENT IN RP FINANCE, LLC (cont.)

\$5 million. In June 2021 and July 2021, Cornerstone Pharmaceuticals called for a total aggregate of \$10 million in draws on the line of RPF Line of Credit and the facility was funded by RP Finance in the amount of \$10 million. In September 2021, Cornerstone Pharmaceuticals called for a \$5 million draw on the RPF Line of Credit and the facility was funded by RP Finance LLC in the amount of \$5 million.

As of July 31, 2023 and 2022, the Company has funded a cumulative total of \$9.375 million in accordance with its 37.5% ownership interests in RP Finance. The Company recorded a reserve on related party interest receivable of \$1.9 million in Interest income, net, on the consolidated statements of operations and comprehensive loss during the year ended July 31, 2022.

Impairment of Equity Method Investment

Due to the Data Events, during the three months ended October 31, 2021, the Company recorded equity in the loss of RP Finance of \$575 thousand. As of July 31, 2023 and 2022, the equity method investment on the Company's balance sheet was \$0, and no additional equity loss of RP Finance was recorded during the year ended July 31, 2023. The Company was not obligated to guarantee obligations of RP Finance and is not committed to provided further financial support for RP Finance. Additionally, during the year ended July 31, 2022, the Company recorded a loss on related party receivables of \$9.375 million related to amounts owed by RP Finance.

NOTE 7 — INVESTMENT IN LIPOMEDIX PHARMACEUTICALS LTD.

LipoMedix is a development-stage, privately held Israeli company focused on the development of an innovative, safe and effective cancer therapy based on liposome delivery.

As of July 31, 2023, the Company held 95% of the issued and outstanding ordinary shares of LipoMedix and has consolidated this investment from the second quarter of fiscal 2018.

In March 2021, the Company provided bridge financing in the principal amount of up to \$400,000 to LipoMedix with a maturity date of September 1, 2021, and an interest rate of 8% per annum. As of September 1, 2021, LipoMedix was in default on the terms of the loan and as such, the interest rate has increased to 15% per annum.

On November 15, 2021, the Company entered into a share purchase agreement with LipoMedix to purchase up to 15,975,000 ordinary shares at \$0.1878 per share for an aggregate purchase price of \$3.0 million (the "LipoMedix SPA"). Additionally, LipoMedix issued the Company a warrant to purchase up to 15,975,000 ordinary shares at an exercise price of \$0.1878 per share which expired on November 11, 2022.

As of the date of the LipoMedix SPA, there was an outstanding loan balance including principal of \$400 thousand and accrued interest of \$21.8 thousand owed by LipoMedix to the Company on a note made by LipoMedix in favor of the Company issued in March 2021. The amount due on the loan was netted against the approximately \$3.0 million aggregate purchase price due to LipoMedix, resulting in a cash payment by the Company of approximately \$2.6 million in exchange for the 15,975,000 shares purchased. As a result of the share purchase, the Company's ownership of LipoMedix increased to approximately 84% with a noncontrolling interest of approximately 16%. The Company recorded approximately \$8 thousand to adjust the carrying amount of the noncontrolling interest to reflect the Company's increased ownership interest in LipoMedix's net assets.

On February 9, 2023, the Company entered into a Share Purchase Agreement with LipoMedix to purchase 70,000,000 ordinary shares at \$0.03 per share for an aggregate purchase price of \$2.1 million (the "2023 LipoMedix SPA"). As a result of the share purchase, the Company's ownership of LipoMedix increased to approximately 95% with a noncontrolling interest of approximately 5%. The Company recorded approximately \$16 thousand to adjust the carrying amount of the noncontrolling interest to reflect the Company's increased ownership interest in LipoMedix's net assets.

RAFAEL HOLDINGS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

NOTE 8 — INVESTMENT IN DAY THREE LABS INC.

On April 7, 2023, the Company entered into a Common Stock Purchase Agreement (the “Day Three Purchase Agreement”) with Day Three. Day Three is a cannabinoid ingredient manufacturer specializing in the development and commercialization of novel cannabis product solutions. Pursuant to the Day Three Purchase Agreement, the Company purchased 4,302,224 shares of common stock representing 38% of the outstanding shares of common stock of Day Three (33.333% on a fully diluted basis), for a purchase price of \$3.0 million. The Company also received a warrant exercisable for 7,528,893 shares of common stock at an aggregate purchase price of \$3.0 million, which expires five years from the date of issuance or earlier based on the occurrence of certain events as defined in the Day Three Purchase Agreement. As of the date of this report, the Company had not exercised the warrant.

The Company has accounted for this investment as an equity method investment in accordance with the guidance in ASC 323, Investments — *Equity Method and Joint Ventures*. The Company determined that a 38% ownership interest in Day Three and its right to designate two members of the Board of Directors of Day Three (out of a current total of seven members) indicates that the Company is able to exercise significant influence. Upon exercise of the warrant, the Company will have the right to appoint a third member of the Day Three Board of Directors.

The Company has determined that Day Three is a VIE; however, the Company is not the primary beneficiary as it does not have the power to direct the activities that most significantly impact Day Three’s economic performance. The Company has therefore concluded it is not required to consolidate Day Three. The Company uses the equity method of accounting to record its investment in Day Three.

Day Three’s fiscal year ends on December 31, and as a result, the Company will recognize its share of Day Three’s earnings/loss on a one-month lag. For the year ended July 31, 2023, the Company recognized approximately \$203 thousand of equity in loss of Day Three, based on its proportionate share of Day Three’s results through June 30, 2023. The assets and operations of Day Three are not significant.

NOTE 9 — INVESTMENT IN CYCLO THERAPEUTICS, INC.

On May 2, 2023, the Company entered into a Securities Purchase Agreement (the “Cyclo SPA”) with Cyclo. Cyclo is a clinical stage biotechnology company, whose common stock is listed on the Nasdaq Capital Market under the symbol CYTH, that develops cyclodextrin-based products for the treatment of neurodegenerative diseases. The Company purchased from Cyclo (i) 2,514,970 common shares (the “Purchased Shares”) and (ii) a warrant to purchase 2,514,970 common shares with an exercise price of \$0.71 per share (the “Cyclo Warrant”), at a combined purchase price equal to \$0.835 per Purchased Share and Cyclo Warrant to purchase one share, for an aggregate purchase price of \$2.1 million. The Cyclo Warrant may be exercised for the seven-year period following the date Cyclo obtains the approval of the stockholders of Cyclo to the exercise of the Cyclo Warrant. On July 31, 2023, the Cyclo stockholders approved the exercise in full of the warrant.

On June 1, 2023, the Company entered into another Securities Purchase Agreement (the “Cyclo II SPA”) with Cyclo. Pursuant to the Cyclo II SPA, the Company agreed to purchase an additional 4,000,000 shares of common stock (the “Cyclo II Shares”), and a warrant to purchase an additional 4,000,000 Shares (the “Cyclo II Warrant”), for an aggregate purchase price of \$5,000,000. The Cyclo II Warrant has an exercise price of \$1.25 per share and is exercisable for a period of seven years following the date of issuance. On July 31, 2023, Cyclo obtained the approval of its stockholders for the transactions contemplated by the Cyclo II SPA.

Subsequent to year end, on August 1, 2023, the Company completed the Cyclo II SPA with Cyclo, whereby the Company purchased 4,000,000 shares of common stock (the “Cyclo II Shares”), and a warrant to purchase an additional 4,000,000 Shares (the “Cyclo II Warrant”), for an aggregate purchase price of \$5,000,000. The August 1, 2023 investment increased the Company’s percentage ownership of Cyclo common stock to 34%. As of the date of this report, the Company had not exercised the Cyclo II Warrant.

Pursuant to the Cyclo II SPA, the Registration Rights Agreement between the Company and Cyclo, dated May 2, 2023, has been amended to require Cyclo to file a registration statement with the Securities and Exchange Commission to register the resale of the Cyclo II Shares and shares of common stock underlying the Cyclo II Warrants, upon

RAFAEL HOLDINGS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

NOTE 9 — INVESTMENT IN CYCLO THERAPEUTICS, INC. (cont.)

the request of the Company, and (ii) Cyclo agreed to appoint a designee of the Company (in addition to William Conkling, the Company’s Chief Executive Officer) to Cyclo’s Board of Directors, and to nominate such designee to serve as a director of Cyclo in connection with Cyclo’s solicitation of proxies for Cyclo’s next Annual Meeting of Stockholders. The Cyclo II SPA purchase price was paid on August 1, 2023, which is the effective date of the second Cyclo investment.

Subsequent to year end, on October 20, 2023, the Company exercised the Cyclo Warrant to purchase 2,514,970 common shares at an exercise price of \$0.71 per share, pursuant to a Securities Purchase Agreement dated October 20, 2023, and in consideration received a new warrant to purchase an additional 2,766,467 common shares at an exercise price of \$0.95 per share which are exercisable for a period of four years following the issuance date (the “Cyclo III Warrant”), for an aggregate purchase price of \$1,785,629.

The Company has elected to account for its investment in Cyclo under the fair value option. The investment was measured at fair value and the Company has recorded the subsequent changes in fair value as unrealized gain (loss) in the consolidated statements of operations and comprehensive loss.

The investment in the Cyclo SPA resulted in an unrealized gain of approximately \$2.1 million as the purchase price was lower than the fair value of the investment. The Company recognized total unrealized gains on its investment of \$2.7 million in the accompanying consolidated statements of operations and comprehensive loss for the year ended July 31, 2023.

Summarized Fair Value (Level 1) Method Investment Details

	Ownership %	Aggregate Fair Value
	July 31, 2023	July 31, 2023
Cyclo.....	16%	\$ 4,763,102

The 16% ownership percentage as of July 31, 2023 is comprised of the shares of common stock owned by the Company and does not include the Cyclo Warrant. The total aggregate fair value of the Cyclo investment of \$4,763,102 as of July 31, 2023 is comprised of common shares with an aggregate fair value of \$3,898,204 and warrants with an aggregate fair value of \$864,898.

Summarized consolidated financial information of Cyclo, reported on a one month lag, is as follows:

	Three Months Ended		Six Months Ended	
	June 30,		June 30,	
	2023	2022	2023	2022
Revenue.....	\$ 117,118	\$ 541,886	\$ 269,529	\$ 736,790
Loss from operations.....	\$ (4,632,942)	\$ (3,456,024)	\$ (9,640,074)	\$ (6,390,481)
Net loss.....	\$ (4,636,455)	\$ (3,451,990)	\$ (9,643,540)	\$ (6,223,581)

NOTE 10 — INVESTMENTS

The Company has classified its investments in corporate bonds, U.S. treasury bills, and convertible note receivable as available-for-sale securities. These securities are carried at estimated fair value with unrealized holding gains and losses included in accumulated other comprehensive loss in stockholders’ equity until realized. Investment transactions are recorded on their trade date. Gains and losses on marketable security transactions are reported on the specific-identification method. Interest income is accrued daily and adjusted for amortization of premiums and accretion of discounts on the corporate bonds and U.S. treasury bills.

RAFAEL HOLDINGS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

NOTE 10 — INVESTMENTS (cont.)

The amortized cost, gross unrealized holding gains, gross unrealized holding losses, and fair value for available-for-sale securities as of July 31, 2023 and 2022 are as follows:

<u>July 31, 2023</u>	<u>Amortized cost</u>	<u>Gross unrealized gains</u>	<u>Gross unrealized (losses)</u>	<u>Fair value</u>
		<i>(in thousands)</i>		
Available-for-sale securities:				
U.S. Treasury Bills	\$ 11,222	\$ 53	\$ —	\$ 11,275
Corporate bonds	46,766	4,333	(4,660)	46,439
Convertible note receivable, related party	2,000	—	(79)	1,921
Total available-for-sale securities	<u>\$ 59,988</u>	<u>\$ 4,386</u>	<u>\$ (4,739)</u>	<u>\$ 59,635</u>
<u>July 31, 2022</u>	<u>Amortized cost</u>	<u>Gross unrealized gains</u>	<u>Gross unrealized (losses)</u>	<u>Fair value</u>
		<i>(in thousands)</i>		
Available-for-sale securities:				
Corporate bonds	\$ 36,761	\$ 81	\$ (144)	\$ 36,698
Total available-for-sale securities	<u>\$ 36,761</u>	<u>\$ 81</u>	<u>\$ (144)</u>	<u>\$ 36,698</u>

During the year ended July 31, 2023, the Company reclassified approximately \$154 thousand of unrealized gains out of accumulated other comprehensive loss related to the sale of available-for-sale securities into consolidated net loss in the consolidated statements of operations and comprehensive loss in realized gain on available-for-sale securities.

Maturities of corporate bonds and U.S. Treasury Bills held as of July 31, 2023 were all due within one year.

Marketable securities in an unrealized loss position as of July 31, 2023 were not deemed impaired at acquisition and subsequent declines in fair value are not deemed attributed to declines in credit quality. The Company believes that it is more likely than not that it will receive a full recovery of par value on the securities, although there can be no assurance that such recovery will occur.

NOTE 11 — 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. To increase the comparability of fair value measures, the following hierarchy prioritizes the inputs to valuation methodologies used to measure fair value:

- **Level 1** — quoted prices in active markets for identical assets or liabilities;
- **Level 2** — quoted prices in active markets for similar assets and liabilities and inputs that are observable for the asset or liability; or
- **Level 3** — unobservable inputs for the asset or liability, such as discounted cash flow models or valuations.

The determination of where assets and liabilities fall within this hierarchy is based upon the lowest level of input that is significant to the fair value measurement.

RAFAEL HOLDINGS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

NOTE 11 — FAIR VALUE MEASUREMENTS (cont.)

The following is a listing of the Company's assets required to be measured at fair value on a recurring basis and where they are classified within the fair value hierarchy as of July 31, 2023 and 2022:

	July 31, 2023			
	Level 1	Level 2	Level 3	Total
	<i>(in thousands)</i>			
Assets:				
Available-for-sale securities – Corporate Bonds	\$ —	\$ 46,439	\$ —	\$ 46,439
Available-for-sale securities – U.S. Treasury Bills	11,275	—	—	11,275
Investment in equity securities	294	—	—	294
Investment in Cyclo Therapeutics Inc. – Common stock . .	3,898	—	—	3,898
Investment in Cyclo Therapeutics Inc. – Warrants	865	—	—	865
Hedge funds	—	—	4,984	4,984
Convertible note receivable, related party	—	—	1,921	1,921
Total	<u>\$ 16,332</u>	<u>\$ 46,439</u>	<u>\$ 6,905</u>	<u>\$ 69,676</u>

	July 31, 2022			
	Level 1	Level 2	Level 3	Total
	<i>(in thousands)</i>			
Assets:				
Available-for-sale securities – Corporate Bonds	\$ —	\$ 36,698	\$ —	\$ 36,698
Hedge funds	—	—	4,764	4,764
Total	<u>\$ —</u>	<u>\$ 36,698</u>	<u>\$ 4,764</u>	<u>\$ 41,462</u>

As of July 31, 2023 and 2022, the Company did not have any liabilities measured at fair value on a recurring basis.

The following table summarizes the changes in the fair value of the assets measured at fair value on a recurring basis using significant unobservable inputs (Level 3):

	Year Ended July 31,	
	2023	2022
	<i>(in thousands)</i>	
Balance, beginning of period	\$ 4,764	\$ 5,268
Total gain (loss) included in earnings	220	(504)
Convertible note receivable, related party	2,000	—
Total loss included in other comprehensive loss	(79)	—
Balance, end of period	<u>\$ 6,905</u>	<u>\$ 4,764</u>

Hedge funds classified as Level 3 include investments and securities which may not be based on readily observable data inputs. The availability of observable inputs can vary from security to security and is affected by a wide variety of factors, including, for example, the type of security, whether the security is new and not yet established in the marketplace, the liquidity of markets, and other characteristics particular to the security. The fair value of these assets is estimated based on information provided by the fund managers or the general partners. Therefore, these assets are classified as Level 3.

Available-for-sale securities classified as Level 3 include a convertible note receivable, related party (see Note 5) which may not be based on readily observable data inputs. The availability of observable inputs can vary and is affected by a wide variety of factors, including, for example, the type of security, whether the security is new and not yet established in the marketplace, the liquidity of markets, and other characteristics particular to the security. The fair value of this asset is estimated using a scenario-based analysis based on the probability-weighted present value of future investments returns, considering each of the possible outcomes available to us, including cash repayment, equity

RAFAEL HOLDINGS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

NOTE 11 — FAIR VALUE MEASUREMENTS (cont.)

conversion, and collateral transfer scenarios. Estimating the fair value of the convertible note requires the development of significant and subjective estimates that may, and are likely to, change over the duration of the instrument with related changes in internal and external market factors. Therefore, this asset is classified as Level 3.

The Company holds \$0.1 and \$0.5 million as of July 31, 2023 and 2022, respectively, in investments in securities in another entity that are not liquid, which were included in Investments — Other Pharmaceuticals in the accompanying consolidated balance sheets. The investment is accounted for under ASC 321, *Investments — Equity Securities*, using the measurement alternative as defined within the guidance, and the Company recorded an impairment loss of \$334 thousand and \$0 for the years ended July 31, 2023 and 2022, respectively.

Fair Value of Other Financial Instruments

The estimated fair value of the Company's other financial instruments was determined using available market information or other appropriate valuation methodologies. However, considerable judgment is required in interpreting these data to develop estimates of fair value. Consequently, the estimates are not necessarily indicative of the amounts that could be realized or would be paid in a current market exchange.

The Company's financial instruments include trade accounts receivable, trade accounts payable, and due from related parties. The recorded carrying amounts of accounts receivable, accounts payable and due to related parties approximate their fair value due to their short-term nature.

NOTE 12 — ACCOUNTS RECEIVABLE

Accounts receivable consisted of the following:

	July 31, 2023	July 31, 2022
	<i>(in thousands)</i>	
Accounts Receivable – Third Party	\$ 247	\$ 196
Accounts Receivable – Related Party	211	158
Less Allowance for Doubtful Accounts	(245)	(197)
Accounts Receivable, net	\$ 213	\$ 157

NOTE 13 — PROPERTY AND EQUIPMENT

Property and equipment consisted of the following:

	July 31, 2023	July 31, 2022
	<i>(in thousands)</i>	
Building and Improvements	\$ 2,505	\$ 2,505
Other	68	68
	2,573	2,573
Less Accumulated Depreciation	(878)	(803)
Total	\$ 1,695	\$ 1,770

Other property and equipment consist of other equipment and miscellaneous computer hardware.

Depreciation expense pertaining to property and equipment was approximately \$78 thousand and \$72 thousand for the years ended July 31, 2023 and 2022, respectively.

The Company's headquarters are located at 520 Broad Street in Newark, New Jersey, where it occupies office space and which was previously owned by the Company. The table above excludes the assets of the 520 Property which were classified as held-for-sale as of July 31, 2022 and subsequently sold on August 22, 2022. Refer to Note 3 for further information on the 520 Property.

RAFAEL HOLDINGS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

NOTE 14 — LOSS PER SHARE

Basic loss per share is computed by dividing net loss attributable to all classes of common stockholders of the Company by the weighted average number of shares of all classes of common stock outstanding during the applicable period. Diluted loss per share includes potentially dilutive securities such as stock options, unvested restricted stock, warrants to purchase common stock, and other convertible instruments unless the result of inclusion would be anti-dilutive.

The securities set forth in the table below have been excluded from the calculation of diluted net loss per share for the years ended July 31, 2023 and 2022 because inclusion of all such securities would have been anti-dilutive for all periods presented.

The following table summarizes the Company’s potentially dilutive securities which have been excluded from the calculation of dilutive loss per share as their effect would be anti-dilutive:

	Year Ended July 31,	
	2023	2022
Shares issuable upon exercise of stock options	388,409	1,021,277
Shares issuable upon vesting of restricted stock	684,766	1,507,373
	1,073,175	2,528,650

The diluted loss per share computation equals basic loss per share for the years ended July 31, 2023 and 2022 because the Company had a net loss from continuing operations in all such periods and the impact of the assumed vesting of restricted shares, and exercise of stock options, and warrants would have been anti-dilutive.

The following table summarizes the basic and diluted loss per share calculations (in thousands, except for share and per share amounts):

	Year Ended July 31,	
	2023	2022
Numerator:		
Net loss from continuing operations	\$ (8,693)	\$ (140,547)
Net loss attributable to noncontrolling interests	(339)	(17,719)
Numerator for net loss from continuing operations	(8,354)	(122,828)
Numerator for discontinued operations	6,478	(1,830)
Net loss attributable to Rafael Holdings, Inc.	\$ (1,876)	\$ (124,658)
Denominator:		
Weighted average basic and diluted shares outstanding	23,263,211	19,767,342
Loss per share attributable to common stockholders		
Basic and diluted:		
Continuing operations	\$ (0.36)	\$ (6.22)
Discontinued operations	0.28	(0.09)
Total basic and diluted loss per share	\$ (0.08)	\$ (6.31)

NOTE 15 — NOTE PAYABLE, HELD-FOR-SALE

On July 9, 2021, the Company, as guarantor, Rafael Holdings Realty, Inc., a wholly-owned subsidiary of the Company (“Realty”), as pledgor, and Broad-Atlantic, a wholly-owned subsidiary of Realty (the “Borrower,” and together with the Company and Realty, the “Borrower Parties”), as borrower, entered into a loan agreement (the “Loan Agreement”) with 520 Broad Street LLC, a third-party lender (the “Lender”). The Loan Agreement provided for a loan in the amount of \$15 million (the “Note Payable”) from Lender to Borrower secured by (i) a first mortgage on 520 Broad Street, Newark, New Jersey 07102; and (ii) a first priority security interest in the equity of the Borrower as set forth in the Pledge and Security Agreement between Realty and Lender.

RAFAEL HOLDINGS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

NOTE 15 — NOTE PAYABLE, HELD-FOR-SALE (cont.)

The Note Payable bore interest at a rate per annum equal to seven and one-quarter percent (7.25%) from July 9, 2021 through July 31, 2021 and thereafter at an interest rate per annum equal to the 30-day LIBOR Rate, as published in *The Wall Street Journal*, plus 6.90% per annum, but in no event less than seven and one-quarter percent (7.25%) per annum. The Note Payable was due on August 1, 2022, subject to the Company's option to extend the maturity date until August 1, 2023 for a fee equal to three-quarters of one percent (0.75%) of the Note Payable.

The Loan Agreement contained customary affirmative covenants, negative covenants and events of default, as defined in the Loan Agreement, including covenants and restrictions that, among other things, restricted the Borrower's ability to incur liens, or transfer, lease or sell the collateral as defined in the Loan Agreement. A failure to comply with these covenants would have permitted the Lender to declare the Borrower's obligations under the Loan Agreement, together with accrued interest and fees, to be immediately due and payable. The Company was in compliance with the covenants in the Loan Agreement as of July 31, 2022. The Company extended the maturity date to November 1, 2022 and paid an extension fee of \$37,500 on July 29, 2022.

In connection with the sale of the 520 Property, on August 22, 2022, the Company paid off the outstanding principal balance of \$15 million and accrued interest of approximately \$87,000 on the Note Payable. Refer to Note 3 for further details on the subsequent sale of the 520 Property.

Interest expense under the Note Payable, which is recognized in loss on discontinued operations, amounted to \$87 thousand for the year ended July 31, 2023, and \$1.2 million for the year ended July 31, 2022.

Unamortized debt issuance costs on the Note Payable totaled approximately \$0 as of July 31, 2023 and 2022. Amortization of the debt discount on the Note Payable totaled approximately \$0 and \$472 thousand for the years ended July 31, 2023 and 2022, respectively.

NOTE 16 — RELATED PARTY TRANSACTIONS

IDT Corporation

The Company has historically maintained an intercompany balance due to/from related parties that relates to cash advances for investments, loan repayments, charges for services provided to the Company by IDT and payroll costs for the Company's personnel that were paid by IDT. IDT billed the Company approximately \$313 thousand and \$343 thousand for services during the years ended July 31, 2023 and 2022, respectively, of which \$70 thousand and \$69 thousand is included in due to related parties at July 31, 2023 and 2022, respectively.

IDT leased, prior to the Company's sale of the property, approximately 80,000 square feet of office space plus parking at the 520 Property and leases approximately 3,600 square feet of office space in Jerusalem, Israel. The Company invoiced IDT approximately \$211 thousand, of which approximately \$102 thousand is included in discontinued operations during the year ended July 31, 2023. The Company invoiced IDT approximately \$2.1 million, of which approximately \$2.0 million is included in discontinued operations for office rent and parking during the year ended July 31, 2022. As of July 31, 2023 and 2022, IDT owed the Company approximately \$210 thousand and \$157 thousand, respectively, for office rent and parking.

Cornerstone Pharmaceuticals

Until October 31, 2021, the Company had provided Cornerstone Pharmaceuticals with administrative, finance, accounting, tax and legal services. Howard S. Jonas and William Conkling currently serve on the Board of Directors of Cornerstone Pharmaceuticals. The Company billed Cornerstone Pharmaceuticals \$120 thousand for the year ended July 31, 2022. As of July 31, 2023 and July 31, 2022, Cornerstone Pharmaceuticals owed the Company \$720 thousand, for which a full allowance for uncollectibility has been recorded.

Due to the Data Events, in the year ended July 31, 2022, the balance owed to the Company by Cornerstone Pharmaceuticals was fully reserved, resulting in a loss on related party receivable of \$720 thousand (see Note 4).

RAFAEL HOLDINGS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

NOTE 16 — RELATED PARTY TRANSACTIONS (cont.)

On March 21, 2023, the Company entered into a Promissory Note with Cornerstone Pharmaceuticals, wherein, Cornerstone Pharmaceuticals promises to pay the Company \$2 million together with all interest accrued on May 22, 2023, or such earlier date as the Promissory Note is required or permitted to be repaid (see Note 5). On May 22, 2023, the Promissory Note was amended to extend the maturity date to November 30, 2023 and to waive the interest increase (see Note 5).

Genie Energy, Ltd.

The Company leased office space at 520 Broad Street to Genie. The Company invoiced Genie approximately \$19 thousand which is included in discontinued operations during the year ended July 31, 2023. Genie pays the Company for payroll costs for certain personnel which totaled approximately \$10 thousand during the year ended July 31, 2023.

Related Party Rental Income

The Company leased space to related parties (including IDT Corporation — see above) which represented approximately 42% and 58% of the Company's total revenue for the years ended July 31, 2023 and 2022, respectively. The portion of related party rental income pertaining to the 520 Property has been classified in discontinued operations on the consolidated statements of operations and comprehensive loss for the years ended July 31, 2023 and 2022.

RP Finance

For the year ended July 31, 2023, the Company recognized \$0 from its ownership interests of 37.5% in RP Finance. For the year ended July 31, 2022, the Company recognized a loss of \$575 thousand in income from its ownership interests of 37.5% in RP Finance.

Howard Jonas, Chairman of the Board and Former Chief Executive Officer

In December 2020, IDT Corporation and Genie Energy Ltd, on whose Boards of Directors Howard Jonas, the Company's Chairman of the Board and Executive Chairman and former Chief Executive Officer serves, each purchased 218,245 shares of Class B common stock for consideration of \$5 million each. In connection with the purchases, each purchaser was granted warrants (the "Issued Warrants") to purchase twenty percent (20%) of the shares of Class B common stock purchased by such purchaser. The Issued Warrants have an exercise price of \$22.91 per share and expired on June 6, 2022. The Issued Warrants were not exercised. The shares and Issued Warrants were issued in reliance on the exemption from registration provided for under Section 4(a)(2) of the Securities Act of 1933, as amended.

On June 22, 2022, the Company entered into a Stock Purchase Agreement (the "I9 SPA") with I9 Plus, LLC, an entity affiliated with members of the family of Howard Jonas. On July 6, 2022, pursuant to the I9 SPA, the Company sold 3,225,806 shares of the Company's Class B common stock to I9 Plus, LLC at a price per share of \$1.86 and an aggregate sale price of \$6 million.

On July 31, 2023, eight trusts, each for the benefit of a child of Howard S. Jonas, the Company's Executive Chairman and Chairman of the Board, with independent trustees, transferred an aggregate of 787,163 shares of Class A common stock of the Company (representing all of the issued and outstanding shares of the Class A common stock of the Company, and 51.3% of the aggregate voting power of all issued and outstanding shares of capital stock of the Company) to a limited partnership. Howard Jonas is the sole manager of the sole general partner of the limited

RAFAEL HOLDINGS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

NOTE 16 — RELATED PARTY TRANSACTIONS (cont.)

partnership, and, therefore, has sole voting and dispositive power over the shares of Class A common stock held by the limited partnership. Following the transfer, Mr. Jonas will be the controlling stockholder of the Company and the Company is a controlled company as defined in Section 303A of the New York Stock Exchange Listed Company Manual.

LipoMedix Pharmaceuticals, Ltd.

As of the date of the LipoMedix SPA, on November 15, 2021, there was an outstanding loan balance including principal of \$400 thousand and accrued interest of \$21.8 thousand owed by LipoMedix to the Company on the note from March 2021. The amount due on the loan was netted against the \$3.0 million aggregate purchase price due LipoMedix, resulting in a cash payment by the Company of approximately \$2.6 million in exchange for the 15,975,000 shares purchased. As a result of the share purchase, the Company’s ownership of LipoMedix increased to approximately 84% with a noncontrolling interest of approximately 16%.

On February 9, 2023, the Company entered into a share purchase agreement with LipoMedix to purchase 70,000,000 ordinary shares at \$0.03 per share for an aggregate purchase price of \$2.1 million. As a result of the share purchase, the Company’s ownership of LipoMedix increased to approximately 95% with a noncontrolling interest of approximately 5%. The Company recorded approximately \$16 thousand to adjust the carrying amount of the noncontrolling interest to reflect the Company’s increased ownership interest in LipoMedix’s net assets.

Investment in Equity Securities

The Company entered into a Cooperation Agreement with Genie, IDT and trusts for the benefit of certain family members of Howard Jonas related to an investment in a third-party publicly traded company. Subsequently, the Company and Genie agreed to share the expenses related to the investment equally and each would retain any return from its own investments. The Company invested \$1.6 million in the third-party company and after selling a portion of its interest made a profit of \$309 thousand.

NOTE 17 — INCOME TAXES

At July 31, 2023, the Company had federal net operating loss (“NOL”) carryforwards from domestic operations of approximately \$63.2 million, to offset future taxable income, state NOLs of \$40.4 million, and NOLs from foreign operations of \$7.6 million. As part of the Tax Act, federal NOLs generated in 2018 and later are not subject to an expiration period and are available to offset 80% of taxable income in the year in which they are utilized. The federal NOL carryforwards generated prior to 2018 will begin to expire in 2026. The state NOLs will begin to expire in 2038 and foreign NOLs do not expire.

The components of loss from continuing operations before income taxes are as follows:

	For the Years Ended	
	July 31,	
	2023	2022
	<i>(in thousands)</i>	
Domestic	\$ (6,056)	\$ (137,978)
Foreign	(2,689)	(1,994)
Loss before income taxes	<u>\$ (8,745)</u>	<u>\$ (139,972)</u>

RAFAEL HOLDINGS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

NOTE 17 — INCOME TAXES (cont.)

Benefit from income taxes as presented in the consolidated statements of operations and comprehensive loss consisted of the following:

	For the Year Ended	
	July 31,	
	2023	2022
	<i>(in thousands)</i>	
Current:		
Foreign	\$ 19	\$ —
Federal	—	—
State	(274)	—
Total current expense (benefit)	(255)	—
Deferred:		
Foreign	—	—
Federal	—	—
State	—	—
Total deferred expense	—	—
Benefit from income taxes	\$ (255)	\$ —

The differences between income taxes expected at the U.S. federal statutory income tax rate attributable to pretax loss from continuing operations and income taxes attributable to pretax loss from continuing operations are reported as follows:

	At July 31,	
	2023	
	2023	2022
	<i>(in thousands)</i>	
U.S. federal income tax at statutory rate	\$ (1,877)	\$ (29,514)
State income tax	(479)	(8,752)
Valuation allowance	2,958	35,001
Foreign tax rate differential	(583)	(459)
Tax law change	—	—
Permanent differences	—	3,632
Rate change	—	—
Sale of state NOLs	(274)	—
Other	—	92
Benefit from income taxes	\$ (255)	\$ —

During the year ended July 31, 2023, the Company received proceeds of approximately \$274 thousand for the sale of the Company's 2018 and 2019 New Jersey tax credits through the New Jersey Technology Business Tax Certificate Transfer Program. The Company has not recorded U.S. income tax expense for foreign earnings because it has not generated any foreign earnings.

RAFAEL HOLDINGS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

NOTE 17 — INCOME TAXES (cont.)

Significant components of the Company's deferred tax assets and deferred tax liabilities are as follows:

	At July 31,	
	2023	2022
	<i>(in thousands)</i>	
Deferred tax assets:		
Net operating loss carryforwards	\$ 17,852	\$ 15,170
Unrealized gain/loss	30,236	31,850
Depreciation	(1)	1
R&D amortization.	689	—
Reserves and accruals.	237	236
Stock-based compensation	1,858	1,839
Gross deferred tax assets.	50,871	49,096
Less valuation allowance	(50,871)	(49,096)
Total deferred tax assets	—	—
Total deferred tax liabilities	—	—
Deferred tax assets, net	\$ —	\$ —

NOTE 18 — BUSINESS SEGMENT INFORMATION

The Company conducts business as two operating segments, Healthcare and Real Estate. The Company's reportable segments are distinguished by types of service, customers and methods used to provide their services. The operating results of these business segments are regularly reviewed by the Company's Chief Executive Officer who is the chief operating decision-maker.

The accounting policies of the segments are the same as the accounting policies of the Company as a whole. The Company evaluates the performance of its Healthcare segment based primarily on research and development efforts and results of clinical trials and the Real Estate segment based primarily on results of operations.

The Healthcare segment is comprised of preferred and common equity interests and the Warrant to purchase equity interests in Cornerstone Pharmaceuticals, a majority equity interest in LipoMedix, Barer, Farber, and Rafael Medical Devices. To date, the Healthcare segment has not generated any revenues.

The Real Estate segment consists of the Company's real estate holdings, which is currently comprised of a portion of a commercial building in Israel. The revenue, (loss) income from operations, and (loss) income before taxes of the 520 Property have been excluded from the Real Estate segment in the figures below due to its classification of held-for-sale and discontinued operations, and the sale of the 520 Property on August 22, 2022.

Operating results for the business segments of the Company are as follows:

<i>(in thousands)</i>	Healthcare	Real Estate	Total
Year Ended July 31, 2023			
Revenues	\$ —	\$ 279	\$ 279
(Loss) income from operations	(15,121)	78	(15,043)
Year Ended July 31, 2022			
Revenues	\$ —	\$ 410	\$ 410
(Loss) income from operations	(60,658)	181	(60,477)

RAFAEL HOLDINGS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

NOTE 18 — BUSINESS SEGMENT INFORMATION (cont.)

Geographic Information

Revenues from tenants located outside of the United States were generated entirely from related parties located in Israel. Revenues from these non-U.S. customers as a percentage of total revenues, which are inclusive of revenue from discontinued operations, were as follows (revenues by country are determined based on the location of the related facility):

Year Ended July 31,	2023	2022
Revenue from tenants located in Israel	53%	7%

Net property, plant, and equipment and total assets held outside of the United States, which are located in Israel, were as follows:

<i>(in thousands)</i>	United States	Israel	Total
July 31, 2023			
Property, plant, and equipment, net	\$ 293	\$ 1,402	\$ 1,695
Total assets	<u>95,244</u>	<u>3,585</u>	<u>98,829</u>
July 31, 2022			
Property, plant, and equipment, net	\$ 305	\$ 1,465	\$ 1,770
Total assets	<u>114,053</u>	<u>4,267</u>	<u>118,320</u>

NOTE 19 — COMMITMENTS AND CONTINGENCIES

Legal Proceedings

The Company may from time to time be subject to legal proceedings that may arise in the ordinary course of business. Although there can be no assurance in this regard, the Company does not expect any of those legal proceedings to have a material adverse effect on the Company's results of operations, cash flows or financial condition.

In December 2022, Broad Atlantic entered into a settlement agreement with a vendor providing for the payment by the Company of \$113 thousand representing payment in full for repair work done on the premises prior to our sale of the 520 Property. This amount is included in discontinued operations on the consolidated statements of operations and comprehensive loss.

NOTE 20 — EQUITY

Share Repurchase Program

In April 2023, the Company's Board of Directors approved a share repurchase program (the "2023 Share Repurchase Program") authorizing the repurchase of up to \$5 million of the Company's Class B common stock. Under the 2023 Share Repurchase Program, which took effect on April 14, 2023, the Company may purchase its shares from time to time until the earlier of June 16, 2023 (the "Plan Termination Date") or when \$5 million worth of shares at \$1.75 per share or below have been purchased. In July 2023, the 2023 Share Repurchase Program was amended to extend the Plan Termination Date to the earlier of July 1, 2024, or when \$5 million worth of shares at \$1.75 per share or below have been purchased.

The timing and amount of any share repurchases under the 2023 Share Repurchase Program will be determined at the Company's discretion and based on market conditions and other considerations. Share repurchases under the authorizations may be made through open market purchases or pursuant to pre-set trading plans meeting the requirements of Rule 10b5-1 under the Securities Exchange Act of 1934. The program does not obligate the Company to acquire any particular amount of its Class B common stock, and the repurchase program may be suspended or discontinued at any time at the Company's discretion.

During the year ended July 31, 2023, the Company did not repurchase any of its Class B common stock.

RAFAEL HOLDINGS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

NOTE 20 — EQUITY (cont.)

Class A Common Stock and Class B Common Stock

The rights of holders of Class A common stock and Class B common stock are identical except for certain voting and conversion rights and restrictions on transferability. The holders of Class A common stock and Class B common stock receive identical dividends per share when and if declared by the Company's Board of Directors. In addition, the holders of Class A common stock and Class B common stock have identical and equal priority rights per share in liquidation. The Class A common stock and Class B common stock do not have any other contractual participation rights. The holders of Class A common stock are entitled to three votes per share and the holders of Class B common stock are entitled to one-tenth of a vote per share. Each share of Class A common stock may be converted into one share of Class B common stock, at any time, at the option of the holder. Shares of Class A common stock are subject to certain limitations on transferability that do not apply to shares of Class B common stock.

On May 27, 2021, the Company filed a Registration Statement on Form S-3, whereby the Company may sell up to \$250 million of Class B common stock. This Registration Statement was declared effective on June 7, 2021.

On June 1, 2021, the Company filed a Registration Statement on Form S-3 to issue 48,859 shares of Class B common stock for payment due on the purchase of Altira, an investment which has been subsequently fully impaired.

On August 19, 2021, the Company entered into a Securities Purchase Agreement (the "Institutional Purchase Agreement") with Institutional Investors and a Securities Purchase Agreement with I9Plus, LLC, (the "Jonas Purchase Agreement"), an entity affiliated with Howard S. Jonas, the Chairman of the Board of Directors of the Company. On August 24, 2021, the Company issued 2,833,425 shares of Class B common stock (the "Institutional Shares"), par value \$0.01 per share, to the Institutional Investors, at a purchase price equal to \$35.00 per share, for aggregate gross proceeds of approximately \$99.2 million, before deducting placement agent fees and other offering expenses. Additionally, pursuant to the Jonas Purchase Agreement, the Company issued 112,501 shares of Class B common stock to I9Plus, LLC, at a purchase price equal to \$44.42 per share, which was equal to the closing price of a share of the Class B common stock on the New York Stock Exchange on August 19, 2021 (the "Jonas Offering"). The Jonas Offering resulted in additional aggregate gross proceeds of approximately \$5.0 million. The total net proceeds from the issuance of shares was \$98.0 million after deducting transaction costs of \$6.2 million.

On August 19, 2021, in connection with the Institutional Purchase Agreement, the Company entered into a Registration Rights Agreement with the Institutional Investors whereby the Company agreed to prepare and file a registration statement with the SEC within 30 days after the earlier of (i) the date of the closing of the Merger Agreement, and (ii) the date the Merger Agreement is terminated in accordance with its terms, for purposes of registering the resale of the Institutional Shares and any shares of Class B common stock issued as a dividend or other distribution with respect to the Institutional Shares.

The 2018 Equity Incentive Plan was created and adopted by the Company in March 2018. On January 19, 2022, the Company's stockholders approved the 2021 Equity Incentive Plan (the "2021 Plan"). The 2018 Equity Incentive Plan was suspended and replaced by the 2021 Plan, and, following January 19, 2022, no new grants are to be awarded under the 2018 Equity Incentive Plan. Existing grants under the 2018 Equity Incentive Plan will not be impacted by the adoption of the 2021 Plan. Any of the Company's employees, directors, consultants, and other service providers, and those of the Company's affiliates, are eligible to participate in the 2021 Plan. In accordance with applicable tax rules, only employees (and the employees of parent or subsidiary corporations) are eligible to be granted incentive stock options. The 2021 Plan authorizes stock options (both incentive stock options or non-qualified stock options), stock appreciation rights, restricted stock, restricted stock units, and cash or other stock-based awards. On January 19, 2022, the Company filed a Registration Statement on Form S-8 registering 1,919,025 shares Class B Common Stock reserved for issuance under the 2021 Plan. On November 28, 2022, the Company's Board of Directors approved an amendment to the 2021 Plan that, among other things, increases the number of shares of the Company's Class B Common Stock available for the grant of awards thereunder by an additional 696,770, which the stockholders approved on January 23, 2023. The maximum number of shares of Class B common stock that may be issued under the 2021 Plan is 2,615,795 shares. As of July 31, 2023, there were 953,516 shares still available for issuance under the 2021 Plan.

RAFAEL HOLDINGS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

NOTE 20 — EQUITY (cont.)

On February 15, 2022, the Company filed a Registration Statement on Form S-3 (as amended on March 2, 2022) registering the resale by institutional investors (the “Institutional Investors”) of the shares purchased by them. The Registration Statement was declared effective on March 7, 2022.

On June 22, 2022, the Company entered into a Stock Purchase Agreement (the “I9 SPA”) with I9 Plus. On July 6, 2022, pursuant to the I9 SPA, the Company sold 3,225,806 shares of the Company’s Class B common stock to I9 Plus at a price per share of \$1.86 and an aggregate sale price of \$6 million, presented in common stock sold to related party within the statement of stockholders’ equity. The price per share was calculated to be the greater of (1) the volume weighted average price for the Class B common stock on the New York Stock Exchange for the five trading days ending on June 21, 2022 (which were the five trading days beginning with the first full trading day following the date that the transaction was approved by the Board of Directors of the Company, and its Corporate Governance Committee which consists solely of independent members of the Board) and (2) the closing price of the Class B common stock on June 21, 2022 (the trading day immediately preceding the date of the I9 SPA to ensure that the sale price was not below the Minimum Price under NYSE Rule 312.03(b)). The shares were issued in reliance on the exemption from registration provided for under Section 4(a)(2) of the Securities Act of 1933, as amended.

Employment Agreement

On June 13, 2022, the Company entered into an employment agreement with Howard S. Jonas (who serves as the Chairman of the Board and Executive Chairman of the Company) (the “Employment Agreement”), which provides, among other things: (i) a term of five years (subject to extension unless either party elects not to renew); (ii) an annual base salary of \$260,000, of which \$250,000 is payable through the issuance of restricted shares of the Company’s Class B common stock (“Class B Stock”) with the value of the shares based upon the volume weighted closing price of the Class B Stock on the NYSE on the thirty days ending with the NYSE trading day immediately preceding the issuance to be issued within thirty days of the date of the Employment Agreement (the “Start Date”) and each annual anniversary, and such shares vesting, contingent on Mr. Jonas’ remaining in continuous service to the Company, in substantially equal amounts on the three, six, nine and twelve month anniversaries of the Start Date or annual anniversary; and (iii) a grant of restricted shares of Class B stock with a value of \$600,000, issuable within 30 days with the value of the shares based upon the volume weighted closing price of the Class B Stock on the NYSE on the thirty days ending with the NYSE trading day immediately preceding the issuance and such shares, and vesting, contingent on Mr. Jonas’ remaining in continuous service to the Company, in substantially equal amounts on the first and second annual anniversaries of the Start Date.

Stock Options

A summary of stock option activity for the Company is as follows:

	Number of Options	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding at July 31, 2021	683,414	\$ 11.13	3.05	\$ 26,982
Granted	518,304	20.54	9.25	—
Cancelled/Forfeited	(180,441)	—	—	—
Outstanding at July 31, 2022	1,021,277	12.11	4.47	—
Granted	175,000	2.08	9.51	—
Expired	(589,205)	—	—	—
Cancelled/Forfeited	(218,663)	—	—	—
Outstanding at July 31, 2023	388,409	\$ 14.51	8.71	\$ —
Exercisable at July 31, 2023	65,456	\$ 20.98	8.13	\$ —

RAFAEL HOLDINGS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

NOTE 20 — EQUITY (cont.)

At July 31, 2023, there is unrecognized compensation costs related to non-vested stock options of \$1.3 million, which are expected to be recognized over the next 3.2 years.

The value of option grants is calculated using the Black-Scholes option pricing model with the following assumptions for options granted during the years ended July 31, 2023 and 2022:

	For the Year Ended July 31,	
	2023	2022
Risk-free interest rate	3.60% – 3.66%	0.67% – 1.7%
Expected term (in years)	6.11	6.04 – 6.11
Expected volatility	95.00%	75% – 93%
Expected dividend yield	—%	—%

The options granted had a \$1.58 and \$3.29 weighted average grant date fair value during the years ended July 31, 2023 and 2022, respectively.

Rafael Medical Devices, Inc. Stock Options

The Rafael Medical Devices, Inc. 2022 Equity Incentive Plan (the “RMD 2022 Plan”) was created and adopted by the Company in May 2022. The RMD 2022 Plan allows for the issuance of up to 10,000 shares of Class B common stock which may be awarded in the form of incentive stock options or restricted shares. There are 4,734 shares available for issuance under the RMD 2022 Plan as of July 31, 2023.

The fair value of Rafael Medical Devices, LLC common stock was estimated for financial reporting purposes based on a valuation of \$4.02 per share as of January 31, 2022. To determine the fair value of the common stock, the Company first determined an enterprise value using accepted valuation approaches; adjusted these valuation approaches with relevant discounts and then allocated the equity value to the common stock and common stock equivalents on a fully diluted basis. The enterprise value was estimated using the generally accepted income approach. The income approach estimates enterprise value based on the estimated present value of future cash flows the business is expected to generate over its remaining life. The estimated present value is calculated using a discount rate reflective of the risks associated with an investment in a similar company in a similar industry or having a similar history of revenue growth. The Company then subtracted the net non-operating assets and applied a discount for lack of marketability to determine equity fair value.

A summary of stock option activity for Rafael Medical Devices, Inc. is as follows:

	Number of Options	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding at July 31, 2021.	—	\$ —	—	\$ —
Granted	5,266	3.82	9.76	—
Outstanding at July 31, 2022.	5,266	\$ 3.82	9.76	\$ —
Granted	—	—	—	—
Outstanding at July 31, 2023	5,266	\$ 3.82	8.76	—
Exercisable at July 31, 2023	2,633	\$ 3.82	8.76	\$ —

At July 31, 2023, there are unrecognized compensation costs related to non-vested stock options of \$5 thousand, which are expected to be recognized over the next 1.44 years.

RAFAEL HOLDINGS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

NOTE 20 — EQUITY (cont.)

Restricted Stock

The fair value of restricted shares of the Company’s Class B common stock is determined based on the closing price of the Company’s Class B common stock on the grant date. Share awards generally vest on a graded basis over three years of service.

In January 2022, the Company granted 33,360 restricted shares of Class B common stock to non-employee directors, 18,336 of which were granted under the 2018 Equity Incentive Plan, and 15,024 of which were granted under the 2021 Plan. The restricted shares vested immediately on the grant date. The share based compensation cost was approximately \$151 thousand, which was included in general and administrative expense in the consolidated statement of operations and comprehensive loss.

On February 1, 2022, the Company issued 986,835 shares of Class B restricted stock to two members of the executive team. Approximately 24% of the restricted shares vest in December 2022, with the remaining shares vesting ratably each quarter through December 2025.

On June 14, 2022, the Company issued 452,130 shares of Class B restricted stock to Howard S. Jonas.

In January 2023, the Company issued 120,019 shares of Class B restricted stock to certain members of its Board of Directors, and 100,000 shares of Class B restricted stock to its new Chief Financial Officer.

During January 2023, 296,759 shares of Class B restricted stock were cancelled or forfeited due to (i) the cancellation of 285,036 shares of restricted stock in connection with the departure of the Company’s former Chief Financial Officer and (ii) the remaining shares forfeited upon the termination of certain employees of the Company.

In connection with Patrick Fabbio’s January 27, 2023 departure as the Company’s Chief Financial Officer, the Company and Mr. Fabbio entered into a Separation and General Release Agreement (the “Separation Agreement”), which provides, among other things, that the Company shall pay Mr. Fabbio severance in the amount of \$307,913, which is included in selling, general and administrative expense on the consolidated statement of operations and comprehensive loss for the year ended July 31, 2023.

In connection with the termination of Mr. Fabbio’s position as Chief Financial Officer of the Company, there was a material forfeiture of his Class B restricted shares and stock options resulting in a reversal of approximately \$915 thousand in stock-based compensation expense for the year ended July 31, 2023 that was previously recorded to selling, general and administrative expense.

A summary of the status of the Company’s grants of restricted shares of Class B common stock is presented below:

	Number of Non-vested Shares	Weighted Average Grant Date Fair Value
Outstanding at July 31, 2021.....	1,007,975	\$ 46.77
Granted	1,533,311	4.24
Vested	(90,608)	16.86
Cancelled/Forfeited.....	(943,305)	(48.50)
Outstanding at July 31, 2022.....	1,507,373	\$ 4.22
Granted	220,019	1.99
Vested	(745,867)	3.37
Cancelled/Forfeited.....	(296,759)	(5.10)
Non-vested shares at July 31, 2023	684,766	\$ 4.04

At July 31, 2023, there was \$1.8 million of total unrecognized compensation cost related to non-vested stock-based compensation arrangements, which is expected to be recognized over the next four years.

RAFAEL HOLDINGS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

NOTE 20 — EQUITY (cont.)

On November 21, 2021, Ameet Mallik resigned as Chief Executive Officer of the Company, effective January 31, 2022. In connection with his resignation, there was a material forfeiture of the former CEO’s Class B restricted shares, resulting in a reversal of approximately \$19.0 million in stock-based compensation expense that was previously recorded to selling, general and administrative expense. Additionally, pursuant to the terms of his employment agreement, the Company paid \$5.0 million relating to his severance payout, which is included in selling, general and administrative expense on the consolidated statement of operations and comprehensive loss for the year ended July 31, 2022.

A summary of the stock-based compensation expense for the Company’s equity incentive plans is presented below (in thousands):

	For the Year Ended	
	July 31,	
	2023	2022
General and administrative	\$ 3,044	\$ 17,270
Research and development	194	791
Forfeiture of RSUs within general and administrative	(931)	(18,978)
Forfeiture of RSUs within research and development	(119)	—
Net stock-based compensation expense	\$ 2,188	\$ (917)

Securities Purchase Agreement

On December 7, 2020, Rafael Holdings entered into a Securities Purchase Agreement (the “SPA”) for the sale of 567,437 shares of the Company’s Class B common stock at a price per share of \$22.91 (which was the closing price for the Class B common stock on the New York Stock Exchange on December 4, 2020, the trading day immediately preceding the date of the SPA) for an aggregate purchase price of \$13 million.

Approximately \$8.2 million of the proceeds received pursuant to the SPA were used by the Company to exercise an additional portion of the Warrant in order to maintain the Company’s relative position in Cornerstone Pharmaceuticals in light of issuances of Cornerstone Pharmaceuticals equity securities to third-party shareholders of Cornerstone Pharmaceuticals, due to warrant exercises by these shareholders. The Company is using the remaining proceeds to fund the operations of its drug development programs including its Barer Institute subsidiary, and for general corporate purposes. Under the SPA, two entities, on whose Boards of Directors Howard Jonas, the Registrant’s Chairman of the Board and former Chief Executive Officer serves, each purchased 218,245 shares of Class B common stock for consideration of \$5 million each. The shares and warrants were issued in reliance on the exemption from registration provided for under Section 4(a)(2) of the Securities Act of 1933, as amended.

Equity-classified Warrants

In connection with the SPA entered into on December 7, 2020, each purchaser was granted warrants to purchase twenty percent (20%) of the shares of Class B common stock purchased by such purchaser. The Company issued warrants to purchase 113,487 shares of Class B common stock to the purchasers. The warrants are exercisable at a per share exercise price of \$22.91, and are exercisable at any time on or after December 7, 2020 through June 6, 2022. The Company determined that these warrants are equity-classified.

During fiscal 2021, IDT and Genie each exercised 43,649 warrants, resulting in a total of 87,298 shares of Class B common stock issued for proceeds of approximately \$2 million.

On June 6, 2022, the Company’s outstanding warrants to purchase 26,189 shares of common stock at an exercise price of \$22.91 per share expired. There were no exercises of warrants during the year ended July 31, 2022. At July 31, 2022, the Company had no outstanding warrants.

RAFAEL HOLDINGS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

NOTE 21 — LEASES

The Company is the lessor of the Israeli property which is leased to tenants under net operating leases with a term expiration date within 2025. Lease income included on the consolidated statements of operations and comprehensive loss was \$0.3 million and \$0.3 million for the years ended July 31, 2023 and 2022, respectively. During the years ended July 31, 2023 and 2022, no real estate property taxes were included in rental income.

The future contractual minimum lease payments to be received (excluding operating expense reimbursements) by the Company as of July 31, 2023, under non-cancellable operating leases which expire on various dates through 2025 are as follows:

<u>Year ending July 31,</u>	<u>Related Parties</u>	<u>Other</u>	<u>Total</u>
		<i>(in thousands)</i>	
2024.	\$ 77	\$ —	\$ 77
2025.	78	—	78
Total Minimum Future Rental Income	<u>\$ 155</u>	<u>\$ —</u>	<u>\$ 155</u>

A related party has the right to terminate the Israeli lease upon four months' notice.

NOTE 22 — SUBSEQUENT EVENTS

Issuance of Class B Common Stock

On August 28, 2023, the Company granted 111,408 restricted shares of Class B common stock of the Company to Howard Jonas, the Chairman of the Board and Executive Chairman and former Chief Executive Officer of the Company and Member of the Board of Cornerstone Pharmaceuticals, pursuant to his employment agreement.

Rafael Medical Devices, LLC outside party investment

During the fourth quarter of the year ended July 31, 2023, the Company received \$825 thousand as a deposit from outside third party investors for the purchase of membership units of Rafael Medical Devices, LLC. On August 1, 2023, the Company received an additional \$100 thousand and closed on the sale of units in exchange of \$925 thousand, whereby the Company will now hold 53.4% (on a fully diluted basis) ownership interests in Rafael Medical Devices, LLC. As of July 31, 2023, the Company recorded the funds received within prepaid expenses and other current assets and other current liabilities within the consolidated balance sheets.

