	Year Ended December 31,				
	2016	2017	2018	2019	2020
Consolidated Statements Of Operations Data:	(USD in thousands, except share and per share data)				
Revenues	165	789	3,820	2,032	763
Operating expenses:					
Research and development expenses, net	(6,115)	(5,106)	(6,075)	(10,976)	(11,951)
General and administrative expenses	(2,733)	(2,868)	(3,159)	(3,063)	(2,951)
Operating loss	(8,683)	(7,185)	(5,414)	(12,007)	(14,139)
Other income	-	769	-	-	-
Financial expenses	(319)	(1,603)	(1,153)	(618)	(304)
Financial income					
Taxes on income	(29)	(29)	(4)	-	-
Net loss	(8,393)	(4,842)	(6,571)	(12,625)	(14,443)
Adjustments arising from translating financial statements from functional currency to presentation currency	119	636	-	-	-
Remeasurements loss from defined benefit plan	-	-	-	-	-
Comprehensive loss	(8,274)	(4,206)	(6,571)	(12,625)	(14,443)
Net loss per ordinary share	(0.30)	(0.14)	(0.17)	(0. 14)	(0.04)
Number of ordinary shares used in computing loss per ordinary share	27,692,668	32,525,138	38,902,214	85,909,859	358,411,297

	As of December 31,				
	2016	2017	2018	2019	2020
Consolidated Balance Sheet Data:	USD in thousands				
Cash and cash equivalents	8,115	3,505	3,615	2,697	8,268
Other receivables and lease deposit	2,017	3,164	4,017	4,383	1,057
Short-term investment	-	-	273	64	75
long-term investments	-	917	-	-	-
Right to use asset	-	-	-	83	73
Other non-current receivables	-	-	-	912	-
Fixed assets	40	28	47	36	50
Total assets	10,172	7,614	7,952	8, 174	9,523
Total liabilities	4,211	2,600	4,937	5,732	3,449
Total shareholders’ equity	5,961	5,014	3,015	2,442	6,074

B. Capitalization and Indebtedness.

Not applicable.

C. Reasons for the Offer and Use of Proceeds.

Not applicable.

D. Risk Factors

You should carefully consider the risks we describe below, in addition to the other information set forth elsewhere in this Annual Report on Form 20-F, including our consolidated financial statements and the related notes beginning on page F-1, before deciding to invest in our ordinary shares and American Depositary Shares, or ADSs. These material risks could adversely impact our results of operations, possibly causing the trading price of our ordinary shares and ADSs to decline, and you could lose all or part of your investment.

Summary Risk Factors

The principal factors and uncertainties that make investing in our ordinary shares risky, include, among others:

Risks Related to Our Financial Position and Capital Requirements

- We have incurred operating losses since our inception and anticipate that we will continue to incur substantial operating losses for the foreseeable future.
- We will need to raise additional capital to meet our business requirements in the future, and such capital raising may be costly or difficult to obtain and will dilute current shareholders' ownership interests.

Risks Related to Our Business and Regulatory Matters

- Our business may be adversely affected by the impact of COVID-19.
- We have not yet commercialized any products or technologies, and we may never become profitable.
- Our product candidates are at various stages of clinical and preclinical development and may never be commercialized.
- Results of earlier clinical trials may not be predictive of the results of later-stage clinical trials.
- We might be unable to develop product candidates that will achieve commercial success in a timely and cost-effective manner, or ever.
- Our current pipeline is based on our platform technology utilizing the Gi protein associated A3AR, as a potent therapeutic target and currently includes three molecules, Piclidenoson, Namodenoson and CF602 product candidates, of which Piclidenoson is the most advanced. Failure to develop these molecules will have a material adverse effect on us.
- Clinical trials are very expensive, time-consuming and difficult to design and implement, and, as a result, we may suffer delays or suspensions in future trials which would have a material adverse effect on our ability to generate revenues.
- The manufacture of our product candidates is a chemical synthesis process and if one of our materials suppliers encounters problems manufacturing our products, our business could suffer.
- We do not currently have sales, marketing or distribution capabilities or experience, and we are unable to effectively sell, market or distribute our product candidates now and we do not expect to be able to do so in the future. The failure to enter into agreements with third parties that are capable of performing these functions would have a material adverse effect on our business and results of operations.
- We depend on key members of our management and key consultants and will need to add and retain additional leading experts. Failure to retain our management and consulting team and add additional leading experts could have a material adverse effect on our business, results of operations or financial condition.
- Our product candidates will remain subject to ongoing regulatory requirements even if they receive marketing approval, and if we fail to comply with these requirements, we could lose these approvals, and the sales of any approved commercial products could be suspended.
- We may not be able to successfully grow and expand our business. Failure to manage our growth effectively will have a material adverse effect on our business, results of operations and financial condition.
- Our cannabinoid initiative is uncertain and may not yield commercial results and is subject to significant regulatory risks.
- We or the third parties upon whom we depend may be adversely affected by natural disasters and/or health epidemics, and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Risks Related to Our Intellectual Property

- We license from Leiden University intellectual property, which protects certain small molecules which target the A3AR, in furtherance of our platform technology, and we could lose our rights to this license if a dispute with Leiden University arises or if we fail to comply with the financial and other terms of the license.

- The failure to obtain or maintain patents, licensing agreements, including our current licensing agreements, and other intellectual property could impact our ability to compete effectively.

- International patent protection is particularly uncertain, and if we are involved in opposition proceedings in foreign countries, we may have to expend substantial sums and management resources.

- We may be unable to protect the intellectual property rights of the third parties from whom we license certain of our intellectual property or with whom we have entered into other strategic relationships.

- Under applicable U.S. and Israeli law, we may not be able to enforce covenants not to compete and therefore, may be unable to prevent our competitors from benefiting from the expertise of some of our former employees. In addition, employees may be entitled to seek compensation for their inventions irrespective of their agreements with us, which in turn could impact our future profitability.

- We may be subject to claims challenging the inventorship of our patents and other intellectual property.

Risks Related to Our Industry

- We expect the healthcare industry to face increased limitations on reimbursement as a result of healthcare reform, which could adversely affect third-party coverage of our products and how much or under what circumstances healthcare providers will prescribe or administer our products.

- Our employees, principal investigators, consultants, commercial partners or vendors may engage in misconduct or other improper activities, including non-compliance with regulatory standards.

Risks Related to Our Operations in Israel

- We conduct our operations in Israel and therefore our results may be adversely affected by political, economic and military instability in Israel and its region.

- Because a certain portion of our expenses is incurred in currencies other than U.S. dollars, our results of operations may be harmed by currency fluctuations and inflation.

Risks Related to Our Ordinary Shares and ADSs

- Our business could be negatively impacted by unsolicited takeover proposals, by shareholder activism or by proxy contests relating to the election of directors or other matters.

- Issuance of additional equity securities may adversely affect the market price of our ADSs or ordinary shares.

- The market price of our ordinary shares and ADSs is subject to fluctuation, which could result in substantial losses by our investors.

- We may not satisfy the NYSE American requirements for continued listing. If we cannot satisfy these requirements, the NYSE American could delist our securities.

- As a foreign private issuer, we are permitted to follow certain home country corporate governance practices instead of applicable SEC and NYSE American requirements, which may result in less protection than is accorded to investors under rules applicable to domestic issuers.

Risks Related to Our Financial Position and Capital Requirements

We have incurred operating losses since our inception and anticipate that we will continue to incur substantial operating losses for the foreseeable future.

We are a clinical-stage biopharmaceutical company focused on developing orally bioavailable small molecule therapeutic products for the treatment of cancer, liver, inflammatory diseases, COVID-19 and erectile dysfunction. Since our incorporation in 1994, we have been focused on research and development activities with a view to developing our product candidates, CF101, also known as Piclidenoson, CF102, also known as Namodenoson, and CF602. We have financed our operations primarily through the sale of equity securities (both in private placements and in public offerings on the TASE and NYSE American) and payments received under out-licensing agreements and have incurred losses in each year since our inception in 1994. We have historically incurred substantial net losses, including net losses of approximately $14.4 million in 2020, $12.6 million in 2019, and $6.6 million in 2018. As of December 31, 2020, we had an accumulated deficit of approximately $125.5 million. We do not know whether or when we will become profitable. To date, we have not commercialized any products or generated any revenues from product sales and accordingly we do not have a revenue stream to support our cost structure. Our losses have resulted principally from costs incurred in development and discovery activities. We expect to continue to incur losses for the foreseeable future, and these losses will likely increase as we:

- initiate and manage pre-clinical development and clinical trials for our current and new product candidates;
- seek regulatory approvals for our product candidates;
- implement internal systems and infrastructures;
- seek to license additional technologies to develop;
- hire management and other personnel; and
- move towards commercialization.

If our product candidates fail in clinical trials or do not gain regulatory clearance or approval, or if our product candidates do not achieve market acceptance, we may never become profitable. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our inability to achieve and then maintain profitability would negatively affect our business, financial condition, results of operations and cash flows. Moreover, our prospects must be considered in light of the risks and uncertainties encountered by an early-stage company and in highly regulated and competitive markets, such as the biopharmaceutical market, where regulatory approval and market acceptance of our products are uncertain. There can be no assurance that our efforts will ultimately be successful or result in revenues or profits.

We will need to raise additional capital to meet our business requirements in the future, and such capital raising may be costly or difficult to obtain and will dilute current shareholders' ownership interests.

As of December 31, 2020 we had cash and cash equivalents of $8.3 million. We believe that our existing financial resources will be sufficient to meet our requirements for the next twelve months from the date of issuance of this Annual Report on Form 20-F. We have expended and believe that we will continue to expend substantial resources for the foreseeable future developing our product candidates. These expenditures will include costs associated with research and development, manufacturing, conducting preclinical experiments and clinical trials and obtaining regulatory approvals, as well as commercializing any products approved for sale. Because the outcome of our planned and anticipated clinical trials is highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development and commercialization of our product candidates. In addition, other unanticipated costs may arise. As a result of these and other factors currently unknown to us, we will require additional funds, through public or private equity or debt financings or other sources, such as strategic partnerships and alliances and licensing arrangements. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans.

Our future capital requirements will depend on many factors, including the progress and results of our clinical trials, the duration and cost of discovery and preclinical development, and laboratory testing and clinical trials for our product candidates, the timing and outcome of regulatory review of our product candidates, the number and development requirements of other product candidates that we pursue, and the costs of activities, such as product marketing, sales, and distribution. Because of the numerous risks and uncertainties associated with the development and commercialization of our product candidates, we are unable to estimate the amounts of increased capital outlays and operating expenditures associated with our anticipated clinical trials.

Our future capital requirements depend on many factors, including:

- the level of research and development investment required to develop our product candidates;
- the failure to obtain regulatory approval or achieve commercial success of our product candidates, including Piclidenoson, Namodenoson and CF602;
- the results of our preclinical studies and clinical trials for our earlier stage product candidates, and any decisions to initiate clinical trials if supported by the preclinical results;
- the costs, timing and outcome of regulatory review of our product candidates that progress to clinical trials;
- our ability to partner or sub-license any of our product candidates;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our issued patents and defending intellectual property-related claims;
- the cost of commercialization activities if any of our product candidates are approved for sale, including marketing, sales and distribution costs;
- the cost of manufacturing our product candidates and any products we successfully commercialize;
- the timing, receipt and amount of sales of, or royalties on, our future products, if any;
- the expenses needed to attract and retain skilled personnel;
- any product liability or other lawsuits related to our products;
- the extent to which we acquire or invest in businesses, products or technologies and other strategic relationships;
- the costs of financing unanticipated working capital requirements and responding to competitive pressures; and
- maintaining minimum shareholders’ equity requirements and complying with other continue listing standards under the NYSE American Company Guide.

Additional funds may not be available when we need them, on terms that are acceptable to us, or at all. General market conditions may make it very difficult for us to seek financing from the capital markets and the recent COVID-19 outbreak could impact the availability or cost of future financings. If adequate funds are not available to us on a timely basis, we may be required to delay, limit, reduce or terminate preclinical studies, clinical trials or other research and development activities for one or more of our product candidates or delay, limit, reduce or terminate our establishment of sales and marketing capabilities or other activities that may be necessary to commercialize our product candidates.

We may incur substantial costs in pursuing future capital financing, including investment banking fees, legal fees, accounting fees, securities law compliance fees, printing and distribution expenses and other costs. We may also be required to recognize non-cash expenses in connection with certain securities we issue, such as convertible notes and warrants, which may adversely impact our financial condition.

Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.

We may seek additional capital through a combination of private and public equity offerings, debt financings, strategic partnerships and alliances and licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interests of existing shareholders will be diluted, and the terms may include liquidation or other preferences that adversely affect shareholder rights. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take certain actions, such as incurring debt, making capital expenditures or declaring dividends. If we raise additional funds through strategic partnerships and alliances and licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies or product candidates, or grant licenses on terms that are not favorable to us. If we are unable to raise additional funds through equity or debt financing when needed, we may be required to delay, limit, reduce or terminate our product development or commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Risks Related to Our Business and Regulatory Matters

Our business may be adversely affected by the impact of COVID-19.

Public health epidemics or outbreaks could adversely impact our business. In late 2019, a novel strain of COVID-19, also known as coronavirus, was reported in Wuhan, China. Initially the outbreak was largely concentrated in China, but it rapidly spread to countries across the globe, including in Israel and the United States. Many countries around the world, including in Israel and the United States, implemented significant governmental measures to control the spread of the virus, including temporary closure of businesses, severe restrictions on travel and the movement of people, and other material limitations on the conduct of business. In response, we implemented remote working and workplace protocols for our employees in accordance Israeli Ministry of Health requirements to ensure employee safety. The extent to which COVID-19 impacts our operations will depend on future developments, which are highly uncertain and cannot be predicted with confidence, including the duration and severity of the outbreak, and the actions that may be required to contain COVID-19 or treat its impact. In particular, the continued spread of the coronavirus globally, could adversely impact our operations and workforce, including our research and clinical trials and our ability to raise capital, could affect the operations of key governmental agencies, such as the FDA, which may delay the development of our product candidates and could result in the inability of our suppliers to deliver components or raw materials on a timely basis or at all, each of which in turn could have an adverse impact on our business, financial condition and results of operation.

We have not yet commercialized any products or technologies, and we may never become profitable.

We have not yet commercialized any products or technologies, and we may never be able to do so. We do not know when or if we will complete any of our product development efforts, obtain regulatory approval for any product candidates incorporating our technologies or successfully commercialize any approved products. Even if we are successful in developing products that are approved for marketing, we will not be successful unless these products gain market acceptance for appropriate indications at favorable reimbursement rates. The degree of market acceptance of these products will depend on a number of factors, including:

- the timing of regulatory approvals in the countries, and for the uses, we seek;
- the competitive environment;
- the establishment and demonstration in the medical community of the safety and clinical efficacy of our products and their potential advantages over existing therapeutic products;
- our ability to enter into distribution and other strategic agreements with pharmaceutical and biotechnology companies with strong marketing and sales capabilities;
- the adequacy and success of distribution, sales and marketing efforts; and
- the pricing and reimbursement policies of government and third-party payors, such as insurance companies, health maintenance organizations and other plan administrators.

Physicians, patients, thirty-party payors or the medical community in general may be unwilling to accept, utilize or recommend, and in the case of third-party payors, cover any of our products or products incorporating our technologies. As a result, we are unable to predict the extent of future losses or the time required to achieve profitability, if at all. Even if we successfully develop one or more products that incorporate our technologies, we may not become profitable.

Our product candidates are at various stages of clinical and preclinical development and may never be commercialized.

Our product candidates are at various stages of clinical development and may never be commercialized. The progress and results of any future pre-clinical testing or future clinical trials are uncertain, and the failure of our product candidates to receive regulatory approvals will have a material adverse effect on our business, operating results and financial condition to the extent we are unable to commercialize any products. None of our product candidates has received regulatory approval for commercial sale. In addition, we face the risks of failure inherent in developing therapeutic products. Our product candidates are not expected to be commercially available for several years, if at all.

In order to receive FDA approval or approval from foreign regulatory authorities to market a product candidate or to distribute our products, we must demonstrate thorough pre-clinical testing and thorough human clinical trials that the product candidate is safe and effective for its intended uses (e.g., treatment of a specific condition in a specific way subject to contraindications and other limitations). If the FDA, or foreign regulatory authorities, determine that data from our pre-clinical testing and clinical trials are not sufficient to support approval, the FDA, or foreign regulatory authorities, may require additional pre-clinical testing or clinical trials for our product candidates. Even if we comply with all FDA requests, the FDA may ultimately reject one or more of our New Drug Applications, or NDA, or grant approval for a narrowly intended use that is not commercially feasible. We might not obtain regulatory approval for our drug candidates in a timely manner, if at all. Failure to obtain FDA approval of any of our drug candidates in a timely manner or at all will severely undermine our business by reducing the number of salable products and, therefore, corresponding product revenues.

Results of earlier clinical trials may not be predictive of the results of later-stage clinical trials.

The results of preclinical studies and early clinical trials of product candidates may not be predictive of the results of later-stage clinical trials. Also, interim results, if at all, during a clinical trial do not necessarily predict final results. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy results despite having progressed through preclinical studies and initial clinical trials. For example, our former subsidiary OphthaliX Inc. (since renamed Wize Pharma, Inc.), or OphthaliX, announced top-line results of a Phase III study with Piclidenoson for dry-eye syndrome in which Piclidenoson did not meet the primary efficacy endpoint of complete clearing of corneal staining, nor the secondary efficacy endpoints, OphthaliX released top-line results from its Phase II clinical trial of Piclidenoson for the treatment of glaucoma in which no statistically significant differences were found between the Piclidenoson treated group and the placebo group in the primary endpoint of lowering intraocular pressure, or IOP. In addition, two Phase IIb studies in rheumatoid arthritis, utilizing Piclidenoson in combination with methotrexate, a generic drug commonly used for treating rheumatoid arthritis patients, or MTX, failed to reach their primary endpoints and we ended our Phase III ACROBAT study after the independent data monitoring committee, or IDMC recommended in a pre-planned interim analysis not to continue this study. A Phase II/III study of Piclidenoson for psoriasis did not meet its primary endpoint although positive data from further analysis of the Phase II/III study suggests Piclidenoson as a potential systemic therapy for patients with moderate-severe psoriasis. Furthermore, a Phase II study for advanced HCC in subjects with Child-Pugh B who failed Nexavar as a first line treatment did not meet its primary endpoint although it showed superiority in overall survival in the largest study subpopulation.

Many companies in the pharmaceutical industry have suffered significant setbacks in advanced clinical trials due to adverse safety profiles or lack of efficacy, notwithstanding promising results in earlier studies. Any delay in, or termination or suspension of, our clinical trials will delay the requisite filings with the FDA, the EMA or other foreign regulatory authorities and, ultimately, our ability to commercialize our product candidates and generate product revenues. If the clinical trials do not support our product claims, the completion of development of such product candidates may be significantly delayed or abandoned, which will significantly impair our ability to generate product revenues and will materially adversely affect our results of operations.

This drug candidate development risk is heightened by any changes in the planned clinical trials compared to the completed clinical trials. As product candidates are developed from preclinical through early to late stage clinical trials towards approval and commercialization, it is customary that various aspects of the development program, such as manufacturing and methods of administration, are altered along the way in an effort to optimize processes and results. While these types of changes are common and are intended to optimize the product candidates for late stage clinical trials, approval and commercialization, such changes do carry the risk that they will not achieve these intended objectives.

Changes in our planned clinical trials or future clinical trials could cause our product candidates to perform differently, including causing toxicities, which could delay completion of our clinical trials, delay approval, if any, of our product candidates, and/or jeopardize our ability to commence product sales and generate revenues.

We might be unable to develop product candidates that will achieve commercial success in a timely and cost-effective manner, or ever.

Even if regulatory authorities approve our product candidates, they may not be commercially successful. Our product candidates may not be commercially successful because government agencies and other third-party payors may not cover the product or the coverage may be too limited to be commercially successful; physicians and others may not use or recommend our products, even following regulatory approval. A product approval, assuming one issues, may limit the uses for which the product may be distributed thereby adversely affecting the commercial viability of the product. Third parties may develop superior products or have proprietary rights that preclude us from marketing our products. We also expect that at least some of our product candidates will be expensive, if approved. Patient acceptance of and demand for any product candidates for which we obtain regulatory approval or license will depend largely on many factors, including but not limited to the extent, if any, of reimbursement of costs by government agencies and other third-party payors, pricing, the effectiveness of our marketing and distribution efforts, the safety and effectiveness of alternative products, and the prevalence and severity of side effects associated with our products. If physicians, government agencies and other third-party payors do not accept our products, we will not be able to generate significant revenue. In addition, government regulators and legislative bodies in the U.S. are considering numerous proposals that may result in limitations on the prices at which we could charge customers for our products if we have products that are ultimately approved for sale. At this time, we are unable to predict how these potential legislative changes might affect our business.

Our pursuit of developing Piclidenoson for the treatment of COVID-19 entails a high level of uncertainty. We cannot assure you that either of them will prove to be a safe and effective treatment for COVID-19 or will be approved for marketing or Emergency Use Authorization by the FDA or other regulatory authorities.

In response to the global pandemic of COVID-19, we are pursuing the study of Piclidenoson for the treatment of moderate to severe COVID-19. We cannot predict the efficacy of Piclidenoson, and we may be unable to provide a treatment that successfully treats COVID-19 and/or its symptoms in a timely manner, if at all. Furthermore, even if we successfully develop a viable therapeutic candidate, we may encounter difficulties developing and scaling up manufacturing processes suitable for production of sufficient supply for our clinical trials or for commercial use. We are also committing financial resources to the development of Piclidenoson for COVID-19, which may cause delays in or otherwise negatively impact our other development programs, despite uncertainties surrounding the longevity and extent of COVID-19 as a global health concern. Our business could be negatively impacted by our allocation of significant resources to a global health threat that is unpredictable and could rapidly dissipate or against which our potential treatments, if developed, may not be partially or fully effective. Further, we may take a decision to discontinue the study of Piclidenoson as potential treatments for COVID-19 for any reason, including if additional parties are successful in developing a more effective treatment or vaccine for COVID-19 or if the pandemic is effectively contained or the risk of COVID-19 infection is diminished or eliminated or if other market or business conditions and considerations support such discontinuation before we can successfully complete clinical development and obtain regulatory approval of Piclidenoson as a treatment for COVID-19. We may be unable to recoup any costs we incur in the evaluation of Piclidenoson for COVID-19 infection and we may never recognize any revenue from the sale of Piclidenoson to treat COVID-19, even if we do receive one or more regulatory approvals. Furthermore, the biotechnology sector is highly competitive and there are numerous companies that are currently pursuing a treatment for COVID-19 and vaccine for COVID-19. In particular, there are efforts by public and private entities to develop additional treatments or vaccines as fast as possible. To date, the FDA and other world health regulators have authorized emergency use of a number of COVID-19 vaccines. Other entities have or we expect will announce positive results from clinical trials for additional COVID-19 vaccine candidates. In addition, to date, there have been several drugs authorized for emergency use in treating COVID-19 patients. These and other public and private entities may develop treatments that are more effective than any we may develop, may develop a COVID-19 treatment that becomes the standard-of-care or at a lower cost or earlier than we are able to, or may be more successful at commercializing their product, which will reduce or eliminate the commercial opportunity for our therapeutic candidates. Many of these other organizations are much larger than we are and have access to larger pools of capital, including government grants and support, and broader manufacturing infrastructure. It is possible that another company or companies will obtain FDA approval for COVID-19 treatments before we obtain emergency use authorization or FDA (or other agency) approval (if ever), in which case, the FDA, the Secretary of the Department of Health and Human Services or other agencies around the world may stop accepting applications for emergency use authorization in connection with COVID-19. Even if we do obtain emergency use authorization or FDA (or other agency) approval for our COVID-19 therapeutic candidate, such authorization will only be effective as long as the public health emergency continues, and the Secretary of the Department of Health and Human Services or FDA (or other agency) may declare an end to such emergency at any time. Finally, if the pandemic ends or is sufficiently controlled, patient accruals for clinical trials will likely become difficult, which will have a material adverse effect on our ability to complete the development of our COVID-19 therapeutic candidate. There are a number of uncertainties and risks associated with our development of a COVID-19 therapeutic candidate, and we cannot guarantee success or profitability and may, instead, face financial and operational hardship as a result of this pursuit.

Our current pipeline is based on our platform technology utilizing the Gi protein associated A3AR, as a potent therapeutic target and currently includes three molecules, Piclidenoson, Namodenoson and CF602 product candidates, of which Piclidenoson is the most advanced. Failure to develop these molecules will have a material adverse effect on us.

Our current pipeline is based on a platform technology where we target the A3AR with highly selective ligands, or small signal triggering molecules that bind to specific cell surface receptors, such as the A3AR, including Piclidenoson, Namodenoson and CF602. A3ARs are structures found in cell surfaces that record and transfer messages from small molecules or ligands, such as Piclidenoson, Namodenoson and CF602 to the rest of the cell. Piclidenoson is the most advanced of our drug candidates. As such, we are currently dependent on only three molecules for our potential commercial success, and any safety or efficacy concerns related to such molecules would have a significant impact on our business. Failure to develop our drug candidates, in whole or in part, will have a material adverse effect on us.

Clinical trials are very expensive, time-consuming and difficult to design and implement, and, as a result, we may suffer delays or suspensions in future trials which would have a material adverse effect on our ability to generate revenues.

Human clinical trials are very expensive and difficult to design and implement, in part because they are subject to rigorous regulatory requirements. Regulatory authorities, such as the FDA, may preclude or prohibit clinical trials from proceeding. Additionally, the clinical trial process is time-consuming, failure can occur at any stage of the trials, and we may encounter problems that cause us to abandon or repeat clinical trials. The commencement and completion of clinical trials may be delayed by several factors, including:

- unforeseen safety issues;
- non-acceptance of an IND by the FDA;
- determination of dosing issues;
- lack of effectiveness or efficacy during clinical trials;
- inability to manufacture sufficient quantities of drug candidate;
- changes in formulation or manufacturing changes;
- failure of third-party suppliers to perform final manufacturing steps for the drug substance;
- slower than expected rates of patient recruitment and enrollment;
- inability to retain patients in clinical trials;
- lack of healthy volunteers and patients to conduct trials;
- inability to monitor patients adequately during or after treatment;
- failure to reach an agreement with contract research organizations or clinical trial sites;
- failure of institutional review boards, or IRBs, to approve our clinical trial protocols or suspension or termination of our clinical trial by the IRB, DSMB, or the FDA;
- failure of institutional review boards to approve our clinical trial protocols;
- inability or unwillingness of clinical investigators and institutional review boards to follow our clinical trial protocols;

- failure of clinical investigators or sites to maintain necessary licenses or permits or comply with good clinical practices, or GCP, or other regulatory requirements;

- debarment of a clinical investigator by FDA or other similar suspension or exclusion by a regulatory authority; and

- lack of sufficient funding to finance the clinical trials.

We have experienced the risks involved with conducting clinical trials, including but not limited to, increased expense and delay and failure to meet end points of the trial. For example, OphthaliX, announced top-line results of a Phase III study with Piclidenoson for dry-eye syndrome in which Piclidenoson did not meet the primary efficacy endpoint of complete clearing of corneal staining, nor the secondary efficacy endpoints and OphthaliX released top-line results from its Phase II clinical trial of Piclidenoson for the treatment of glaucoma in which no statistically significant differences were found between the Piclidenoson treated group and the placebo group in the primary endpoint of lowering IOP. In addition, two Phase IIb studies in rheumatoid arthritis, utilizing Piclidenoson in combination with MTX failed to reach their primary end points and we ended our Phase III ACROBAT study after the IDMC recommended in a pre-planned interim analysis not to continue this study. A Phase II/III study of Piclidenoson for psoriasis did not meet its primary endpoint although positive data from further analysis of the Phase II/III study suggests Piclidenoson as a potential systemic therapy for patients with moderate-severe psoriasis. Furthermore, a Phase II study of namodenoson for advanced HCC in subjects with Child-Pugh B who failed Nexavar as a first line treatment did not meet its primary endpoint although it showed superiority in overall survival in the largest study subpopulation.

In addition, we or regulatory authorities may suspend our clinical trials at any time if it appears that we are exposing participants to unacceptable health risks or if the regulatory authorities find deficiencies in our regulatory submissions or the conduct of these trials. Any suspension of clinical trials will delay possible regulatory approval, if any, increase costs, and adversely impact our ability to develop products and generate revenue.

We seek to partner with third-party collaborators with respect to the development and commercialization of Piclidenoson and and for any other product candidate, and we may not succeed in establishing and maintaining collaborative relationships, which may significantly limit our ability to develop and commercialize our product candidates successfully, if at all.

Our business strategy relies in part on partnering with pharmaceutical companies to complement our internal development efforts. We will be competing with many other companies as we seek partners for Piclidenoson, Namodenoson and for any other product candidate and we may not be able to compete successfully against those companies. If we are not able to enter into collaboration arrangements for Piclidenoson, Namodenoson and for any other product candidate, we may be required to undertake and fund further development, clinical trials, manufacturing and commercialization activities solely at our own expense and risk. If we are unable to finance and/or successfully execute those expensive activities, or we delay such activities due to capital availability, our business could be materially and adversely affected, and potential future product launch could be materially delayed, be less successful, or we may be forced to discontinue clinical development of these product candidates. The process of establishing and maintaining collaborative relationships is difficult, time-consuming and involves significant uncertainty, including:

- a collaboration partner may shift its priorities and resources away from our product candidates due to a change in business strategies, or a merger, acquisition, sale or downsizing;

- a collaboration partner may seek to renegotiate or terminate their relationships with us due to unsatisfactory clinical results, manufacturing issues, a change in business strategy, a change of control or other reasons;

- a collaboration partner may cease development in therapeutic areas which are the subject of our strategic collaboration;

- a collaboration partner may not devote sufficient capital or resources towards our product candidates;

- a collaboration partner may change the success criteria for a drug candidate thereby delaying or ceasing development of such candidate;

- a significant delay in initiation of certain development activities by a collaboration partner will also delay payment of milestones tied to such activities, thereby impacting our ability to fund our own activities;

- a collaboration partner could develop a product that competes, either directly or indirectly, with our drug candidate;

- a collaboration partner with commercialization obligations may not commit sufficient financial or human resources to the marketing, distribution or sale of a product;

- a collaboration partner with manufacturing responsibilities may encounter regulatory, resource or quality issues and be unable to meet demand requirements;

- a partner may exercise a contractual right to terminate a strategic alliance;

- a dispute may arise between us and a partner concerning the research, development or commercialization of a drug candidate resulting in a delay in milestones, royalty payments or termination of an alliance and possibly resulting in costly litigation or arbitration which may divert management attention and resources; and

- a partner may use our products or technology in such a way as to invite litigation from a third party.

Any collaborative partners we enter into agreements with in the future may shift their priorities and resources away from our product candidates or seek to renegotiate or terminate their relationships with us. If any collaborator fails to fulfill its responsibilities in a timely manner, or at all, our research, clinical development, manufacturing or commercialization efforts related to that collaboration could be delayed or terminated, or it may be necessary for us to assume responsibility for expenses or activities that would otherwise have been the responsibility of our collaborator. If we are unable to establish and maintain collaborative relationships on acceptable terms or to successfully transition terminated collaborative agreements, we may have to delay or discontinue further development of one or more of our product candidates, undertake development and commercialization activities at our own expense or find alternative sources of capital.

If we acquire or license additional technology or product candidates, we may incur a number of costs, may have integration difficulties and may experience other risks that could harm our business and results of operations.

We may acquire and license additional product candidates and technologies. Any product candidate or technology we license from others or acquire will likely require additional development efforts prior to commercial sale, including extensive pre-clinical or clinical testing, or both, and approval by the FDA and applicable foreign regulatory authorities, if any. All product candidates are prone to risks of failure inherent in pharmaceutical product development, including the possibility that the product candidate or product developed based on licensed technology will not be shown to be sufficiently safe and effective for approval by regulatory authorities. In addition, we cannot assure you that any product candidate that we develop based on acquired or licensed technology that is granted regulatory approval will be manufactured or produced economically, successfully commercialized or widely accepted in the marketplace. Moreover, integrating any newly acquired product candidates could be expensive and time-consuming. If we cannot effectively manage these aspects of our business strategy, our business may not succeed.

The manufacture of our product candidates is a chemical synthesis process and if one of our materials suppliers encounters problems manufacturing our products, our business could suffer.

The FDA and foreign regulators require manufacturers to register manufacturing facilities. The FDA and foreign regulators also inspect these facilities to confirm compliance with requirements that the FDA or foreign regulators establish. We do not intend to engage in the manufacture of our products other than for pre-clinical and clinical studies, but we or our materials suppliers may face manufacturing or quality control problems causing product production and shipment delays or a situation where we or the supplier may not be able to maintain compliance with the FDA's or foreign regulators' requirements necessary to continue manufacturing our drug substance. Drug manufacturers are subject to ongoing periodic unannounced inspections by the FDA, the U.S. Drug Enforcement Agency, or DEA, and corresponding foreign regulators to ensure strict compliance with requirements and other governmental regulations and corresponding foreign standards. Any failure to comply with DEA requirements or FDA or foreign regulatory requirements could adversely affect our clinical research activities and our ability to develop our product candidates, and delay possible regulatory approval.

We do not currently have sales, marketing or distribution capabilities or experience, and we are unable to effectively sell, market or distribute our product candidates now and we do not expect to be able to do so in the future. The failure to enter into agreements with third parties that are capable of performing these functions would have a material adverse effect on our business and results of operations.

We do not currently have and we do not expect to develop sales, marketing and distribution capabilities. If we are unable to enter into agreements with third parties to perform these functions, we will not be able to successfully market any of our platforms or product candidates. In order to successfully market any of our platform or product candidates, we must make arrangements with third parties to perform these services.

As we do not intend to develop a marketing and sales force with technical expertise and supporting distribution capabilities, we will be unable to market any of our product candidates directly. To promote any of our potential products through third parties, we will have to locate acceptable third parties for these functions and enter into agreements with them on acceptable terms, and we may not be able to do so. Any third-party arrangements we are able to enter into may result in lower revenues than we could achieve by directly marketing and selling our potential products. In addition, to the extent that we depend on third parties for marketing and distribution, any revenues we receive will depend upon the efforts of such third parties, as well as the terms of our agreements with such third parties, which cannot be predicted in most cases at this time. As a result, we might not be able to market and sell our products in the United States or overseas, which would have a material adverse effect on us.

We will to some extent rely on third parties to implement our manufacturing and supply strategies. Failure of these third parties in any respect could have a material adverse effect on our business, results of operations and financial condition.

If our current and future manufacturing and supply strategies are unsuccessful, then we may be unable to conduct and complete any future pre-clinical or clinical trials or commercialize our product candidates in a timely manner, if at all. Completion of any potential future pre-clinical or clinical trials and commercialization of our product candidates will require access to, or development of, facilities to manufacture a sufficient supply of our product candidates. We do not have the resources, facilities or experience to manufacture our product candidates for commercial purposes on our own and do not intend to develop or acquire facilities for the manufacture of product candidates for commercial purposes in the foreseeable future. We may rely on contract manufacturers to produce sufficient quantities of our product candidates necessary for any pre-clinical or clinical testing we undertake in the future. Such contract manufacturers may be the sole source of production and they may have limited experience at manufacturing, formulating, analyzing, filling and finishing our types of product candidates.

We also intend to rely on third parties to supply the requisite materials needed for the manufacturing of our active pharmaceutical ingredients, or API. There may be a limited supply of these requisite materials. We might not be able to enter into agreements that provide us assurance of availability of such components in the future from any supplier. Our potential suppliers may not be able to adequately supply us with the components necessary to successfully conduct our pre-clinical and clinical trials or to commercialize our product candidates. In particular, as a result of the recent COVID-19 outbreak, the continued spread of COVID-19 globally could result in the inability of our suppliers to deliver components or raw materials on a timely basis or at all. If we cannot acquire an acceptable supply of the requisite materials to produce our product candidates, we will not be able to complete pre-clinical and clinical trials delaying possible regulatory approval, and adversely impacting our ability to develop products, and will not be able to market or commercialize our product candidates, if approved.

We depend on key members of our management and key consultants and will need to add and retain additional leading experts. Failure to retain our management and consulting team and add additional leading experts could have a material adverse effect on our business, results of operations or financial condition.

We are highly dependent on our executive officers and other key management and technical personnel. Our failure to retain our Chief Executive Officer, Pnina Fishman, Ph.D., who has developed much of the technology we utilize today, or any other key management and technical personnel, could have a material adverse effect on our future operations. Our success is also dependent on our ability to attract, retain and motivate highly trained technical, and management personnel, among others, to continue the development and commercialization, if approved, of our current and future product candidates.

Our success also depends on our ability to attract, retain and motivate personnel required for the development, maintenance and expansion of our activities. There can be no assurance that we will be able to retain our existing personnel or attract additional qualified employees or consultants. The loss of key personnel or the inability to hire and retain additional qualified personnel in the future could have a material adverse effect on our business, financial condition and results of operation.

We face significant competition and continuous technological change, and developments by competitors may render our products or technologies obsolete or non-competitive. If we cannot successfully compete with new or existing products, our marketing and sales will suffer and we may not ever be profitable.

We will compete against fully integrated pharmaceutical and biotechnology companies and smaller companies that are collaborating with larger pharmaceutical companies, academic institutions, government agencies and other public and private research organizations. In addition, many of these competitors, either alone or together with their collaborative partners, operate larger research and development programs than we do, and have substantially greater financial resources than we do, as well as significantly greater experience in:

- developing drugs;
- undertaking pre-clinical testing and human clinical trials;
- obtaining FDA approval, addressing various regulatory matters and other regulatory approvals of drugs;
- formulating and manufacturing drugs; and
- launching, marketing and selling drugs.

If our competitors develop and commercialize products faster than we do, or develop and commercialize products that are superior to our product candidates, our commercial opportunities will be reduced or eliminated. The extent to which any of our product candidates achieve market acceptance will depend on competitive factors, many of which are beyond our control. Competition in the biotechnology and biopharmaceutical industry is intense and has been accentuated by the rapid pace of technology development. Our competitors include large integrated pharmaceutical companies, biotechnology companies that currently have drug and target discovery efforts, universities, and public and private research institutions. Almost all of these entities have substantially greater research and development capabilities and financial, scientific, manufacturing, marketing and sales resources than we do. These organizations also compete with us to:

- attract parties for acquisitions, joint ventures or other collaborations;
- license proprietary technology that is competitive with the technology we are developing;
- attract funding; and
- attract and hire scientific talent and other qualified personnel.

Our competitors may succeed in developing and commercializing products earlier and obtaining regulatory approvals from the FDA or foreign regulators more rapidly than we do. Our competitors may also develop products or technologies that are superior to those we are developing, and render our product candidates or technologies obsolete or non-competitive. If we cannot successfully compete with new or existing products, our marketing and sales will suffer and we may not ever be profitable.

Our competitors currently include companies with marketed products and/or an advanced research and development pipeline. The major competitors in the psoriasis therapeutic field include Amgen, J&J, Pfizer, Novartis, Abbvie, Eli Lilly, Bristol-Myers Squibb, and more. Competitors in the HCC field include companies such as Bayer, Exelixis, Merck, Roche, and Bristol-Myers Squibb. Competitors in the NASH field include companies such as Gilead, Genfit, Galmed, Intercept, Madrigal, Akero, 89Bio, Viking, and Terns. Competitors in the COVID-19 field include Pfizer, BioNTech, Moderna, Johnson & Johnson, AstraZeneca, Novavax, Eli Lilly, and Regeneron. Competitors in the erectile dysfunction field include Pfizer, Eli Lilly and Bayer. See “Item 4. Information on the Company—B. Business Overview—Competition.”

Moreover, several companies have reported the commencement of research projects related to the A3AR. Such companies include CV Therapeutics Inc. (which was acquired by Gilead), King Pharmaceuticals R&D Inv. (which was acquired by Pfizer), Hoechst Marion Roussel Inc. (which was acquired by Aventis), Novo Nordisk A/S and Inotek Pharmaceuticals. However, to the best of our knowledge, there is no approved drug currently on the market, which is similar to our A3AR agonists, nor are we aware of any allosteric modulator in the A3AR product pipeline similar to our allosteric modulator with respect to chemical profile and mechanism of action.

We may suffer losses from product liability claims if our product candidates cause harm to patients.

Any of our product candidates could cause adverse events. Although data from clinical trials to date encompassing more than 1,300 humans dosed with Piclidenoson indicate that Piclidenoson is generally well-tolerated at doses up to 4.0 mg administered twice daily for up to 12-48 weeks, there were incidences (less than or equal to 5%) of adverse events in eight completed and fully analyzed trials in inflammatory disease. Such adverse events included nausea, diarrhea, abdominal pain, vomiting, constipation, common bacterial and viral syndromes (such as tonsillitis, otitis and respiratory and urinary tract infections), abdominal pain, vomiting, myalgia, arthralgia, dizziness, headache and pruritus. We observed an even lower incidence (less than or equal to 2%) of serious adverse events, although only one type of event was reported in more than a single Piclidenoson-treated subject, which was exacerbation of chronic obstructive lung disease reported in two subjects. Notwithstanding the foregoing, the placebo group in such studies had a higher incidence of overall adverse events than the pooled Piclidenoson groups. In addition, in normal volunteers, Piclidenoson at doses 3-4-fold higher than those to be used in therapeutic trials, but not at therapeutic doses, was associated with prolongation of the electrocardiographic QT intervals. No new safety concerns have been identified and no novel or unexpected safety concerns have appeared over 48 weeks of treatment in more recent trials.

There is also a risk that certain adverse events may not be observed in clinical trials, but may nonetheless occur in the future. If any of these adverse events occur, they may render our product candidates ineffective or harmful in some patients, and our sales would suffer, materially adversely affecting our business, financial condition and results of operations.

In addition, potential adverse events caused by our product candidates could lead to product liability lawsuits. If product liability lawsuits are successfully brought against us, we may incur substantial liabilities and may be required to limit the marketing and commercialization of our product candidates. Our business exposes us to potential product liability risks, which are inherent in the testing, manufacturing, marketing and sale of pharmaceutical products. We may not be able to avoid product liability claims. Product liability insurance for the pharmaceutical and biotechnology industries is generally expensive, if available at all. If, at any time, we are unable to obtain sufficient insurance coverage on reasonable terms or to otherwise protect against potential product liability claims, we may be unable to clinically test, market or commercialize our product candidates. A successful product liability claim brought against us in excess of our insurance coverage, if any, may cause us to incur substantial liabilities, and, as a result, our business, liquidity and results of operations would be materially adversely affected.

Our product candidates will remain subject to ongoing regulatory requirements even if they receive marketing approval, and if we fail to comply with these requirements, we could lose these approvals, and the sales of any approved commercial products could be suspended.

Even if we receive regulatory approval to market a particular product candidate, the product will remain subject to extensive regulatory requirements, including requirements relating to manufacturing, labelling, packaging, adverse event reporting, storage, advertising, promotion, distribution and recordkeeping. Even if regulatory approval of a product is granted, the approval may be subject to limitations on the uses for which the product may be marketed or the conditions of approval, or may contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the product, which could negatively impact us or our collaboration partners by reducing revenues or increasing expenses, and cause the approved product candidate not to be commercially viable. In addition, as clinical experience with a drug expands after approval, typically because it is used by a greater number and more diverse group of patients after approval than during clinical trials, side effects and other problems may be observed after approval that were not seen or anticipated during pre-approval clinical trials or other studies. Any adverse effects observed after the approval and marketing of a product candidate could result in limitations on the use of or withdrawal of any approved products from the marketplace. Absence of long-term safety data may also limit the approved uses of our products, if any. If we fail to comply with the regulatory requirements of the FDA and other applicable U.S. and foreign regulatory authorities, or previously unknown problems with any approved commercial products, manufacturers or manufacturing processes are discovered, we could be subject to administrative or judicially imposed sanctions or other setbacks, including the following:

- Restrictions on the products, manufacturers or manufacturing process;
- Warning or other enforcement letters;
- Civil or criminal penalties, fines and injunctions;
- Product seizures or detentions;
- Import or export bans or restrictions;
- Voluntary or mandatory product recalls and related publicity requirements;
- Suspension or withdrawal of regulatory approvals;
- Total or partial suspension of production; and
- Refusal to approve pending applications for marketing approval of new products or supplements to approved applications.

If we or our collaborators are slow or unable to adapt to changes in existing regulatory requirements or adoption of new regulatory requirements or policies, marketing approval for our product candidates may be lost or cease to be achievable, resulting in decreased revenue from milestones, product sales or royalties, which would have a material adverse effect on our results of operations.

We deal with hazardous materials and must comply with environmental, health and safety laws and regulations, which can be expensive and restrict how we do business.

Our activities and those of our third-party manufacturers on our behalf involve the controlled storage, use and disposal of hazardous materials, including corrosive, explosive and flammable chemicals and other hazardous compounds. We and our manufacturers are subject to U.S. federal, state, and local, and Israeli and other foreign laws and regulations governing the use, manufacture, storage, handling and disposal of these hazardous materials. Although we believe that our safety procedures for handling and disposing of these materials comply with the standards prescribed by these laws and regulations, we cannot eliminate the risk of accidental contamination or injury from these materials. In addition, if we develop a manufacturing capacity, we may incur substantial costs to comply with environmental regulations and would be subject to the risk of accidental contamination or injury from the use of hazardous materials in our manufacturing process.

In the event of an accident, government authorities may curtail our use of these materials and interrupt our business operations. In addition, we could be liable for any civil damages that result, which may exceed our financial resources and may seriously harm our business. Although our Israeli insurance program covers certain unforeseen sudden pollutions, we do not maintain a separate insurance policy for any of the foregoing types of risks. In addition, although the general liability section of our life sciences policy covers certain unforeseen, sudden environmental issues, pollution in the United States and Canada is excluded from the policy. In the event of environmental discharge or contamination or an accident, we may be held liable for any resulting damages, and any liability could exceed our resources. In addition, we may be subject to liability and may be required to comply with new or existing environmental laws regulating pharmaceuticals or other medical products in the environment.

Our business and operations may be materially adversely affected in the event of computer system failures or security breaches.

Despite the implementation of security measures, our internal computer systems, and those of our contract research organizations, or CROs, and other third parties on which we rely, are vulnerable to damage from computer viruses, unauthorized access, cyber-attacks, natural disasters, fire, terrorism, war, and telecommunication and electrical failures. If such an event were to occur and interrupt our operations, it could result in a material disruption of our drug development programs. For example, the loss of clinical trial data from ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of or damage to our data or applications, loss of trade secrets or inappropriate disclosure of confidential or proprietary information, including protected health information or personal data of employees or former employees, access to our clinical data, or disruption of the manufacturing process, we could incur liability and the further development of our drug candidates could be delayed. We may also be vulnerable to cyber-attacks by hackers or other malfeasance. This type of breach of our cybersecurity may compromise our confidential information and/or our financial information and adversely affect our business or result in legal proceedings. Further, these cybersecurity breaches may inflict reputational harm upon us that may result in decreased market value and erode public trust.

We may not be able to successfully grow and expand our business. Failure to manage our growth effectively will have a material adverse effect on our business, results of operations and financial condition.

We may not be able to successfully grow and expand. Successful implementation of our business plan will require management of growth, including potentially rapid and substantial growth, which will result in an increase in the level of responsibility for management personnel and place a strain on our human and capital resources. To manage growth effectively, we will be required to continue to implement and improve our operating and financial systems and controls to expand, train and manage our employee base. Our ability to manage our operations and growth effectively requires us to continue to expend funds to enhance our operational, financial and management controls, reporting systems and procedures and to attract and retain sufficient numbers of talented personnel. If we are unable to scale up and implement improvements to our control systems in an efficient or timely manner, or if we encounter deficiencies in existing systems and controls, then we will not be able to make available the products required to successfully commercialize our technology. Failure to attract and retain sufficient numbers of talented personnel will further strain our human resources and could impede our growth or result in ineffective growth. Moreover, the management, systems and controls currently in place or to be implemented may not be adequate for such growth, and the steps taken to hire personnel and to improve such systems and controls might not be sufficient. If we are unable to manage our growth effectively, it will have a material adverse effect on our business, results of operations and financial condition.

If we are unable to obtain adequate insurance, our financial condition could be adversely affected in the event of uninsured or inadequately insured loss or damage. Our ability to effectively recruit and retain qualified officers and directors could also be adversely affected if we experience difficulty in obtaining adequate directors' and officers' liability insurance.

We may not be able to obtain insurance policies on terms affordable to us that would adequately insure our business and property against damage, loss or claims by third parties. To the extent our business or property suffers any damages, losses or claims by third parties, which are not covered or adequately covered by insurance, our financial condition may be materially adversely affected.

We may be unable to maintain sufficient insurance as a public company to cover liability claims made against our officers and directors. Our insurance costs have increased for directors' and officers' liability insurance, and we may be required to incur further substantial increased costs to maintain the same or similar coverage or be forced to accept reduced coverage in future. If we are unable to adequately insure our officers and directors, we may not be able to retain or recruit qualified officers and directors to manage us.

Our cannabinoid initiative is uncertain and may not yield commercial results and is subject to significant regulatory risks.

We are developing formulations of cannabis components for the treatment of diseases in which there is an overexpression of A3AR. While we believe there are substantial business opportunities for us in this field, there can be no assurance that our activities will be successful, or that any research and development and product testing efforts will result in commercially saleable products, or that the market will accept or respond positively to our products. In addition, our current and potential involvement in cannabis-related activity, , may expose us to legal and reputational risks. Such risks include:

- Medical-use cannabis remains illegal under U.S. federal law, and therefore, strict enforcement of federal laws regarding medical-use cannabis would likely result in our inability to market any products;
- FDA has not approved a marketing application for the treatment of any disease or condition;
- Changes in laws, regulations and guidelines related to cannabis may result in significant additional compliance costs for us or limit our ability to operate in certain jurisdictions;
- Certain banks will not accept deposits from or provide other bank services to businesses involved with cannabis and U.S. federal money laundering laws make it a federal crime to engage in financial transactions involving the proceeds of some form of unlawful activity; and
- Third parties with whom we do business may perceive that they are exposed to reputational risk as a result of our cannabis-related business activities and may ultimately elect not to do business with us.

Complying with laws and regulations relating to cannabinoids is evolving, complex and expensive, and may divert management's attention and resources from other aspects of our business. Failure to maintain compliance with such laws and regulations may result in regulatory action that could have a material adverse effect on our business, results of operations and financial condition. The DEA, FDA or state agencies may seek civil penalties, refuse to renew necessary registrations, or initiate proceedings to revoke those registrations. In certain circumstances, violations could lead to criminal proceedings.

We or the third parties upon whom we depend may be adversely affected by natural disasters and/or health epidemics, and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Natural disasters could severely disrupt our operations and have a material adverse effect on our business, results of operations, financial condition and prospects. If a natural disaster, power outage, health epidemic or other event occurred that prevented us from using all or a significant portion of our office, manufacturing and/or lab spaces, that damaged critical infrastructure, such as the manufacturing facilities of our third-party contract manufacturers, CROs, clinical sites, third parties ongoing activities and schedules or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our plans and business for a substantial period of time.

In late 2019, a novel strain of COVID-19, also known as coronavirus, was reported in Wuhan, China and began spreading to various parts of the world. In particular, our clinical trial sites are based in areas currently affected by COVID-19. Epidemics such as this can adversely impact our business as they can cause disruptions, such as travel bans, quarantines, and interruptions to access the trial sites and supply chain, which could result in material delays and complications with respect to our research and development programs and clinical trials. Moreover, as a result of COVID-19, there is a general unease of conducting unnecessary activities in medical centers. It is too early to assess the full impact of the COVID-19 outbreak on our clinical trials however COVID-19 may affect our ability to complete recruitment in our original timeframe and could materially affect the operations of key governmental agencies, such as the FDA. The extent to which COVID-19 impacts our operations will depend on future developments, which are highly uncertain and cannot be predicted with confidence, including the duration and severity of the outbreak, and the actions that may be required to contain COVID-19 or treat its impact. A health epidemic or other outbreak, including the current COVID-19 outbreak, may materially and adversely affect our business, financial condition and results of operations.

The disaster recovery and business continuity plans we have in place may prove inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which could have a material adverse effect on our business.

Risks Related to Our Intellectual Property

The termination of the National Institute of Health, or NIH, license agreement between us and NIH due to patent expiration may diminish our proprietary position.

As a result of the termination of the NIH license agreement between us and NIH in June 2015 due to patent expiration, we no longer hold rights to a family of composition of matter patents relating to Piclidenoson that were licensed from NIH. Nevertheless, because Piclidenoson may be a new chemical entity, or NCE, following approval of an NDA, we, if we are the first applicant to obtain NDA approval, may be entitled to five years of data exclusivity in the United States with respect to such NCEs. Analogous data and market exclusivity provisions, of varying duration, may be available in Europe and other foreign jurisdictions. We also have rights under our pharmaceutical use issued patents with respect to Piclidenoson and Namodenoson, which provide patent exclusivity within our field of activity until the mid- to late-2020s. While we believe that we may be able to protect our exclusivity through such use patent portfolio and such period of exclusivity, the lack of composition of matter patent protection may diminish our ability to maintain a proprietary position for our intended uses of Piclidenoson. Moreover, we cannot be certain that we will be the first applicant to obtain an FDA approval for any indication of Piclidenoson and we cannot be certain that we will be entitled to NCE exclusivity. In addition, we have discontinued the prosecution of a family of pending patent applications under joint ownership of us and NIH pertaining to the use of A3AR agonists for the treatment of uveitis. Such diminution of our proprietary position could have a material adverse effect on our business, results of operation and financial condition.

We license from Leiden University intellectual property, which protects certain small molecules which target the A3AR, in furtherance of our platform technology, and we could lose our rights to this license if a dispute with Leiden University arises or if we fail to comply with the financial and other terms of the license.

We have licensed intellectual property from Leiden University pursuant to a license agreement. The license agreement imposes certain payment, reporting, confidentiality and other obligations on us. In the event that we were to breach any of the obligations and fail to cure, Leiden University would have the right to terminate the license agreement. In addition, Leiden University has the right to terminate the license agreement upon our bankruptcy, insolvency, or receivership. If any dispute arises with respect to our arrangements with Leiden University, such dispute may disrupt our operations and may have a material adverse impact on us if resolved in a manner that is unfavorable to us.

The failure to obtain or maintain patents, licensing agreements, including our current licensing agreements, and other intellectual property could impact our ability to compete effectively.

To compete effectively, we need to develop and maintain a proprietary position with regard to our own technologies, intellectual property, licensing agreements, product candidates and business. Legal standards relating to the validity and scope of claims in the biotechnology and biopharmaceutical fields are still evolving. Therefore, the degree of future protection for our proprietary rights in our core technologies and any products that might be made using these technologies is also uncertain. The risks and uncertainties that we face with respect to our patents and other proprietary rights include the following:

- while the patents we license have been issued, the pending patent applications we have filed may not result in issued patents or may take longer than we expect to result in issued patents;
- we may be subject to interference proceedings;
- we may be subject to opposition proceedings in foreign countries;
- any patents that are issued may not provide meaningful protection;
- we may not be able to develop additional proprietary technologies that are patentable;
- other companies may challenge patents licensed or issued to us or our customers;
- other companies may independently develop similar or alternative technologies, or duplicate our technologies;
- other companies may design around technologies we have licensed or developed; and
- enforcement of patents is complex, uncertain and expensive.

If patent rights covering our products and methods are not sufficiently broad, they may not provide us with any protection against competitors with similar products and technologies. Furthermore, if the United States Patent and Trademark Office, or the USPTO, or foreign patent officers issue patents to us or our licensors, others may challenge the patents or design around the patents, or the patent office or the courts may invalidate the patents. Thus, any patents we own or license from or to third parties may not provide any protection against our competitors.

We cannot be certain that patents will be issued as a result of any pending applications, and we cannot be certain that any of our issued patents will give us adequate protection from competing products. For example, issued patents, including the patents licensed by us, may be circumvented or challenged, declared invalid or unenforceable, or narrowed in scope. In addition, since publication of discoveries in the scientific or patent literature often lags behind actual discoveries, we cannot be certain that we were the first to make our inventions or to file patent applications covering those inventions.

It is also possible that others may obtain issued patents that could prevent us from commercializing our products or require us to obtain licenses requiring the payment of significant fees or royalties in order to enable us to conduct our business. As to those patents that we have licensed, our rights depend on maintaining our obligations to the licensor under the applicable license agreement, and we may be unable to do so.

In addition to patents and patent applications, we depend upon trade secrets and proprietary know-how to protect our proprietary technology. We require our employees, consultants, advisors and collaborators to enter into confidentiality agreements that prohibit the disclosure of confidential information to any other parties. We require our employees and consultants to disclose and assign to us their ideas, developments, discoveries and inventions. These agreements may not, however, provide adequate protection for our trade secrets, know-how or other proprietary information in the event of any unauthorized use or disclosure.

Costly litigation may be necessary to protect our intellectual property rights and we may be subject to claims alleging the violation of the intellectual property rights of others.

We may face significant expense and liability as a result of litigation or other proceedings relating to patents and other intellectual property rights of others. In the event that another party has also filed a patent application or been issued a patent relating to an invention or technology claimed by us in pending applications, we may be required to participate in an interference proceeding declared by the USPTO to determine priority of invention, which could result in substantial uncertainties and costs for us, even if the eventual outcome were favorable to us. We, or our licensors, also could be required to participate in interference proceedings involving issued patents and pending applications of another entity. An adverse outcome in an interference proceeding could require us to cease using the technology or to license rights from prevailing third parties.

The cost to us of any patent litigation or other proceeding relating to our licensed patents or patent applications, even if resolved in our favor, could be substantial. Our ability to enforce our patent protection could be limited by our financial resources, and may be subject to lengthy delays. If we are unable to effectively enforce our proprietary rights, or if we are found to infringe the rights of others, we may be in breach of our License Agreement.

A third party may claim that we are using inventions claimed by their patents and may go to court to stop us from engaging in our normal operations and activities, such as research, development and the sale of any future products. Such lawsuits are expensive and would consume time and other resources. There is a risk that the court will decide that we are infringing the third party’s patents and will order us to stop the activities claimed by the patents, redesign our products or processes to avoid infringement or obtain licenses (which may not be available on commercially reasonable terms). In addition, there is a risk that a court will order us to pay the other party damages for having infringed their patents.

Moreover, there is no guarantee that any prevailing patent owner would offer us a license so that we could continue to engage in activities claimed by the patent, or that such a license, if made available to us, could be acquired on commercially acceptable terms. In addition, third parties may, in the future, assert other intellectual property infringement claims against us with respect to our product candidates, technologies or other matters.

We rely on confidentiality agreements that could be breached and may be difficult to enforce, which could result in third parties using our intellectual property to compete against us.

Although we believe that we take reasonable steps to protect our intellectual property, including the use of agreements relating to the non-disclosure of confidential information to third parties, as well as agreements that purport to require the disclosure and assignment to us of the rights to the ideas, developments, discoveries and inventions of our employees and consultants while we employ them, the agreements can be difficult and costly to enforce. Although we seek to obtain these types of agreements from our contractors, consultants, advisors and research collaborators, to the extent that employees and consultants utilize or independently develop intellectual property in connection with any of our projects, disputes may arise as to the intellectual property rights associated with our products. If a dispute arises, a court may determine that the right belongs to a third party. In addition, enforcement of our rights can be costly and unpredictable. We also rely on trade secrets and proprietary know-how that we seek to protect in part by confidentiality agreements with our employees, contractors, consultants, advisors or others. Despite the protective measures we employ, we still face the risk that:

- these agreements may be breached;
- these agreements may not provide adequate remedies for the applicable type of breach;
- our trade secrets or proprietary know-how will otherwise become known; or
- our competitors will independently develop similar technology or proprietary information.

International patent protection is particularly uncertain, and if we are involved in opposition proceedings in foreign countries, we may have to expend substantial sums and management resources.

Patent law outside the United States is different than in the United States. Further, the laws of some foreign countries may not protect our intellectual property rights to the same extent as the laws of the United States, if at all. A failure to obtain sufficient intellectual property protection in any foreign country could materially and adversely affect our business, results of operations and future prospects. Moreover, we may participate in opposition proceedings to determine the validity of our foreign patents or our competitors' foreign patents, which could result in substantial costs and divert management's resources and attention.

Although most jurisdictions in which we have applied for, intend to apply for, or have been issued patents have patent protection laws similar to those of the United States, some of them do not. For example, we expect to do business in Brazil and India in the future. However, the Brazilian drug regulatory agency, ENVISA, has the authority to nullify patents on the basis of its perceived public interest and the Indian patent law does not allow patent protection for new uses of pharmaceuticals (many of our current patent applications are of such nature). Additionally, due to uncertainty in patent protection law, we have not filed applications in many countries where significant markets exist, including Indonesia, Pakistan, Russia, African countries and Taiwan.

We may be unable to protect the intellectual property rights of the third parties from whom we license certain of our intellectual property or with whom we have entered into other strategic relationships.

Certain of our intellectual property rights are currently licensed from Leiden University, and, in the future, we intend to continue to license intellectual property from Leiden University and/or other universities and/or strategic partners. Such third parties may determine not to protect the intellectual property rights that we license from them and we may be unable to defend such intellectual property rights on our own or we may have to undertake costly litigation to defend the intellectual property rights of such third parties. There can be no assurances that we will continue to have proprietary rights to any of the intellectual property that we license from such third parties or otherwise have the right to use through similar strategic relationships. Any loss or limitations on use with respect to our right to use such intellectual property licensed from third parties or otherwise obtained from third parties with whom we have entered into strategic relationships could have a material adverse effect on our business, results of operations and financial condition.

Under applicable U.S. and Israeli law, we may not be able to enforce covenants not to compete and therefore, may be unable to prevent our competitors from benefiting from the expertise of some of our former employees. In addition, employees may be entitled to seek compensation for their inventions irrespective of their agreements with us, which in turn could impact our future profitability.

We generally enter into non-competition agreements with our employees and certain key consultants, or our employment and consulting agreements contain non-competition provisions. These agreements, to the extent they are in place and in effect, prohibit our employees and certain key consultants, if they cease working for us, from competing directly with us or working for our competitors or clients for a limited period of time. We may be unable to enforce these agreements under the laws of the jurisdictions in which our employees work and it may be difficult for us to restrict our competitors from benefitting from the expertise our former employees or consultants developed while working for us. For example, Israeli courts have required employers seeking to enforce non-compete undertakings of a former employee to demonstrate that the competitive activities of the former employee will harm one of a limited number of material interests of the employer which have been recognized by the courts, such as the secrecy of a company's confidential commercial information or the protection of its intellectual property. If we cannot demonstrate that such interests will be harmed, we may be unable to prevent our competitors from benefiting from the expertise of our former employees or consultants and our ability to remain competitive may be diminished.

In addition, Chapter 8 to the Israeli Patents Law, 5727-1967, or the Patents Law, deals with inventions made in the course of an employee's service and during his or her term of employment, whether or not the invention is patentable, or service inventions. Section 134 of the Patents Law provides that if there is no agreement that explicitly determines whether the employee is entitled to compensation for the service inventions and the extent and terms of such compensation, such determination will be made by the Compensation and Rewards Committee, a statutory committee of the Israeli Patents Office. Although our employees have agreed to assign to us service invention rights, we may face claims demanding remuneration in consideration for assigned inventions. As a consequence of such claims, we could be required to pay additional remuneration or royalties to our current and/or former employees, or be forced to litigate such claims, which could negatively affect our business.

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

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business, or permit us to maintain our competitive advantage. The following examples are illustrative:

- Others may be able to make compounds that are the same as or similar to our product candidates but that are not covered by the claims of the patents that we own or have exclusively licensed;
- We or our licensors or any future strategic partners might not have been the first to make the inventions covered by the issued patent or pending patent application 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 advantages, 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; and
- We may not develop additional proprietary technologies that are patentable.

We may be subject to claims challenging the inventorship of our patents and other intellectual property.

We may be subject to claims that former employees, collaborators or other third parties have an interest in our patents or other intellectual property as an inventor or co-inventor. For example, we may have inventorship disputes arise from conflicting obligations of consultants or others who are involved in developing our product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. 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.

Risks Related to Our Industry

We are subject to government regulations and we may experience delays in obtaining required regulatory approvals in the United States to market our proposed product candidates.

Various aspects of our operations are subject to federal, state or local laws, and rules and regulations, any of which may change from time to time. Costs arising out of any regulatory developments could be time-consuming and expensive and could divert management resources and attention and, consequently, could adversely affect our business operations and financial performance.

Delays in regulatory approval, limitations in regulatory approval and withdrawals of regulatory approval may have a material adverse effect on us. If we experience significant delays in testing or receiving approvals or sign-offs to conduct clinical trials, our product development costs, or our ability to license product candidates, will increase. If the FDA grants regulatory approval to market a product, this approval will be limited to those disease states and conditions and populations for which the product has demonstrated, through clinical trials, to be safe and effective. Any product approvals that we receive in the future could also include significant restrictions on the use or marketing of our products. Product approvals, if granted, can be withdrawn for failure to comply with regulatory requirements or upon the occurrence of adverse events following commercial introduction of the products. Failure to comply with applicable FDA or other applicable regulatory requirements may result in criminal prosecution, civil penalties, recall or seizure of products, total or partial suspension of production or injunction, as well as other regulatory action against our product candidates or us. If approval is withdrawn for a product, or if a product were seized or recalled, we would be unable to sell or license that product and our revenues would suffer. In addition, outside the United States, our ability to market any of our potential products is contingent upon receiving market application authorizations from the appropriate regulatory authorities and these foreign regulatory approval processes include all of the risks associated with the FDA approval process described above.

We expect the healthcare industry to face increased limitations on reimbursement as a result of healthcare reform, which could adversely affect third-party coverage of our products and how much or under what circumstances healthcare providers will prescribe or administer our products.

In both the United States and other countries, sales of our products will depend in part upon the availability of reimbursement from third-party payors, which include governmental authorities, managed-care organizations and other private-health insurers. Third-party payors are increasingly challenging the price and examining the cost effectiveness of medical products and services.

Increasing expenditures for healthcare have been the subject of considerable public attention in the United States. Both private and government entities are seeking ways to reduce or contain healthcare costs. Numerous proposals that would effect changes in the U.S. healthcare system have been introduced or proposed in Congress and in some state legislatures, including reducing reimbursement for prescription products and reducing the levels at which consumers and healthcare providers are reimbursed for purchases of pharmaceutical products.

In 2010, the U.S. congress enacted the Patient Protection and Affordable Care Act of 2010, or the Affordable Care Act. The Affordable Care Act seeks to reduce the federal deficit and the rate of growth in healthcare spending through, among other things, stronger prevention and wellness measures, increased access to primary care, changes in healthcare delivery systems and the creation of health insurance exchanges. Enrollment in the health insurance exchanges began in October 2013. The Affordable Care Act requires the pharmaceutical industry to share in the costs of reform, by, among other things, increasing Medicaid rebates and expanding Medicaid rebates to cover Medicaid managed-care programs. Other components of healthcare reform include funding of pharmaceutical costs for Medicare patients in excess of the prescription drug coverage limit and below the catastrophic coverage threshold. Under the Affordable Care Act, pharmaceutical companies are now obligated to fund 50% of the patient obligation for branded prescription pharmaceuticals in this gap, or “donut hole.”

There have been judicial and congressional challenges to the Affordable Care Act. If a law is enacted, many if not all of the provisions of the Affordable Care Act may no longer apply to prescription drugs. While we are unable to predict what changes may ultimately be enacted, to the extent that future changes affect how any future products are paid for and reimbursed by government and private payers, our business could be adversely impacted. On December 14, 2018, a federal district court in Texas ruled that the Affordable Care Act is unconstitutional as a result of the Tax Cuts and Jobs Act and the federal income tax reform legislation previously passed by Congress and signed by President Trump on December 22, 2017, that eliminated the individual mandate portion of the Affordable Care Act. The case, Texas, et al. v. United States of America, et al., (N.D. Texas), is an outlier, but in 2019, the Fifth Circuit Court of Appeals subsequently upheld the lower court decision, which was then appealed to the U.S. Supreme Court. The U.S. Supreme Court declined to hear the appeal on an expedited basis and so no decision will be forthcoming until the next Supreme Court term in early 2021. We are not able to state with any certainty what will be the impact of this court decision on our business pending further court action and possible appeals. In November 2020, Joseph Biden was elected President and, in January 2021, the Democratic Party obtained control of the Senate. As a result of these electoral developments, it is unlikely that continued legislative efforts will be pursued to repeal PPACA. Instead, it is possible that legislation will be pursued to enhance or reform PPACA. We are not able to state with certainty what the impact of potential legislation will be on our business.

In addition, other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. In August 2011, President Obama signed into law the Budget Control Act of 2011, which, among other things, created the Joint Select Committee on Deficit Reduction to recommend to Congress proposals in spending reductions. The Joint Select Committee did not achieve a targeted deficit reduction of an amount greater than $1.2 trillion for the years 2013 through 2021, triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions to Medicare payments to healthcare providers of up to 2.0% per fiscal year, starting in 2013. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several categories of healthcare providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. If we ever obtain regulatory approval and commercialization of our products, these laws may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on our customers and accordingly, our financial operations. Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We 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 marketing approvals of our products may be. Further, the Deficit Reduction Act of 2010, directed Centers for Medicare & Medicaid Services to contract a vendor to determine "retail survey prices for covered outpatient drugs that represent a nationwide average of consumer purchase prices for such drugs, net of all discounts and rebates (to the extent any information with respect to such discounts and rebates is available)." This survey information can be used to determine the National Average Drug Acquisition Cost, or NADAC. Some states have indicated that they will reimburse based on the NADAC and this can result in further reductions in the prices paid for various outpatient drugs.

As part of its reform of the 340B discount drug program, on October 31, 2018, the Health Resources and Services Administration, or HRSA, at the HHS, issued a notice of proposed rulemaking to move up the effective date of a final rule that would give HHS authority to impose Civil Monetary Penalties on pharmaceutical manufacturers who knowingly and intentionally charged a covered entity more than the statutorily allowed ceiling price for a covered outpatient drug. The final rule is intended to encourage compliance by manufacturers in offering the mandatory 340B ceiling purchase price to eligible purchasers, such as certain qualified health systems or individual hospitals.

Various states, such as California, have also taken steps to consider and enact laws or regulations that are intended to increase the visibility of the pricing of pharmaceutical products with the goal of reducing the prices at which we are able to sell our products. Because these various actual and proposed legislative changes are intended to operate on a state-by-state level rather than a national one, we cannot predict what the full effect of these legislative activities may be on our business in the future.

Although we cannot predict the full effect on our business of the implementation of existing legislation, including the Affordable Care Act or the enactment of additional legislation, we believe that legislation or regulations that reduce reimbursement for or restrict coverage of our products could adversely affect how much or under what circumstances healthcare providers will prescribe or administer our products. This could materially and adversely affect our business by reducing our ability to generate revenue, raise capital, obtain additional collaborators and market our products, following marketing approval. In addition, we believe the increasing emphasis on managed care in the United States has and will continue to put pressure on the price and usage of pharmaceutical products, which may adversely impact any future product sales.

If we or any of our independent contractors, consultants, collaborators, manufacturers, or service providers fail to comply with healthcare and data privacy laws and regulations, we or they could be subject to enforcement actions, which could result in penalties and affect our ability to develop, market and sell our product candidates and may harm our reputation.

We are or may in the future be subject to federal, state, and foreign healthcare and data privacy laws and regulations pertaining to, among other things, fraud and abuse of patients' rights. These laws and regulations include:

- The federal Anti-Kickback Statute prohibits, among other things, knowingly and willfully soliciting, offering, receiving, or paying any remuneration, directly or indirectly, in cash or in kind, to induce or reward purchasing, ordering or arranging for or recommending the purchase or order of any item or service for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid. Liability may be established without a person or entity having actual knowledge of the federal Anti-Kickback Statute or specific intent to violate it. This statute has been interpreted to apply broadly to arrangements between pharmaceutical manufacturers on the one hand and prescribers, patients, purchasers and formulary managers on the other. In addition, the Affordable Care Act amended the Social Security Act to provide that the U.S. 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, or the FCA. A conviction for violation of the Anti-Kickback Statute requires mandatory exclusion from participation in federal healthcare programs. Although there are a number of statutory exemptions and regulatory safe harbors protecting certain common activities from prosecution, the exemptions and safe harbors are drawn narrowly, and those activities may be subject to scrutiny or penalty if they do not qualify for an exemption or safe harbor;

- The FCA prohibits, among other things, knowingly presenting, or causing to be presented claims for payment of government funds that are false or fraudulent, or knowingly making, using or causing to be made or used a false record or statement material to such a false or fraudulent claim, or knowingly concealing or knowingly and improperly avoiding, decreasing, or concealing an obligation to pay money to the federal government. This statute also permits a private individual acting as a “whistleblower” to bring actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery. The FCA prohibits anyone from knowingly presenting, conspiring to present, making a false statement in order to present, or causing to be presented, for payment to federal programs (including Medicare and Medicaid) claims for items or services, including drugs, that are false or fraudulent, claims for items or services not provided as claimed, or claims for medically unnecessary items or services. This law also prohibits anyone from knowingly underpaying an obligation owed to a federal program. Increasingly, U.S. federal agencies are requiring nonmonetary remedial measures, such as corporate integrity agreements in FCA settlements. The U.S. Department of Justice announced in 2016 its intent to follow the “Yates Memo,” taking a far more aggressive approach in pursuing individuals as FCA defendants in addition to the corporations. FCA liability is potentially significant in the healthcare industry because the statute provides for treble damages and mandatory penalties of $5,500 to $11,000 per false claim or statement ($10,781 to $21,563 per false claim or statement for penalties assessed after August 1, 2016 for violations occurring after November 2, 2015, and $10,957 to $21,916 per false claim or statement for penalties assessed after February 3, 2017 for violations occurring after November 2, 2015). Government enforcement agencies and private whistleblowers have investigated pharmaceutical companies for or asserted liability under the FCA for a variety of alleged promotional and marketing activities, such as providing free product to customers with the expectation that the customers would bill federal programs for the product; providing consulting fees and other benefits to physicians to induce them to prescribe products; engaging in promotion for “off-label” uses; and submitting inflated best price information to the Medicaid Rebate Program;

- The federal False Statements Statute prohibits knowingly and willfully falsifying, concealing, or covering up a material fact or making any materially false, fictitious or fraudulent statement or representation, or making or using any false writing or document knowing the same to contain any materially false, fictitious or fraudulent statement or entry, in connection with the delivery of or payment for healthcare benefits, items, or services;

- The federal Civil Monetary Penalties Law authorizes the imposition of substantial civil monetary penalties against an entity, such as a pharmaceutical manufacturer, that engages in activities including, among others (1) knowingly presenting, or causing to be presented, a claim for services not provided as claimed or that is otherwise false or fraudulent in any way; (2) arranging for or contracting with an individual or entity that is excluded from participation in federal healthcare programs to provide items or services reimbursable by a federal healthcare program; (3) violations of the federal Anti-Kickback Statute; or (4) failing to report and return a known overpayment;

- The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of, or payment for, healthcare benefits, items or services; similar to the 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, which imposes requirements on certain types of people and entities relating to the privacy, security, and transmission of individually identifiable health information, and requires notification to affected individuals and regulatory authorities of certain breaches of security of individually identifiable health information;

- The federal Physician Payment Sunshine Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program, to report annually to the Centers for Medicare & Medicaid Services information related to payments and other transfers of value to physicians, other healthcare providers and teaching hospitals, and ownership and investment interests held by physicians and other healthcare providers and their immediate family members, which is published in a searchable form on an annual basis;

- State laws comparable to each of the above federal laws, such as, for example, anti-kickback and false claims laws that may be broader in scope and also apply to commercial insurers and other non-federal payor;

- Requirements for mandatory corporate regulatory compliance programs, and laws relating to patient data privacy and security. Other state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government; require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; and state and foreign laws 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; and

- In the European Union, the General Data Protection Regulation, or the GDPR—Regulation EU 2016/679—which was adopted in May 2016 and has become applicable on May 25, 2018. The GDPR is further intended to harmonize data protection requirements across the European Union member states by establishing new and expanded operational requirements for entities that collect, process or use personal data generated in the European Union, including consent requirements for disclosing the way personal information will be used, information retention requirements, and notification requirements in the event of a data breach.

- The California Consumer Privacy Act of 2018, or CCPA, effective as of January 1, 2020, gives California residents expanded rights to access and require deletion of their personal information, opt out of certain personal information sharing, and receive detailed information about how their personal information is used. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches, that is expected to increase data breach litigation.

- In addition, failure to comply with the Israeli Privacy Protection Law of 1981, and its regulations, as well as the guidelines of the Israeli Privacy Protection Authority, may expose us to administrative fines, civil claims (including class actions) and in certain cases criminal liability. Current pending legislation may result in a change of the current enforcement measures and sanctions.

If our operations are found to be in violation of any such healthcare laws and regulations, we may be subject to penalties, including administrative, civil and criminal penalties, monetary damages, disgorgement, imprisonment, the curtailment or restructuring of our operations, loss of eligibility to obtain approvals from the FDA or foreign regulatory authorities, or exclusion from participation in government contracting, healthcare reimbursement or other government programs, including Medicare and Medicaid, any of which could adversely our financial results. Any action against us for an alleged or suspected violation could cause us to incur significant legal expenses and could divert our management's attention from the operation of our business, even if our defense is successful. In addition, achieving and sustaining compliance with applicable laws and regulations may be costly to us in terms of money, time and resources.

Our employees, principal investigators, consultants, commercial partners or vendors may engage in misconduct or other improper activities, including non-compliance with regulatory standards.

We are also exposed to the risk of employees, independent contractors, principal investigators, consultants, commercial partners or vendors engaging in fraud or other misconduct. Misconduct by employees, independent contractors, principal investigators, consultants, commercial partners and vendors could include intentional failures to comply with EU regulations, to provide accurate information to the EMA or EU Member States authorities or to comply with manufacturing or quality standards we have or will have established. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices such as promotion of products by medical practitioners. The EU Member States in which we operate have different statutory provisions regulating the cooperation of pharmaceutical companies with healthcare professionals. In addition to these statutory provisions, codes of conduct issued by business associations or other non-statutory standards may be applicable to our activities. Both statutory provisions and non-statutory codes or standards restrict payments or other benefits provided to healthcare professionals, and in case of non-compliance, may result in severe sanctions such as bans, administrative fines, criminal fines or even imprisonment. The advertising of medicinal products for human use in the EU is regulated by Title VIII of European Directive 2001/83/EC. These provisions have been implemented into the law of the EU member States. Such laws inter alia restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Misconduct could also involve the improper use of information obtained in the course of clinical studies, which could result in regulatory sanctions and serious and irreparable harm to our reputation.

This could also apply with respect to data privacy. In the EU, the EU Directive 95/46/EEC was replaced by the GDPR on May 25, 2018. The GDPR as an EU regulation does not have to be implemented into Member States' national law, but applies directly in all Member States since May 25, 2018. It applies to companies with an establishment in the European Economic Area (EEA) and to certain other companies not in the EEA that offer or provide goods or services to individuals located in the EEA or monitor individuals located in the EEA. The GDPR implements more stringent operational requirements for controllers of personal data, including, for example, expanded disclosures about how personal information is to be used, limitations on retention of information, increased requirements pertaining to health data and pseudonymized (i.e., key-coded) data, increased cyber security requirements, mandatory data breach notification requirements and higher standards for controllers to demonstrate that they have obtained a valid legal basis for certain data processing activities. The GDPR provides that EU Member States may continue to make their own further laws and regulations in relation to the processing of genetic, biometric or health data, which could result in continued or new differences between Member States, limit our ability to use and share personal data or could cause our costs to increase, and harm our business and financial condition. We are also subject to evolving and strict rules on the transfer of personal data out of the European Union to the United States. Further prospective revision of the Directive on privacy and electronic communications (Directive 2002/58/EC), or ePrivacy Directive, may affect our marketing communications.

Our actual or alleged failure to comply with this regulation, or to protect personal data, could result in enforcement actions and significant penalties against us, which could result in negative publicity, increase our operating costs, subject us to claims or other remedies and have a material adverse effect on our business, financial condition, and results of operations. It is not always possible to identify and deter misconduct by employees or other parties. The precautions we take to detect and prevent such activity may not protect us from legal or regulatory action resulting from a failure to comply with applicable laws or regulations. Misconduct by our employees, principal investigators, consultants, commercial partners or vendors could result in significant financial penalties, criminal sanctions, civil law claims and/or negative media coverage, and thus have a material adverse effect on our business, including through the imposition of significant fines or other sanctions, and our reputation. In particular, failure to comply with EU laws, including failure under the GDPR, ePrivacy Directive and other laws relating to the security of personal data may result in fines up to €20,000,000 or up to 4% of the total worldwide annual turnover of the preceding financial year, if greater, and other administrative penalties including criminal liability, which may be onerous and adversely affect our business, financial condition, results of operations and prospects. Failure to comply with the GDPR and related laws may also give risk to increase risk of private actions, including a new form of class action that is available under the GDPR.

Risks Related to Our Operations in Israel

We conduct our operations in Israel and therefore our results may be adversely affected by political, economic and military instability in Israel and its region.

Our headquarters, all of our operations and some of our suppliers and third party contractors are located in central Israel and our key employees, officers and most of our directors are residents of Israel. Accordingly, political and economic instability, war or acts of terrorism or natural disasters, emergence of a pandemic, or other widespread health emergencies (or concerns over the possibility of such an emergency, including for example, the COVID-19 outbreak), may directly affect our business. Since the establishment of the State of Israel in 1948, a number of armed conflicts have taken place between Israel and its Arab neighbors. Any hostilities involving Israel or the interruption or curtailment of trade within Israel or between Israel and its trading partners could adversely affect our operations and results of operations and could make it more difficult for us to raise capital. During the winter of 2008, winter of 2012 and the summer of 2014, Israel was engaged in an armed conflict with Hamas, a militia group and political party operating in the Gaza Strip, and during the summer of 2006, Israel was engaged in an armed conflict with Hezbollah, a Lebanese Islamist Shiite militia group and political party. Israel faces political tension with respect to its relationships with Turkey, Iran and certain Arab neighbor countries. In addition, recent conflicts involved missile strikes against civilian targets in various parts of Israel, and negatively affected business conditions in Israel. Recent political uprisings and social unrest in various countries in the Middle East and North Africa are affecting the political stability of those countries. This instability may lead to deterioration of the political relationships that exist between Israel and these countries, and have raised concerns regarding security in the region and the potential for armed conflict. Any armed conflicts, terrorist activities or political instability in the region could adversely affect business conditions and could harm our results of operations. For example, any major escalation in hostilities in the region could result in a portion of our employees and service providers being called up to perform military duty for an extended period of time. Parties with whom we do business have sometimes declined to travel to Israel during periods of heightened unrest or tension, forcing us to make alternative arrangements when necessary. In addition, the political and security situation in Israel may result in parties with whom we have agreements involving performance in Israel claiming that they are not obligated to perform their commitments under those agreements pursuant to force majeure provisions in such agreements. Any future deterioration in the political and security situation in Israel will negatively impact our business.

Our commercial insurance does not cover losses that may occur as a result of events associated with the security situation in the Middle East. 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. Any losses or damages incurred by us could have a material adverse effect on our business. Any armed conflicts or political instability in the region would likely negatively affect business conditions and could harm our results of operations.

Further, in the past, the State of Israel and Israeli companies have been subjected to an economic boycott. Several countries still restrict business with the State of Israel and with Israeli companies. These restrictive laws and policies may have an adverse impact on our operating results, financial condition or the expansion of our business.

The legislative power of the State resides in the Knesset, a unicameral parliament that consists of 120 members elected by nationwide voting under a system of proportional representation. Israel’s most recent general elections were held on March 23, 2021. The uncertainty surrounding the results of the recent elections may continue. Actual or perceived political instability in Israel or any negative changes in the political environment, may individually or in the aggregate adversely affect the Israeli economy and, in turn, our business, financial condition, results of operations and prospects.

Our operations may be disrupted as a result of the obligation of Israeli citizens to perform military service.

Many Israeli citizens, including Motti Farbstein, our Chief Operating and Financial Officer, are obligated to perform one month, and in some cases more, of annual military reserve duty until they reach the age of 40 (or older, for reservists with certain occupations) and, in the event of a military conflict, may be called to active duty. In response to increases in terrorist activity, there have been periods of significant call-ups of military reservists. It is possible that there will be military reserve duty call-ups in the future. Our operations could be disrupted by such call-ups, which may include the call-up of Motti Farbstein. Such disruption could materially adversely affect our business, financial condition and results of operations.

Because a certain portion of our expenses is incurred in currencies other than U.S. dollars, our results of operations may be harmed by currency fluctuations and inflation.

From our inception through January 1, 2018, our functional and presentation currency was the NIS. Management conducted a review of the functional currency and decided to change its functional and presentation currency to U.S. dollars from the NIS effective January 1, 2018. These changes were based on an assessment by our management that U.S. dollars is the primary currency of the economic environment in which we operate. Part of our expenses are payable in U.S. dollars or in Euros as well as the revenues from our licensing arrangements that are payable in U.S. dollars and Canadian dollars, we expect our revenues from future licensing arrangements to be denominated in U.S. dollars or in Euros. To date, we have not engaged in hedging transactions. Although the Israeli rate of inflation has not had a material adverse effect on our financial condition during 2018, 2019 or 2020 to date, we may, in the future, decide to enter into currency hedging transactions to decrease the risk of financial exposure from fluctuations in the exchange rates of the currencies mentioned above in relation to U.S. dollars. These measures, however, may not adequately protect us from material adverse effects.

It may be difficult to enforce a U.S. judgment against us and our officers and directors named in this Annual Report on Form 20-F in Israel or the United States, or to serve process on our officers and directors.

We are incorporated in Israel. All of our executive officers and directors listed in this Annual Report on Form 20-F reside outside of the United States, and all of our assets and most of the assets of our executive officers and directors are located outside of the United States. Therefore, a judgment obtained against us or most of our executive officers and all of our directors in the United States, including one based on the civil liability provisions of the U.S. federal securities laws, may not be collectible in the United States and may not be enforced by an Israeli court. It also may be difficult for you to effect service of process on these persons in the United States or to assert U.S. securities law claims in original actions instituted in Israel.

Your rights and responsibilities as a shareholder will be governed by Israeli law which may differ in some respects from the rights and responsibilities of shareholders of U.S. companies.

We are incorporated under Israeli law. The rights and responsibilities of the holders of our shareholders are governed by our Amended and Restated Articles of Association and Israeli law. These rights and responsibilities differ in some respects from the rights and responsibilities of shareholders in typical U.S.-based corporations. In particular, a shareholder of an Israeli company has a duty to act in good faith toward the company and other shareholders and to refrain from abusing its power in the company, including, among other things, in voting at the general meeting of shareholders on matters such as amendments to a company's articles of association, increases in a company's authorized share capital, mergers and acquisitions and interested party transactions requiring shareholder approval. In addition, a shareholder who knows that it possesses the power to determine the outcome of a shareholder vote or to appoint or prevent the appointment of a director or executive officer in the company has a duty of fairness toward the company. There is limited case law available to assist us in understanding the implications of these provisions that govern shareholders' actions. These provisions may be interpreted to impose additional obligations and liabilities of our shareholders that are not typically imposed on shareholders of U.S. corporations.

Provisions of Israeli law may delay, prevent or otherwise impede a merger with, or an acquisition of, our Company, which could prevent a change of control, even when the terms of such a transaction are favorable to us and our shareholders.

Israeli corporate law regulates mergers, requires tender offers for acquisitions of shares above specified thresholds, requires special approvals for transactions involving directors, officers or significant shareholders and regulates other matters that may be relevant to these types of transactions. For example, a merger may not be consummated unless at least 50 days have passed from the date that a merger proposal was filed by each merging company with the Israel Registrar of Companies and at least 30 days from the date that the shareholders of both merging companies approved the merger. In addition, a majority of each class of securities of the target company must approve a merger. Moreover, a full tender offer can only be completed if the acquirer receives at least 95% of the issued share capital; provided that, pursuant to an amendment to the Companies Law, 5759-1999, as amended, or the Israeli Companies Law, effective as of May 15, 2011, a majority of the offerees that do not have a personal interest in such tender offer shall have approved the tender offer; except that, if the total votes to reject the tender offer represent less than 2% of our issued and outstanding share capital, in the aggregate, approval by a majority of the offerees that do not have a personal interest in such tender offer is not required to complete the tender offer, and the shareholders, including those who indicated their acceptance of the tender offer, may, at any time within six months following the completion of the tender offer, petition the court to alter the consideration for the acquisition (unless the acquirer stipulated in the tender offer that a shareholder that accepts the offer may not seek appraisal rights).

Furthermore, Israeli tax considerations may make potential transactions unappealing to us or to our shareholders whose country of residence does not have a tax treaty with Israel exempting such shareholders from Israeli tax. For example, Israeli tax law does not recognize tax-free share exchanges to the same extent as U.S. tax law. With respect to mergers, Israeli tax law allows for tax deferral in certain circumstances but makes the deferral contingent on the fulfillment of numerous conditions, including a holding period of two years from the date of the transaction during which sales and dispositions of shares of the participating companies are restricted. Moreover, with respect to certain share swap transactions, the tax deferral is limited in time, and when such time expires, the tax becomes payable even if no actual disposition of the shares has occurred.

These and other similar provisions could delay, prevent or impede an acquisition of us or our merger with another company, even if such an acquisition or merger would be beneficial to us or to our shareholders. See "Description of the Offered Securities—Articles of Association."

Risks Related to Our Ordinary Shares and ADSs

There can be no assurance that we will not be a passive foreign investment company, or PFIC, for U.S. federal income tax purposes in 2020 or in any subsequent year. If we are a PFIC, there may be negative tax consequences for U.S. taxpayers that are holders of our ordinary shares, ADSs, Warrants, or Pre-funded Warrants.

We will be treated as a PFIC for U.S. federal income tax purposes in any taxable year in which either (i) at least 75% of our gross income is "passive income" or (ii) on average at least 50% of our assets by value produce passive income or are held for the production of passive income. Passive income for this purpose generally includes, among other things, certain dividends, interest, royalties, rents and gains from commodities and securities transactions and from the sale or exchange of property that gives rise to passive income. Passive income also includes amounts derived by reason of the temporary investment of funds, including those raised in a public offering. In determining whether a non-U.S. corporation is a PFIC, a proportionate share of the income and assets of each corporation in which it owns, directly or indirectly, at least a 25% interest (by value) is taken into account.

Based on our analysis of our income, assets, and operations, we do not believe that we were a PFIC for 2020. Because the PFIC determination is highly fact intensive, there can be no assurance that we will not be a PFIC in 2021 or in any other taxable year. If we were to be characterized as a PFIC for U.S. federal income tax purposes in any taxable year during which a U.S. shareholder owns our ordinary shares, ADSs, Warrants, or Pre-funded Warrants, then "excess distributions" to such U.S. shareholder, and any gain realized on the sale or other disposition of our ordinary shares, ADSs, Warrants, or Pre-funded Warrants, as applicable, will be subject to special rules. Under these rules: (i) the excess distribution or gain would be allocated ratably over the U.S. shareholder's holding period for the ordinary shares (or ADSs, Warrants, or Pre-funded Warrants, as the case may be); (ii) the amount allocated to the current taxable year and any period prior to the first day of the first taxable year in which we were a PFIC would be taxed as ordinary income; and (iii) the amount allocated to each of the other taxable years would be subject to tax at the highest rate of tax in effect for the applicable class of taxpayer for that year, and an interest charge for the deemed deferral benefit would be imposed with respect to the resulting tax attributable to each such other taxable year. Certain of the adverse consequences of PFIC status can be mitigated if a U.S. shareholder makes an election to treat us as a "qualified electing fund," or QEF, or makes a "mark-to-market" election. A QEF election is unavailable with respect to our Warrants, and a mark-to-market election is unavailable with respect to our Warrants and Pre-funded Warrants. In addition, if the U.S. Internal Revenue Service, or IRS, determines that we are a PFIC for a year with respect to which we have determined that we were not a PFIC, it may be too late for a U.S. shareholder to make a timely QEF or mark-to-market election. U.S. shareholders who hold our ordinary shares, ADSs, Warrants or Pre-funded Warrants during a period when we are a PFIC will be subject to the foregoing rules, even if we cease to be a PFIC in subsequent years, subject to exceptions for U.S. shareholders who made a timely QEF or mark-to-market election (to the extent available). A U.S. shareholder can make a QEF election by completing the relevant portions of and filing IRS Form 8621 in accordance with the instructions thereto. Upon request, we intend to annually furnish U.S. shareholders with information needed in order to complete IRS Form 8621 (which form would be required to be filed with the IRS on an annual basis by the U.S. shareholder) and to make and maintain a valid QEF election for any year in which we or any of our subsidiaries that we control is a PFIC.

Provisions of our charter documents and Israeli law may discourage, delay, prevent or otherwise impede a merger with, or an acquisition of, our Company, which could prevent a change of control, even when the terms of such a transaction are favorable to us and our shareholders.

Provisions in articles of association may discourage, delay, prevent or otherwise impede a merger, acquisition or other change in control of us that shareholders may consider favorable, including transactions in which they might otherwise receive a premium for their ADSs. On February 20, 2020, we amended our articles of association to establish a staggered Board of Directors, which divides the board into three groups, with directors in each group serving a three-year term. The existence of a staggered board can make it more difficult for shareholders to replace or remove incumbent members of our Board of Directors. As such, these provisions could also limit the price that investors might be willing to pay in the future for our ADSs, thereby depressing the market price of our ADSs. In addition, because our Board of Directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our shareholders to replace or remove our current management by making it more difficult for shareholders to replace members of our Board of Directors.

In addition, Israeli corporate law regulates mergers, requires tender offers for acquisitions of shares above specified thresholds, requires special approvals for transactions involving directors, officers or significant shareholders and regulates other matters that may be relevant to these types of transactions. For example, a merger may not be consummated unless at least 50 days have passed from the date that a merger proposal was filed by each merging company with the Israel Registrar of Companies and at least 30 days from the date that the shareholders of both merging companies approved the merger. In addition, a majority of each class of securities of the target company must approve a merger. Moreover, a full tender offer can only be completed if the acquirer receives at least 95% of the issued share capital; provided that, pursuant to an amendment to the Companies Law, 5759-1999, as amended, or the Israeli Companies Law, effective as of May 15, 2011, a majority of the offerees that do not have a personal interest in such tender offer shall have approved the tender offer; except that, if the total votes to reject the tender offer represent less than 2% of our issued and outstanding share capital, in the aggregate, approval by a majority of the offerees that do not have a personal interest in such tender offer is not required to complete the tender offer, and the shareholders, including those who indicated their acceptance of the tender offer, may, at any time within six months following the completion of the tender offer, petition the court to alter the consideration for the acquisition (unless the acquirer stipulated in the tender offer that a shareholder that accepts the offer may not seek appraisal rights).

Furthermore, Israeli tax considerations may make potential transactions unappealing to us or to our shareholders whose country of residence does not have a tax treaty with Israel exempting such shareholders from Israeli tax. For example, Israeli tax law does not recognize tax-free share exchanges to the same extent as U.S. tax law. With respect to mergers, Israeli tax law allows for tax deferral in certain circumstances but makes the deferral contingent on the fulfillment of numerous conditions, including a holding period of two years from the date of the transaction during which sales and dispositions of shares of the participating companies are restricted. Moreover, with respect to certain share swap transactions, the tax deferral is limited in time, and when such time expires, the tax becomes payable even if no actual disposition of the shares has occurred.

Our business could be negatively impacted by unsolicited takeover proposals, by shareholder activism or by proxy contests relating to the election of directors or other matters.

Our business could be negatively affected as a result of an unsolicited takeover proposal, by shareholder activism or a proxy contest. During 2019, an activist shareholder sought to make changes to our Board of Directors, among other matters, which ultimately resulted in us entering into a settlement agreement with the shareholder, and for which considerable costs were incurred and absorbed significant time and attention by management and the Board of Directors. See “Item 8. Financial Information—B. Consolidated Financial Statements and Other Financial Information—Legal Matters”. A future proxy contest, unsolicited takeover proposal, or other shareholder activism relating to the election of directors or other matters would most likely require us to incur significant legal fees and proxy solicitation expenses and require significant time and attention by management and our Board of Directors. The potential of a proxy contest, unsolicited takeover proposal, or other shareholder activism could interfere with our ability to execute our strategic plan, give rise to perceived uncertainties as to our future direction, result in the loss of potential business opportunities or make it more difficult to attract and retain qualified personnel, any of which could materially and adversely affect our business and operating results.

Issuance of additional equity securities may adversely affect the market price of our ADSs or ordinary shares.

We are currently authorized to issue 1,000,000,000 ordinary shares. As of the date of this Annual Report, we had 515,746,293 ordinary shares issued and outstanding and we had no preferred shares outstanding. As of the date of this Annual Report, we also had warrants to purchase 177,265,456 ordinary shares and options to purchase 11,816,200 ordinary shares outstanding, of which options to purchase 3,513,075 ordinary shares are currently fully vested or vest within the next 60 days.

To the extent that ADSs or ordinary shares are issued or options and warrants are exercised, holders of our ADSs and our ordinary shares will experience dilution. In addition, in the event of any future issuances of equity securities or securities convertible into or exchangeable for ADSs or ordinary shares, holders of our ADSs or our ordinary shares may experience dilution. We also consider from time to time various strategic alternatives that could involve issuances of additional ADSs or ordinary shares, including but not limited to acquisitions and business combinations, but do not currently have any definitive plans to enter into any of these transactions.

We have no plans to pay dividends on our ordinary shares, and you may not receive funds without selling our ADSs or ordinary shares.

We have not declared or paid any cash dividends on our ordinary shares, nor do we expect to pay any cash dividends on our ordinary shares for the foreseeable future. We currently intend to retain any additional future earnings to finance our operations and growth and for future stock repurchases and, therefore, we have no plans to pay cash dividends on our ordinary shares at this time. Any future determination to pay cash dividends on our ordinary shares will be at the discretion of our Board of Directors and will be dependent on our earnings, financial condition, operating results, capital requirements, any contractual restrictions, and other factors that our Board of Directors deems relevant. Accordingly, you may have to sell some or all of our ADSs or ordinary shares in order to generate cash from your investment. You may not receive a gain on your investment when you sell our ADSs or ordinary shares and may lose the entire amount of your investment.

The market price of our ordinary shares and ADSs is subject to fluctuation, which could result in substantial losses by our investors.

The stock market in general and the market price of our ordinary shares on the TASE and our ADSs on the NYSE American is subject to fluctuation, and changes in our share price may be unrelated to our operating performance. The market price of our ordinary shares and ADSs are and will be subject to a number of factors, including:

- announcements of technological innovations or new products by us or others;
- announcements by us of significant strategic partnerships, out-licensing, in-licensing, joint ventures, acquisitions or capital commitments;
- expiration or terminations of licenses, research contracts or other collaboration agreements;
- public concern as to the safety of drugs we, our licensees or others develop;
- general market conditions;
- the volatility of market prices for shares of biotechnology companies generally;
- success of research and development projects;
- success in clinical and preclinical studies;
- departure of key personnel;

- developments concerning intellectual property rights or regulatory approvals;
- variations in our and our competitors' results of operations;
- changes in earnings estimates or recommendations by securities analysts, if our ordinary shares or ADSs are covered by analysts;
- changes in government regulations or patent decisions;
- developments by our licensees; and
- general market conditions and other factors, including factors unrelated to our operating performance, such as natural disasters and political and economic instability, including wars, terrorism, political unrest, results of certain elections and votes, emergence of a pandemic, or other widespread health emergencies (or concerns over the possibility of such an emergency, including for example, the COVID-19 outbreak), boycotts, adoption or expansion of government trade restrictions, and other business restrictions.

These factors and any corresponding price fluctuations may materially and adversely affect the market price of our ordinary shares and our ADSs and result in substantial losses by our investors.

Additionally, market prices for securities of biotechnology and pharmaceutical companies historically have been very volatile. The market for these securities has from time to time experienced significant price and volume fluctuations for reasons unrelated to the operating performance of any one company. In the past, following periods of market volatility, shareholders have often instituted securities class action litigation and we have been named in the past in a lawsuit requesting recognition as a class action, in which we ultimately prevailed. If we were involved in securities litigation, it could have a substantial cost and divert resources and attention of management from our business, even if we are successful.

Future sales of our ordinary shares or ADSs could reduce the market price of our ordinary shares and ADSs.

Substantial sales of our ordinary shares or our ADSs either on the TASE or on the NYSE American, as applicable, may cause the market price of our ordinary shares or our ADSs to decline.

Sales by us or our security-holders of substantial amounts of our ordinary shares or our ADSs, or the perception that these sales may occur in the future, could cause a reduction in the market price of our ordinary shares or our ADSs. The issuance of any additional ordinary shares or ADSs, or any securities that are exercisable for or convertible into our ordinary shares or our ADSs, may have an adverse effect on the market price of our ordinary shares or our ADSs, as applicable, and will have a dilutive effect on our shareholders.

We may not satisfy the NYSE American requirements for continued listing. If we cannot satisfy these requirements, the NYSE American could delist our securities.

Our ADSs are listed on the NYSE American under the symbol "CANF." To continue to be listed on the NYSE American, we are required to satisfy a number of conditions, including maintaining a share price and shareholders' equity above certain thresholds. If we are delisted from the NYSE American, trading in our securities may be conducted, if available, on the OTC Markets or, if available, via another market. In the event of such delisting, our shareholders would likely find it significantly more difficult to dispose of, or to obtain accurate quotations as to the value of our securities, and our ability to raise future capital through the sale of our securities could be severely limited. In addition, if our securities were delisted from the NYSE American, our ADSs could be considered a "penny stock" under the U.S. federal securities laws. Additional regulatory requirements apply to trading by broker-dealers of penny stocks that could result in the loss of an effective trading market for our securities. Moreover, if our ADSs were delisted from the NYSE American, we will no longer be exempt from certain provisions of the Israeli Securities Law, and therefore will have increased disclosure requirements.

ADS holders are not shareholders and do not have shareholder rights.

The Bank of New York Mellon, as Depositary, delivers our ADSs. Each ADS represents two of our ordinary shares. ADS holders will not be treated as shareholders and do not have the rights of shareholders. The Depositary will be the holder of the shares underlying our ADSs. Holders of ADSs will have ADS holder rights. A deposit agreement among us, the Depositary, ADS holders and the beneficial owners of ADSs sets out ADS holder rights as well as the rights and obligations of the Depositary. New York law governs the deposit agreement and our ADSs. Our shareholders have shareholder rights. Israeli law and our Amended and Restated Articles of Association govern shareholder rights. ADS holders do not have the same voting rights as our shareholders. Shareholders are entitled to our notices of general meetings and to attend and vote at our general meetings of shareholders. At a general meeting, every shareholder present (in person or by proxy, attorney or representative) and entitled to vote has one vote. This is subject to any other rights or restrictions which may be attached to any shares. ADS holders may instruct the Depositary how to vote the number of deposited shares their ADSs represent. *Otherwise, you won't be able to exercise your right to vote unless you withdraw the shares. However, you may not know about the meeting enough in advance to withdraw the shares. Th*e Depositary will notify ADS holders of shareholders' meetings and arrange to deliver our voting materials to them if we ask it to. Those materials will describe the matters to be voted on and explain how ADS holders may instruct the Depositary how to vote. For instructions to be valid, they must reach the Depositary by a date set by the Depositary. The Depositary will try, as far as practical, subject to the laws of Israel and our Amended and Restated Articles of Association or similar documents, to vote or to have its agents vote the shares or other deposited securities as instructed by ADS holders. The Depositary will only vote or attempt to vote as instructed. We cannot assure you that you will receive the voting materials in time to ensure that you can instruct the Depositary to vote your shares. In addition, the Depositary and its agents are not responsible for failing to carry out voting instructions or for the matter of carrying out voting instructions. Th*is means that you may not be able to exercise your right to vote and there may be nothing you can do if your shares are not voted as requested.*

ADS holders do not have the same rights to receive dividends or other distributions as our shareholders. Subject to any special rights or restrictions attached to a share, the directors may determine that a dividend will be payable on a share and fix the amount, the time for payment and the method for payment (although we have never declared or paid any cash dividends on our ordinary shares and we do not anticipate paying any cash dividends in the foreseeable future). Dividends and other distributions payable to our shareholders with respect to our ordinary shares generally will be payable directly to them. Any dividends or distributions payable with respect to ordinary shares deposited in the ADS facility will be paid to the Depositary, which has agreed to pay to ADS holders the cash dividends or other distributions it or the custodian receives on shares or other deposited securities, after deducting its fees and expenses. ADS holders will receive these distributions in proportion to the number of ordinary shares their ADSs represent. In addition, there may be certain circumstances in which the Depositary may not pay ADS holder's amounts distributed by us as a dividend or distribution.

Our ordinary shares and our ADSs are traded on different markets and this may result in price variations.

Our ordinary shares have traded on the TASE since October 2005 and our ADSs have been listed on the NYSE American since November 2013. Trading on these markets will take place in different currencies (U.S. dollars on the NYSE American and NIS on the TASE), and at different times (resulting from different time zones, different trading days and different public holidays in the United States and Israel). The trading prices of our securities on these two markets may differ due to these and other factors. Any decrease in the price of our securities on one of these markets could cause a decrease in the trading price of our securities on the other market.

We have incurred significant additional increased costs as a result of the listing of our ADSs for trading on the NYSE American, and our management is required to devote substantial time to new compliance initiatives as well as to compliance with ongoing U.S. and Israeli reporting requirements.

As a public company in the United States, we incur additional significant accounting, legal and other expenses that we did not incur before becoming a reporting company in the United States. We also incur costs associated with corporate governance requirements of the SEC and the NYSE American Company Guide, as well as requirements under Section 404 and other provisions of the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act as a result of our ADSs being listed on the NYSE American. These rules and regulations have increased our legal and financial compliance costs, introduced new costs such as investor relations, stock exchange listing fees and shareholder reporting, and made some activities more time consuming and costly. Since we are no longer an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, and are no longer able to take advantage of certain exemptions from various reporting requirements that are applicable to public companies that are "emerging growth companies" and that were applicable to us prior to January 1, 2020, we may incur additional compliance costs in the future. The implementation and testing of such processes and systems may require us to hire outside consultants and incur other significant costs. Any future changes in the laws and regulations affecting public companies in the United States and Israel, including Section 404 and other provisions of the Sarbanes-Oxley Act, the rules and regulations adopted by the SEC and the NYSE American Company Guide, as well as applicable Israeli reporting requirements, for so long as they apply to us, may result in increased costs to us as we respond to such changes. These laws, rules and regulations could make it more difficult or more costly for us to obtain certain types of insurance, including director and officer liability insurance, and we may be forced to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. The impact of these requirements could also make it more difficult for us to attract and retain qualified persons to serve on our Board of Directors, our Board committees or as executive officers.

As a foreign private issuer, we are permitted to follow certain home country corporate governance practices instead of applicable SEC and NYSE American requirements, which may result in less protection than is accorded to investors under rules applicable to domestic issuers.

As a foreign private issuer, we will be permitted to follow certain home country corporate governance practices instead of those otherwise required under the NYSE American Company Guide for domestic issuers. For instance, we may follow home country practice in Israel with regard to, among other things, composition and function of the audit committee and other committees of our Board of Directors and certain general corporate governance matters. In addition, in certain instances we will follow our home country law, instead of the NYSE American Company Guide, which requires that we obtain shareholder approval for certain dilutive events, such as an issuance that will result in a change of control of the company, certain transactions other than a public offering, involving issuances of a 20% or more interest in the company and certain acquisitions of the stock or assets of another company. We comply with the director independence requirements of the NYSE American Company Guide, including the requirement that a majority of the Board of Directors be independent. Following our home country governance practices as opposed to the requirements that would otherwise apply to a U.S. company listed on the NYSE American may provide less protection than is accorded to investors under the NYSE American Company Guide applicable to domestic issuers.

In addition, as a foreign private issuer, we are exempt from the rules and regulations under the U.S. Securities Exchange Act of 1934, as amended, or the Exchange Act, related to the furnishing and content of proxy statements, and our officers, directors and principal shareholders are exempt from the reporting and short-swing profit recovery provisions contained in Section 16 of the Exchange Act. In addition, we will not be required under the Exchange Act to file annual, quarterly and current reports and financial statements with the SEC as frequently or as promptly as domestic companies whose securities are registered under the Exchange Act.

Because we became a reporting company under the Exchange Act by means of filing a Form 20-F, we may have difficulty attracting the attention of research analysts at major brokerage firms.

Because we did not become a reporting company by conducting an underwritten initial public offering in the United States, we may have difficulty attracting the attention of security analysts at major brokerage firms in order for them to provide coverage of our company. The failure to receive research coverage or support in the market for our shares will have an adverse effect on our ability to develop a liquid market for our ADSs.

If we are unable to satisfy the requirements of Section 404 of the Sarbanes-Oxley Act as they apply to a foreign private issuer that is listed on a U.S. exchange, or our internal control over financial reporting is not effective, the reliability of our financial statements may be questioned and our share price and the ADS price may suffer.

We are subject to the requirements of the Sarbanes-Oxley Act. Section 404 of the Sarbanes-Oxley Act requires companies subject to the reporting requirements of the U.S. securities laws to do a comprehensive evaluation of its and its subsidiaries' internal control over financial reporting. To comply with this statute, we must document and test our internal control procedures and our management and issue a report concerning our internal control over financial reporting. In addition, as long as we do not become an accelerated or large accelerated filer, we are exempt from the auditor attestation requirements of Section 404(b) of the Sarbanes-Oxley Act. Under this exemption, our auditor will not be required to attest to and report on our management's assessment of our internal control over financial reporting until the date we are no longer a non-accelerated filer. We will need to prepare for compliance with Section 404 by strengthening, assessing and testing our system of internal controls to provide the basis for our report. However, the continuous process of strengthening our internal controls and complying with Section 404 is complicated and time-consuming. Furthermore, as our business continues to grow both domestically and internationally, our internal controls will become more complex and will require significantly more resources and attention to ensure our internal controls remain effective overall. During the course of the testing, our management may identify material weaknesses or significant deficiencies, which may not be remedied in a timely manner to meet the deadline imposed by the Sarbanes-Oxley Act. If our management cannot favorably assess the effectiveness of our internal control over financial reporting, or our independent registered public accounting firm identifies material weaknesses in our internal controls, investor confidence in our financial results may weaken, and the market price of our securities may suffer.