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

Amendment No. 1 to
FORM 20-F

☐ REGISTRATION STATEMENT PURSUANT TO SECTION 12(b) OR (g) OF THE SECURITIES EXCHANGE ACT OF 1934

OR

☒ ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended December 31, 2021

OR

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

OR

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

Date of event requiring this shell company report _____

Commission file number 001-38367

Sol-Gel Technologies Ltd.
(Exact name of Registrant as specified in its charter)

N/A
(Translation of Registrant's name into English)

Israel
(Jurisdiction of incorporation or organization)

7 Golda Meir St., Weizmann Science Park, Ness Ziona, 7403650, Israel
(Address of principal executive offices)

Gilad Mamlok, Chief Financial Officer
7 Golda Meir St., Weizmann Science Park, Ness Ziona, 7403650, Israel
Tel: 972-8-9313429; Fax: 972-153-523044444
(Name, Telephone, E-mail and/or Facsimile number and Address of Company Contact Person)

Securities registered or to be registered pursuant to Section 12(b) of the Act.

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Ordinary Shares, par value NIS 0.1 per share	SLGL	The Nasdaq Stock Market LLC

Securities registered or to be registered pursuant to Section 12(g) of the Act:

None

(Title of Class)

Securities for which there is a reporting obligation pursuant to Section 15(d) of the Act:

None

(Title of Class)

Indicate the number of outstanding shares of each of the issuer's classes of capital or common stock as of the close of the period covered by the annual report: 23,126,804 Ordinary Shares, par value NIS 0.1 per share

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act.

Yes ☐ No ☒

If this report is an annual or transition report, indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Securities Exchange Act 1934.

Yes ☐ No ☒

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days.

Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files).

Yes ☒ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, or a non-accelerated filer. See definition of "accelerated filer and large accelerated filer" in Rule 12b-2 of the Exchange Act. (Check one):

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

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

Indicate by check mark whether the registrant has fi led a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☐

Indicate by check mark which basis of accounting the registrant has used to prepare the financial statements included in this filing:

U.S. GAAP ☒

International Financing Reporting Standards as issued by the International Accounting Standards Board ☐ Other ☐

If "Other" has been checked in response to the previous question, indicate by check mark which financial statement item the registrant has elected to follow.

Item 17 ☐ Item 18 ☐

If this is an annual report, indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act).

Yes ☐ No ☒

EXPLANATORY NOTE

On April 4, 2022, Sol-Gel Technologies Ltd. (the "Company") filed its Annual Report on Form 20-F for the fiscal year ended December 31, 2021 (the "Original Form 20-F"). This Amendment No. 1 (the "Amendment") amends the Original Form 20-F solely to (i) correct typographical errors in Item 4 – Information on the Company and (ii) add the date of the report of our independent accounting firm, Kesselman & Kesselman, a member of PricewaterhouseCoopers International Limited.

This Amendment speaks as of the original filing date and does not reflect events occurring after the filing of the Original Form 20-F. No revisions are being made to the Company's financial statements or any other disclosure contained in the Original Form 20-F. This Amendment does not otherwise update any exhibits as originally filed or previously amended.

In addition, as required by Rule 12b-15 under the Securities Exchange Act of 1934, as amended (the "Exchange Act"), new certifications by the Company's principal executive officer and principal financial officer are filed herewith as exhibits to this Amendment pursuant to Rule 13a-14(a) of the Exchange Act and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. 1350).

ITEM 4. INFORMATION ON THE COMPANY

A. History and Development of the Company

Our legal and commercial name is Sol-Gel Technologies Ltd. Our company was incorporated on October 28, 1997 and was registered as a private company limited by shares under the laws of the State of Israel. Our principal executive offices are located at 7 Golda Meir St., Weizmann Science Park, Ness Ziona, 7403650 Israel and our telephone number is 972-8-931 3433. Our website address is http://www.sol-gel.com. The information contained therein, or that can be accessed therefrom, does not constitute a part of this annual report and is not incorporated by reference herein. We have included our website address in this annual report solely for informational purposes. Our agent for service of process in the United States is Cogency Global Inc., located at 10 E. 40th Street, 10th Floor, New York, NY 10016, and its telephone number is +1 (800) 221-0102.

In February 2018 we completed our initial public offering on The Nasdaq Global Market, pursuant to which we issued 7,187,500 Ordinary Shares for aggregate gross proceeds of approximately $86.25 million before deducting underwriting discounts and commissions and offering expenses payable by us, including the full exercise by the underwriters of their option to purchase additional shares. Our Ordinary Shares are traded on The Nasdaq Global Market under the symbol "SLGL".

Our capital expenditures for the years ended December 31, 2019, 2020 and 2021 were approximately $597 thousand, $449 thousand and $143 thousand, respectively. Our current capital expenditures involve equipment and leasehold improvements.

B. Business Overview

We are a dermatology company focused on identifying, developing and commercializing investigational and generic topical drug products for the treatment of skin diseases. In addition to Twyneo®, which has been approved by the FDA, our current product candidate pipeline consists of clinical stage and early-stage investigational product candidates, some of which leverage our development platform, and several generic product candidates across multiple indications.

Our FDA-approved product, Twyneo®, is a novel, once-daily, non-antibiotic topical cream containing a fixed-dose combination of encapsulated benzoyl peroxide and encapsulated tretinoin, that we developed for the treatment of acne vulgaris, or acne.

On December 30, 2019, we announced top-line results from two pivotal Phase 3 clinical trials evaluating Twyneo® for the treatment of acne. Twyneo® met all co-primary endpoints in both Phase 3 trials. The Phase 3 program enrolled an aggregate of 858 patients aged nine and older in two multicenter, randomized, double-blind, parallel group, vehicle-controlled trials at 63 sites across the United States. Twyneo® demonstrated statistically significant improvement in each of the co-primary endpoints of (1) the proportion of patients who succeeded in achieving at least a two grade reduction from baseline and Clear (grade 0) or Almost Clear (grade 1) at Week 12 on a 5-point Investigator Global Assessment (IGA) scale, (2) an absolute change from baseline in inflammatory lesion count at Week 12, and (3) and an absolute change from baseline in non-inflammatory lesion count at Week 12. In addition, Twyneo® was found to be well-tolerated.

Our investigational product candidate, Epsolay®, is a novel, once-daily investigational topical cream containing encapsulated benzoyl peroxide, that we are developing for the treatment of papulopustular (subtype II) rosacea. On July 8, 2019, we announced positive top-line results from our Phase 3 program evaluating Epsolay®. The program enrolled 733 patients aged 18 and older in two identical, double-blind, vehicle-controlled Phase 3 clinical trials at 54 sites across the United States. Epsolay® demonstrated statistically significant improvement in both co-primary endpoints of (1) the number of patients achieving "clear" or "almost clear" in the Investigator Global Assessment (IGA) relative to baseline at week 12 and (2) absolute mean reduction from baseline in inflammatory lesion count at week 12. In an additional analysis, Epsolay® demonstrated rapid efficacy, achieving statistically significant improvements on both co-primary endpoints compared with vehicle as early as Week 2. In addition, Epsolay® was found to be well- tolerated. Our NDA for Epsolay® was accepted for filing by the FDA, which originally assigned a PDUFA goal date of April 26, 2021, which has since been delayed due to COVID-19 related travel restrictions. The FDA conducted a pre-approval inspection of the production site for Epsolay® during the week of February 14, 2022.

In June 2021, we entered into two five-year exclusive license agreements with Galderma pursuant to which Galderma has the exclusive right to, and is responsible for, all U.S. commercial activities for Twyneo®, and, if approved by the FDA, Epsolay®.

Other investigational product candidates are SGT-210 that we are developing for the treatment of various keratodermas; SGT-310, an investigational aryl hydrocarbon receptor agonist; and SGT-510.

We designed our proprietary, silica-based microencapsulation technology platform to enhance the tolerability and stability of topical drugs while maintaining their efficacy. Topical drugs often struggle to balance achieving both high efficacy and high tolerability. Our technology platform entraps active ingredients in an inert, inorganic silica shell, which creates an unnoticeable barrier between the active ingredient and the skin. The resulting microcapsules are designed to allow the entrapped active ingredients to gradually migrate through the pores of the shell and deliver active ingredient doses onto the skin in a controlled manner, resulting in improved tolerability and stability without sacrificing efficacy. By separately encapsulating active ingredients within protective silica shells, our technology platform also enables the production of novel fixed-dose active ingredient combinations that otherwise would not be stable. We believe that our microencapsulation technology has the potential to be used for topical drug products to treat a variety of skin diseases. As a result of the FDA having already approved silica as a safe excipient for topical drug products, both Twyneo® and Epsolay® were submitted for approval through the FDA's 505(b)(2) regulatory pathway.

In November 2021, we announced that we had signed an agreement with Padagis, pursuant to which we sold our rights related to 10 generic collaborative programs and retained the collaboration rights to two generic programs related to four generic drug candidates for skin diseases. Under the terms of the agreement with Padagis, effective as of November 1, 2021, we are to unconditionally receive $21.5 million over 24 months, in lieu of our share in ten generic programs, two of which were approved by the FDA, and eight of which were unapproved.

Twyneo®, a novel, once-daily, non-antibiotic topical cream, developed for the treatment of acne, containing a fixed-dose combination of encapsulated benzoyl peroxide, or E-BPO, and encapsulated tretinoin. Acne is one of the three most prevalent skin diseases in the world and is the most commonly treated skin disease in the United States. According to the American Academy of Dermatology, acne affects approximately 40 to 50 million people in the United States, of which approximately 10% are treated with prescription medications. Tretinoin and benzoyl peroxide, the two active components in Twyneo®, are both widely-used therapies for the treatment of acne that historically have not been conveniently co-administered due to stability concerns. On December 30, 2019, we announced top-line results from two pivotal Phase 3 clinical trials evaluating Twyneo® for the treatment of acne. Twyneo® met all co-primary endpoints in both Phase 3 trials. The Phase 3 program enrolled an aggregate of 858 patients aged nine and older in two multicenter, randomized, double-blind, parallel group, vehicle-controlled trials at 63 sites across the United States. Twyneo® demonstrated statistically significant improvement in each of the co-primary endpoints of (1) the proportion of patients who succeeded in achieving at least a two grade reduction from baseline and Clear (grade 0) or Almost Clear (grade 1) at Week 12 on a 5-point Investigator Global Assessment (IGA) scale, (2) an absolute change from baseline in inflammatory lesion count at Week 12, and (3) and an absolute change from baseline in non-inflammatory lesion count at Week 12. In addition, Twyneo® was found to be well-tolerated. Twyneo® was approved for marketing by the FDA in July 2021.

Our leading investigational product candidate, Epsolay®, is a topical cream containing 5% encapsulated benzoyl peroxide, which we are developing for the treatment of papulopustular (subtype II) rosacea. Rosacea is a chronic skin disease characterized by facial redness, inflammatory lesions, burning and stinging. According to the U.S. National Rosacea Society, approximately 16 million people in the United States are affected by rosacea. According to a study we commissioned in 2017, approximately 4.8 million people in the United States experience subtype II symptoms. Subtype II rosacea is characterized by small, dome-shaped erythematous papules, tiny surmounting pustules on the central aspects of the face, solid facial erythema and edema, and thickening/overgrowth of skin. Subtype II rosacea resembles acne, except that comedowns are absent, and patients may report associated burning and stinging sensations. Current topical therapies for subtype II rosacea are limited due to tolerability concerns. For example, BPO, a common therapy for acne, is not used for the treatment of subtype II rosacea due to side effects. As encapsulated BPO, Epsolay® is designed to redefine the standard of care for the treatment of subtype II rosacea. If approved by the FDA, we expect Epsolay® to be the first product containing BPO that is marketed for the treatment of subtype II rosacea. On July 8, 2019, we announced positive top-line results from our Phase 3 program evaluating Epsolay®. The program enrolled 733 patients aged 18 and older in two identical, double-blind, vehicle-controlled Phase 3 clinical trials at 54 sites across the United States. Epsolay® demonstrated statistically significant improvement in both co-primary endpoints of (1) the number of patients achieving "clear" or "almost clear" in the Investigator Global Assessment (IGA) relative to baseline at week 12 and (2) absolute mean reduction from baseline in inflammatory lesion count at week 12. In an additional analysis, Epsolay® demonstrated rapid efficacy, achieving statistically significant improvements on both co-primary endpoints compared with vehicle as early as Week 2. In addition, Epsolay® was found to be well-tolerated. On February 12, 2020, we announced positive topline results from our open-label, long-term safety study, evaluating Epsolay® for a treatment duration up to 52 weeks. Our NDA for Epsolay® has been accepted for filing by the FDA, which originally assigned a PDUFA goal date of April 26, 2021, which has since been delayed due to COVID-19 related travel restrictions. The FDA conducted a pre-approval inspection of the production site for Epsolay® during the week of February 14, 2022.

We maintain exclusive, worldwide commercial rights for our other investigational product candidates, which consist of:

- SGT-210 that we are developing for the treatment of various keratoderma, such as PC, PPK, etc. a group of skin conditions characterized by thickening of the skin. SGT-210 is designed to be used alone or in combination for the treatment of hyperproliferation and hyperkeratinization disorders, including PPK. On January 2, 2020, we announced the initiation of a Phase 1 clinical study of SGT-210 in patients with palmoplantar keratoderma. The Phase 1 study SGT-84-01 is a single-center, single-blinded, vehicle-controlled study designed to evaluate the bioavailability, safety and tolerability of SGT-210 as well as inform on potential efficacy. During the third quarter of 2021, we reported that the study with respect to six (6) palmoplantar keratoderma (PPK) patients has been completed and indicated modest improvement and a favorable safety profile.

- We are conducting pre-clinical testing to explore the possible activity of SGT-210, SGT-310 and SGT-510 in various new pharmaceutical indications. A total of 25 provisional patent applications for these investigational drug candidates have been submitted to date, including patent applications covering the use of tapinarof in ophthalmic disorders such as dry eye, uveitis, and blepharitis with or without demodex involvement.

We are also currently developing a portfolio of two generic programs related to four generic drug candidates in collaboration with Padagis, by assignment from Perrigo.

In June 2021, we entered into two exclusive license agreements with Galderma, each for a period of five years following Galderma's first commercial sale of the applicable product in the U.S., pursuant to which Galderma has the exclusive right to, and is responsible for, all U.S. commercial activities for Twyneo®, and, if approved by the FDA, Epsolay®, including promotion and distribution, and we are responsible for obtaining all regulatory approvals of the products until approval in the U.S. Following approval, Galderma will assume responsibility for all filings and communications with regulatory authorities in the U.S. until expiration of the applicable license agreement. In connection with the licenses, we and Galderma have entered into a three party supply agreement with Douglas Manufacturing Limited, which will supply Galderma the Twyneo® product, and Galderma is responsible for entering into a supply agreement with a third party for the supply of the Epsolay® product, once approved. In consideration for the grant of such rights, we are entitled to of up to $11 million in upfront payments to us and regulatory approval milestone payments. We are also eligible to receive tiered double-digit royalties ranging from mid-teen to high-teen percentage of net sales as well as up to $9 million in sales milestone payments.

The following chart represents our current investigational and generic product candidate pipeline:

Our Approved Product and Investigational Product Candidates

Twyneo® for Acne

Using our proprietary, silica-based microencapsulation technology platform, we developed Twyneo® to become a preferred treatment for acne by dermatologists and their patients.

Twyneo® is a novel, once-daily, non-antibiotic topical cream containing a fixed-dose combination of encapsulated benzoyl peroxide and encapsulated tretinoin that we developed for the treatment of acne. Studies have shown that benzoyl peroxide and tretinoin are effective in treating acne as monotherapies; moreover, according to an article in the American Academy of Dermatology (2009), dermatologists recommend combining the two monotherapies as a first-line approach for acne, but a drug-drug interaction that causes the degradation of tretinoin has previously prohibited the development of a combination therapy. By encapsulating the two agents separately through the use of our technology platform, Twyneo® is designed to be a fixed-dose combination that otherwise would not be stable. Similar to other combination drug products, such as clindamycin and benzoyl peroxide, Twyneo® is required to be kept refrigerated throughout the supply chain and then stored in ambient conditions upon its distribution to patients. Pre-clinical data suggests that Twyneo® may be more tolerable than generic tretinoin gel 0.1% and Epiduo, a branded fixed-dose combination of benzoyl peroxide and adapalene, without a corresponding loss in efficacy. In addition, Epiduo and its successor Epiduo Forte contain adapalene as opposed to tretinoin, which is widely considered to be more effective than adapalene, but generally causes greater irritation. We expect that Twyneo® will compete directly with Winlevi, Aklief, Epiduo and Epiduo Forte. We have utilized the FDA's 505(b)(2) regulatory pathway in seeking approval of Twyneo® in the United States.

On December 30, 2019, we announced top-line results from two pivotal Phase 3 clinical trials evaluating Twyneo® for the treatment of acne. Twyneo® met all co-primary endpoints in both Phase 3 trials. The Phase 3 program enrolled an aggregate of 858 patients aged nine and older in two multicenter, randomized, double-blind, parallel group, vehicle-controlled trials at 63 sites across the United States. Twyneo® demonstrated statistically significant improvement in each of the co-primary endpoints of (1) the proportion of patients who succeeded in achieving at least a two grade reduction from baseline and Clear (grade 0) or Almost Clear (grade 1) at Week 12 on a 5-point Investigator Global Assessment (IGA) scale, (2) an absolute change from baseline in inflammatory lesion count at Week 12, and (3) and an absolute change from baseline in non-inflammatory lesion count at Week 12. Twyneo® was approved for marketing by the FDA in July 2021.

Acne Market Opportunity

Acne is a disease characterized by areas of scaly red skin, non-inflammatory blackheads and whiteheads, inflammatory lesions, papules and pustules and occasionally boils and scarring that occur on the face, neck, chest, back, shoulders and upper arms. The development of acne lesions is caused by genetic and environmental factors that arise from the interplay of the following pathogenic factors:

- blockage of hair follicles through abnormal keratinization in the follicle, which narrows pores;
- increase in oils, or sebum production, secreted by the sebaceous gland;
- overgrowth of naturally occurring bacteria caused by the colonization by the anaerobic lipohilic bacterium *Propionibacterium acnes*, or *P. acnes*;
- inflammatory response due to relapse of pro-inflammatory mediators into the skin.

Due to the frequency of recurrence and relapse, acne is characterized as a chronic inflammatory disease, which may require treatment over a prolonged period of time. Acne is one of the three most prevalent skin diseases in the world and is the most commonly treated skin disease in the United States. According to the American Academy of Dermatology, acne affects approximately 40 to 50 million people in the United States and approximately 85% of people between the ages of 12 and 24 experience some form of acne. Acne patients suffer from the appearance of lesions on areas of the body with a large concentration of oil glands, such as the face, chest, neck and back. These lesions can be inflamed (papules, pustules, nodules) or non-inflamed (comedones). Early effective treatment is recommended to lessen the overall long-term impact. For most people, acne diminishes over time and tends to disappear, or at least to decrease, by the age of 25. There is, however, no way to predict how long it will take for symptoms to disappear entirely, and some individuals continue to suffer from acne well into adulthood.

Current Treatment Landscape for Acne

The treatment options for acne depend on the severity of the disease and consist of topical and oral drugs:

- **Mild acne**: characterized by few papules or pustules (both comedonal and inflammatory); treated with an over-the-counter product or topical prescription therapies.
- **Moderate acne**: characterized by multiple papules and pustules with moderate inflammation and seborrhea (scaly red skin); treated with a combination of oral antibiotics and topical therapies.

- **Severe acne**: characterized by substantial papulopustular disease, many nodules and/or cysts and significant inflammation and seborrhea; treated with oral and topical combination therapies and photodynamic therapy as a third-line treatment.

Topical therapies dominate the acne market as physicians and patients often prefer therapies that act locally on the skin, while minimizing side effects. For more pronounced symptoms, patients are typically treated with a combination of topical and oral therapies.

The acne prescription treatment landscape is comprised of four classes of topical products and two classes of oral products:

- **Topical over-the-counter monotherapies** such as adapalene 0.1%, benzoyl peroxide and salicylic acid, in different concentrations, are the most commonly used therapies. These are generally tolerable first-line treatments for mild acne, but less efficacious than prescription therapies.

- **Topical prescription antibiotic monotherapies** such as clindamycin and erythromycin that are most commonly used as topical therapies in cases of mild-to-moderate acne.

- **Topical prescription retinoid monotherapies** such as tretinoin, adapalene 0.3% and tazarotene. Physicians view retinoids as moderately efficacious, but they have high rates of skin irritation.

- **Topical prescription combination products** such as combinations of BPO/adapalene, BPO/clindamycin, BPO/erythromycin and clindamycin/tretinoin. These target multiple components that contribute to the development of acne, though topical side effects are common.

- **Oral prescription antibiotics** such as doxycycline and minocycline. These are typically used as step-up treatments for more severe cases of acne, with risk of systemic side effects.

- **Oral prescription isotretinoin**, which is primarily used for severe cystic acne and acne that has not responded to other treatments. The use of oral prescription isotretinoin is tightly controlled due to tolerability issues.

Twyneo® Phase 3 Trial Design

The pivotal Phase 3 clinical program evaluating the safety and efficacy of Twyneo® in subjects with acne vulgaris enrolled an aggregate of 858 patients aged nine and older, with moderate-to-severe acne in two multicenter, randomized, double-blind, parallel group, vehicle-controlled trials at 63 sites across the United States. Patients were randomized at a 2:1 ratio to be treated once-daily with either Twyneo® (n=571) or vehicle cream (n=287) for 12 weeks.

The primary and secondary efficacy endpoints were assessed at the end of the 12-week treatment period. Three primary efficacy endpoints were defined for this trial:

- the proportion of subjects who achieve at least a two-grade reduction in the IGA score and either “clear” or “almost clear” at week 12;

- the mean absolute change from baseline in the number of inflammatory acne lesions at week 12; and

- the mean absolute change from baseline in the number of non-inflammatory acne lesions at week 12.

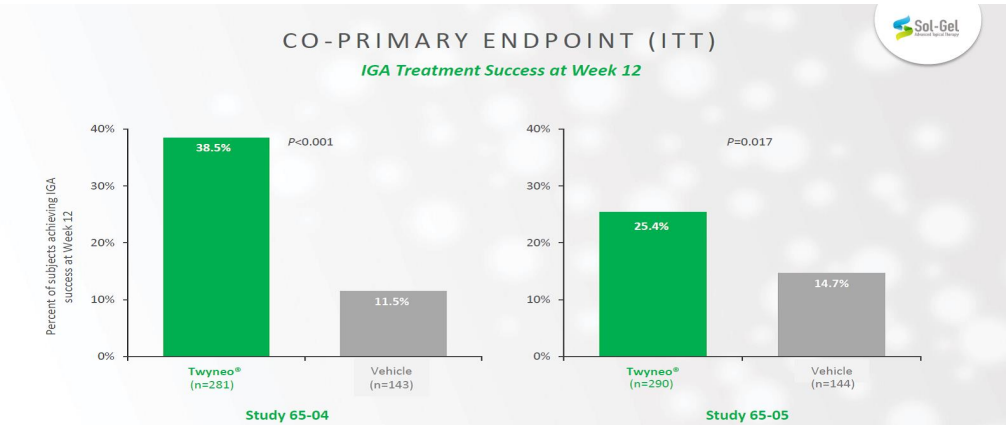
Twyneo® Phase 3 Trial Results

As outlined below Twyneo® met all co-primary endpoints in both Phase 3 trials. Twyneo® demonstrated statistically significant improvement in each of the co-primary endpoints described above.

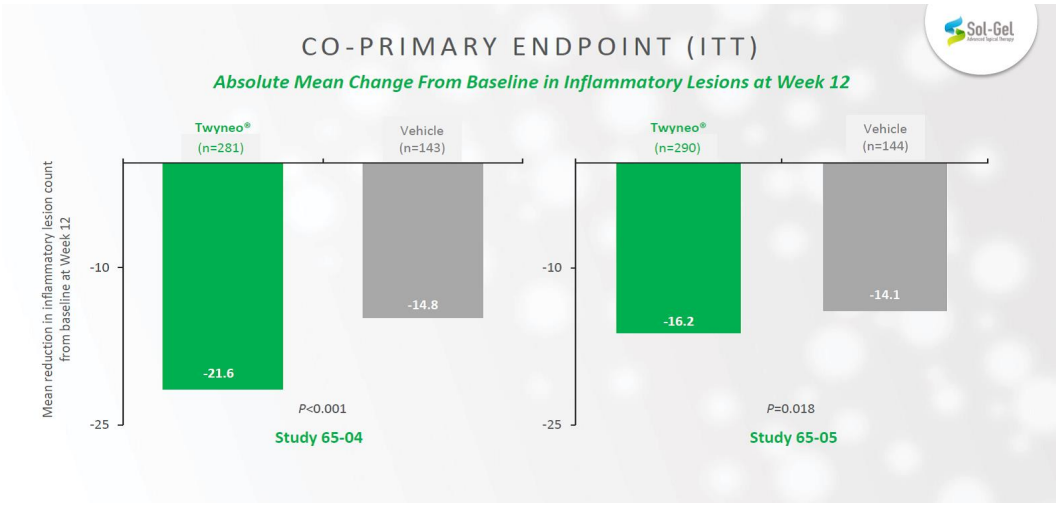
In trial SGT-65-04, 39.9% of patients treated with Twyneo® achieved success in IGA versus 14.3% in the vehicle treated group (P<0.001) at week 12. In trial SGT-65-05, 26.8% of patients treated with Twyneo® achieved success in IGA versus 15.1% in the vehicle group (P=0.017) at week 12. In trial SGT-65-04, the absolute mean change from baseline of inflammatory lesion count for Twyneo® was -21.6 versus -14.8 for the vehicle group (P<0.001) at week 12. In trial SGT-65-05, the absolute change from baseline of inflammatory lesion count for Twyneo® was -16.2 versus -14.1 for the vehicle group (P=0.021) at week 12. In trial SGT-65-04, the absolute mean change from baseline of non-inflammatory lesion count for Twyneo® was -29.7 versus -19.8 for the vehicle group (P<0.001). In trial SGT-65-05, the absolute mean change from baseline of non-inflammatory lesion count for Twyneo was -24.2 versus -17.4 for the vehicle group (P<0.001) at week 12.

In both trials, Twyneo® appeared to be generally safe and well-tolerated and the majority of local skin reactions, when reported, were mild or moderate and improved over time. A total of 18 subjects discontinued treatment in both trials due to treatment emergent adverse events. There were no treatment-related serious adverse events and four unrelated serious adverse events (one Twyneo® (depression), three vehicle) were reported across both trials.

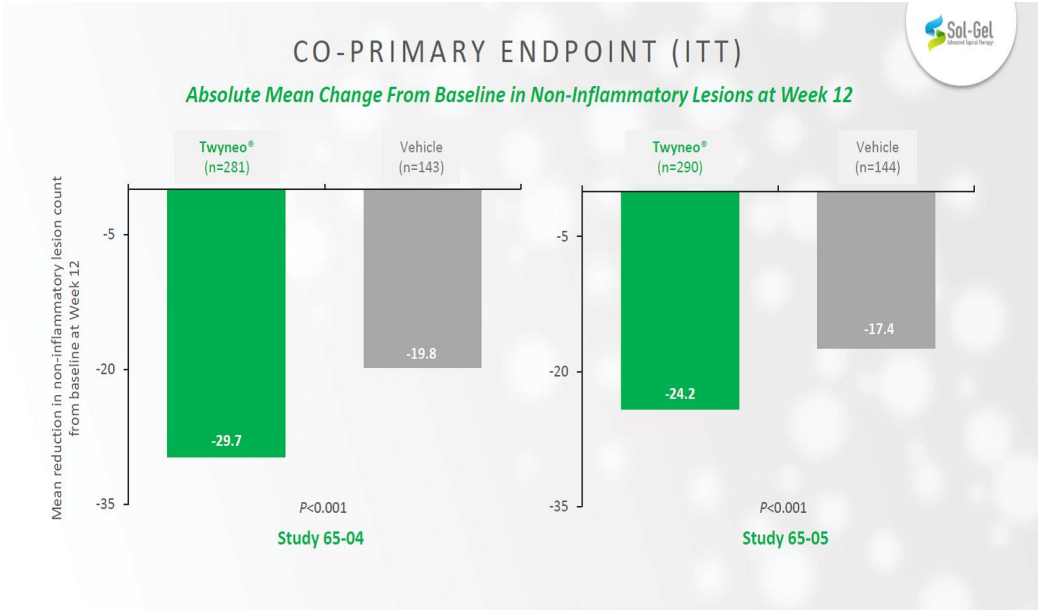
The following chart presents the proportion of subjects in the ITT population in studies SGT 65-04 and SGT 65-05 who achieved a successful improvement in the severity of their disease at week 12, as assessed using the IGA:



The following chart presents the absolute mean change from baseline in the number of inflammatory acne lesions at week 12:



The following chart presents the absolute mean change from baseline in the number of non-inflammatory acne lesions at week 12:



We also assessed cutaneous tolerability by recording the erythema (redness), scaling, pigmentation, dryness, itching, burning and stinging on a four-point scale from 0 to 3 at baseline and at each visit. These measurements are either measured by the physician or reported by the subject. Overall, Twyneo® was generally well tolerated. The majority of cutaneous adverse events were mild.

Out of the 858 subjects who enrolled in both studies, 754 subjects were included in the safety population, and a combined total of 16 subjects discontinued treatment due to an adverse event across both trials. The most common reasons for subjects not completing the study in both groups (active and vehicle) were the withdrawal of informed consent (41 subjects, 4.8%), and loss to follow-up (39 subjects, 4.5%).

Epsolay® for Subtype II Rosacea

Epsolay® *Overview*

Epsolay® is a once-daily investigational topical cream containing 5% encapsulated benzoyl peroxide that we have developed for the treatment of papulopustular (subtype II) rosacea. We believe Epsolay® has the potential to become the first product to contain encapsulated benzoyl peroxide for the treatment of subtype II rosacea and, if approved by the FDA, has the potential to redefine the standard of care for the treatment of inflammatory lesions associated with subtype II rosacea. Subtype II rosacea is characterized by small, dome-shaped erythematous papules, tiny surmounting pustules on the central aspects of the face, solid facial erythema and edema, and thickening/overgrowth of skin. Subtype II rosacea resembles acne, except that comedones are absent, and patients may report associated burning and stinging sensations. We expect that Epsolay®, if approved by the FDA, will compete directly with Soolantra. We utilized the FDA's 505(b)(2) regulatory pathway in seeking approval of Epsolay® in the United States. On July 8, 2019, we announced positive top-line results from our Phase 3 program evaluating Epsolay®. The program enrolled 733 patients aged 18 and older in two identical, double-blind, vehicle-controlled Phase 3 clinical trials at 54 sites across the United States. Epsolay® demonstrated statistically significant improvement in both co-primary endpoints of (1) the number of patients achieving "clear" or "almost clear" in the Investigator Global Assessment (IGA) relative to baseline at week 12 and (2) absolute mean reduction from baseline in inflammatory lesion count at week 12. In an additional analysis, Epsolay® demonstrated rapid efficacy, achieving statistically significant improvements on both co-primary endpoints compared with vehicle as early as Week 2. In addition, Epsolay® was found to be well- tolerated. On February 12, 2020, we announced positive topline results from our open-label, long-term safety study, evaluating Epsolay® for a treatment duration up to 52 weeks. Our NDA for Epsolay® has been accepted for filing by the FDA, which originally assigned a PDUFA goal date of April 26, 2021, which has since been delayed due to COVID-19 related travel restrictions. The FDA conducted a pre-approval inspection of the production site for Epsolay® during the week of February 14, 2022.

Current Treatment Landscape for Subtype II Rosacea

As there is no cure for rosacea, treatment is largely focused on managing the disease. We believe that a significant market opportunity exists for a subtype II rosacea treatment option that can provide both efficacy and higher tolerability than existing treatments. There are currently five approved drugs for the treatment of subtype II rosacea: Soolantra, Metrogel, Oracea, Zilixi and generic metronidazole. In certain cases, dermatologists often prescribe oral antibiotics either as monotherapies or in conjunction with approved medications.

Our Solution for Subtype II Rosacea — Epsolay®

Benzoyl peroxide is approved by the FDA for the treatment of acne and is widely considered to be safe and effective. Currently, there is no approved benzoyl peroxide product in the rosacea treatment landscape as a result of potential tolerability issues, despite clinical studies showing that treatment with benzoyl peroxide could be efficacious. According to a published study, benzoyl peroxide was found to be an effective treatment for rosacea but caused irritation. Using our proprietary, silica-based microencapsulation technology platform, we believe our Epsolay® candidate for the treatment of papulopustular (subtype II) rosacea can improve on current subtype II rosacea treatments in the following ways:

- Epsolay® creates a silica-based barrier between benzoyl peroxide crystals and the skin and, as a result, can reduce irritation typically associated with topical application of benzoyl peroxide, increasing the potential for more tolerable application to rosacea-affected skin.

- Epsolay®'s release of the drug can reduce irritation while maintaining efficacy.

Epsolay® is an innovative topical cream, and if approved by the FDA, would be the first product containing benzoyl peroxide for the treatment of subtype II rosacea.

Epsolay® Phase 3 Trial Design

In June 2018, we announced dosing of the first subject in our pivotal Phase 3 clinical program of Epsolay® in subjects with papulopustular rosacea. The program enrolled 733 patients aged 18 and older in two identical, double-blind, vehicle-controlled Phase 3 clinical trials at 54 sites across the United States. Patients were randomized at a 2:1 ratio to be treated once-daily with either Epsolay (n=493) or vehicle cream (n=240) for 12 weeks. After the initiation of treatment, clinical and safety evaluations were performed at Weeks 2, 4, 6, 8 and 12.

The primary efficacy endpoints for both trials were success in the IGA defined as two-grade reduction in IGA on a stage of 0 to 4 with a “clear” (0) or “almost clear” (1) at week 12, and a reduction in mean inflammatory lesion count at week 12.

Epsolay® Phase 3 Trial Results

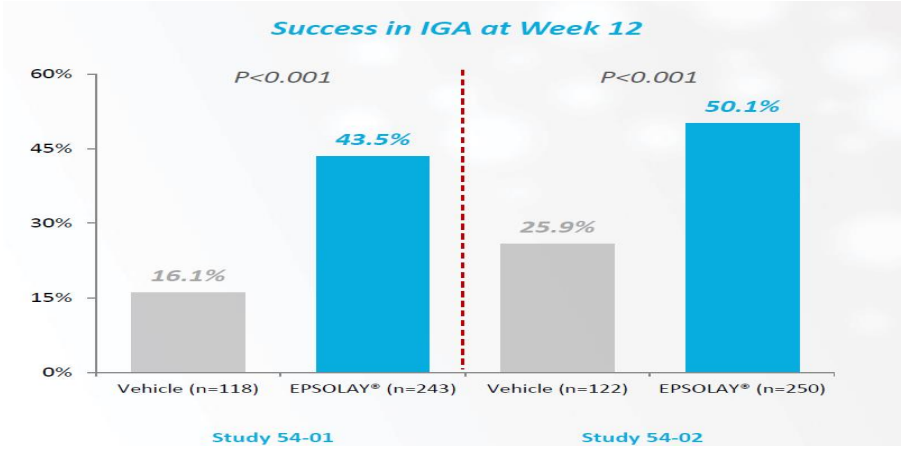
As outlined below, Epsolay demonstrated statistically significant improvement in both co-primary endpoints of (1) the number of patients achieving “clear” or “almost clear” in the IGA relative to baseline at week 12 and (2) absolute mean reduction from baseline in inflammatory lesion count at week 12. In an additional analysis, Epsolay® demonstrated rapid efficacy, achieving statistically significant improvements on both co-primary endpoints compared with vehicle as early as Week 2. Epsolay® demonstrated a favorable safety and tolerability profile similar to vehicle.

In study SGT 54-01, patients in the Epsolay® and vehicle treatment groups had a baseline mean inflammatory lesion count of 25.7 and 26.3, respectively. The proportion of patients with "moderate" (3) or "severe" (4) IGA in the Epsolay® treatment group was 86.4% and 13.6%, respectively, and 88.1% and 11.9%, respectively, in the vehicle treatment group. In study SGT 54-02, patients in Epsolay® and vehicle treatment groups had a baseline mean inflammatory lesion count of 29.8 and 27.5, respectively. The proportion of patients with "moderate" (3) or "severe" (4) IGA in the Epsolay treatment group was 90.8% and 9.2%, respectively, and 91.8% and 8.2%, respectively, in the vehicle treatment group.

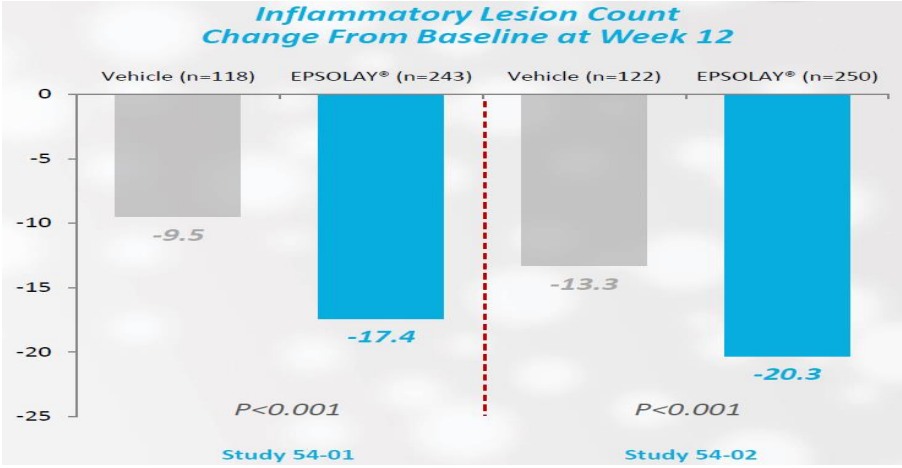
As outlined below, Epsolay® met all co-primary endpoints in both Phase 3 trials. Epsolay® demonstrated statistically significant improvement in each of the co-primary endpoints described above.

In study SGT 54-01, 43.5% of patients treated with Epsolay achieved success in IGA versus 16.1% in the vehicle treated group (P<0.001) at week 12. In Study 54-02, 50.1% of patients treated with Epsolay® achieved success in IGA versus 25.9% in the vehicle group (P<0.001) at week 12. In study SGT 54-01, the absolute change from baseline of inflammatory lesion count for Epsolay was -17.4 versus -9.5 for the vehicle group (P<0.001) at week 12. In study SGT 54-02, the absolute change from baseline of inflammatory lesion count for Epsolay was -20.3 versus -13.3 for the vehicle group (P<0.001) at week 12.

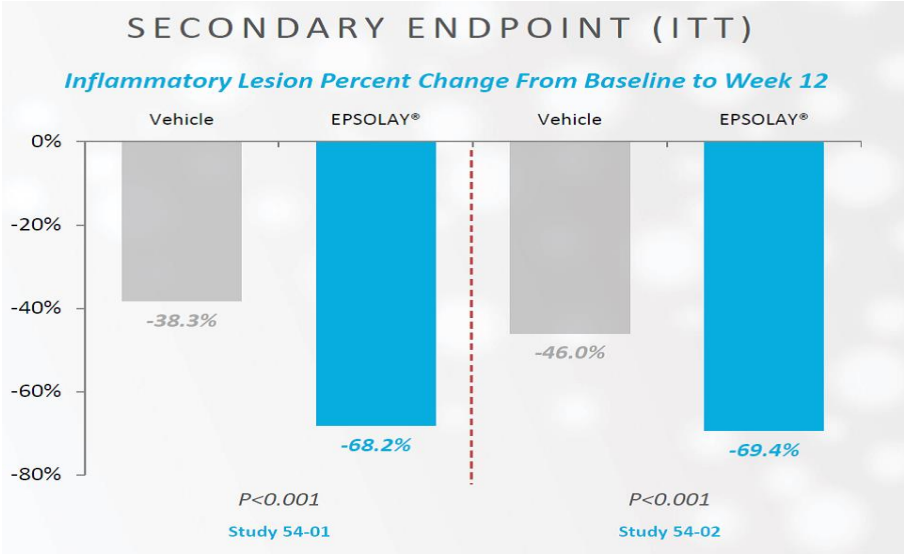
The following chart presents the proportion of subjects in the ITT population in studies SGT 54-01 and SGT 54-02 who achieved a successful improvement in the severity of their disease at week 12, as assessed using the IGA:



The following chart presents the absolute change from baseline in the number of inflammatory acne lesions at week 12:



The following chart presents the percent change from baseline in the number of inflammatory acne lesions at week 12:



In both studies, Epsolay® demonstrated a favorable safety and tolerability profile similar to vehicle, with a low rate of cutaneous side effects (e.g., dryness, scaling, itching and burning/stinging) comparable to vehicle. Adverse events were primarily mild to moderate in severity with the most frequently reported adverse events across both studies being application site erythema and application site pain reported by less than 3.4% of subjects. There were no treatment-related serious adverse events, with a combined total of two unrelated serious adverse events (1 Epsolay®, 1 vehicle) reported across both trials.

Out of the 733 subjects who enrolled in both studies, 721 subjects were included in the safety population, and a combined total of 10 subjects (9 Epsolay®, 1 vehicle) discontinued treatment due to an adverse event across both trials. The most common reasons for subjects not completing the study in both groups (active and vehicle) were the withdrawal of informed consent (25 subjects, 3.4%), and loss to follow-up (17 subjects, 2.3%).

Long-Term Safety Study Results for Epsolay®

On February 12, 2020, we announced positive topline results from our open-label, long-term safety study, SGT -54-07, evaluating Epsolay® for a treatment duration up to 52 weeks. The study enrolled 547 subjects, all of whom had completed 12 weeks of treatment with Epsolay® or vehicle in the preceding double-blind Phase 3 studies. Patients continued onto open-label treatment with Epsolay® once-daily for up to an additional 40 weeks. The safety population of 535 subjects received Epsolay® therapy for an overall period of at least 28 weeks. Of these 535 subjects, 209 subjects completed 52 weeks of treatment with Epsolay, exceeding the sample size requirements previously defined by the FDA for the Epsolay® one-year safety evaluation.

Non-cutaneous adverse events were similar in frequency and type to those observed in the preceding Phase 3 trials. The most common adverse event reported was nasopharyngitis (5.4%). Less than 3% of patients experienced application site adverse events that were considered to be drug-related, and no serious drug-related adverse events were reported.

At every study visit, the investigator conducted Local Tolerability and Cutaneous Safety Assessments. At the end of 52 weeks more than 90% of subjects had “none” or “mild” signs or symptoms (burning or stinging, itching, dryness and scaling) and no “severe” tolerability scores were recorded.

Although the study was designed to evaluate long-term safety, subjects also continued to undergo evaluation according to the Investigator Global Assessment (IGA) 5-point scale. Of the 209 patients treated with Epsolay for 52 weeks, 73.2% reported an IGA score of 0 ("clear") or 1 ("almost clear") at 52 weeks.

SGT-210 for Keratodermas

SGT-210 that we are developing for the treatment of keratoderma, such as PPK, a group of skin conditions characterized by thickening of the skin. SGT-210 is designed to be used alone or in combination for the treatment of hyperproliferation and hyperkeratinization disorders, including PPK. On January 2, 2020, we announced the initiation of a Phase 1 clinical study of SGT-210 in patients with palmoplantar keratoderma. The Phase 1 concept study SGT-84-01 is a single-center, single-blinded, vehicle-controlled study designed to evaluate the bioavailability, safety and tolerability of SGT-210 as well as inform on potential efficacy. During the third quarter of 2021, we reported that the study with respect to six (6) palmoplantar keratoderma (PPK) patients has been completed and indicated modest improvement and a favorable safety profile

SGT-210, SGT-310 and SGT-510 potentially for psoriasis and other medical conditions

We are conducting pre-clinical testing to explore the possible activity of SGT-210, SGT-310, and SGT-510 in various new pharmaceutical indications. Approximately 25 provisional patent applications for these project candidates have been submitted to date, including patent applications covering the use of tapinarof in ophthalmic disorders such as dry eye, uveitis, and blepharitis with or without demodex involvement.

Generic Drug Product Candidates

In addition to our investigational product candidates, we are also currently developing a portfolio of two generic topical dermatological related to four generic drug candidates in collaboration with Padagis by assignment from Perrigo. Padagis has significant experience in the development of generic drugs.

We previously had collaboration arrangements with Perrigo to develop a portfolio of 11 generic topical dermatological products. In November 2021, we announced that we had signed an agreement with Padagis, pursuant to which we sold our rights related to 10 generic collaborative agreements between the parties. Under the terms of this agreement with Padagis, effective as of November 1, 2021, we are to unconditionally receive $21.5 million over 24 months, in lieu of our share in the ten generic programs, two of which were approved by the FDA, and eight of which are unapproved. Pursuant to the agreement, effective as of November 1, 2021, we ceased paying any outstanding and future operational costs related to these 10 collaborative agreements.

We currently have two collaboration agreements with Padagis for the development, manufacturing and commercialization of two generic product candidates. Under such agreements, Padagis will conduct the regulatory (if relevant), scientific, clinical and technical activities necessary to develop the generic product candidates and seek regulatory approval with the FDA for the generic product candidates. If approved by the FDA, Padagis has agreed to commercialize the generic product candidates in the United States. We and Padagis will share the development costs and the gross profits generated from the sales of the generic product candidates, if approved by the FDA.

Our Proprietary Silica-Based Microencapsulation Technology Platform

Encapsulation of a drug substance can be made using a variety of techniques, such as solvent evaporation, coacervation, and interfacial polymerization. Most encapsulations involve organic polymers, such as poly-methyl methacrylate, chitosan and cellulose. The resultant encapsulated drug substance can be an aqueous dispersion of varying payload and volume fraction or a dried powder. Control over the encapsulation process when organic polymers are used is challenging and is mainly limited to shell thickness. Other properties of the organic polymer encapsulating material are hard to control.

In contrast, we use proprietary 'sol-gel' processes to shape silica on site to form microcapsule shells of almost any size and release profile. Sol-gel is a chemical process whereby amorphous silica, or other metal oxides, are made by forming interconnections among colloidal particles (the "sol") under increasing viscosity until a rigid silica shell (the "gel") is formed. The drug substance that is added during the sol-gel reaction is encapsulated, using a patented technique, by which a core-shell structure is formed. The drug substance is in the core and the silica is the capsule shell. At the end of the process, the microcapsules are in the shape of small beads ranging from 1 – 50 micron in size. This process results in an aqueous suspension in which the drug substances are entrapped in silica particles.

Intellectual Property

Our intellectual property and proprietary technology are directed to the development, manufacture and sale of Twyneo®, Epsolay® and our other investigational product candidates, SGT-210, SGT-310, SGT-510 . We seek to protect our intellectual property, core technologies and other know-how, through a combination of patents, trademarks, trade secrets, non-disclosure and confidentiality agreements, assignments of invention and other contractual arrangements with our employees, consultants, partners, suppliers, customers and others.

We will be able to protect our technology from unauthorized use by third parties only to the extent it is covered by valid and enforceable patents or is effectively maintained as trade secrets. Patents and other proprietary rights are an essential element of our business. If any of the below described applications are not approved, or any of the below described patents are invalidated, deemed unenforceable or otherwise successfully challenged, such loss would have a material effect on the commercialization of our Investigational product candidates and our future prospects.

Our patent portfolio that is directed to Twyneo® Epsolay® and our other investigational product candidates includes 144 patents and patent applications and claims processes for manufacture (including silica microencapsulation platform and other technologies), formulations, composition of matter, and methods of use. Of these 144 patents and patent applications, 78 are granted patents (11 in the United States and 67 in other countries) and 66 are pending applications (32 in the United States and 34 in other countries).

For Twyneo®, we have obtained patent protection for the composition of matter in the United States, Canada, Japan, Mexico (with a term until 2028) and we have an allowed application claiming composition of matter in the European Patent Office. There are four patent families protecting the process for the encapsulation of the active agents of our Twyneo® product (one patent family has patents granted in Canada, India, Mexico, Europe (validated in France, Germany, Ireland, Italy, Spain, Switzerland and the United Kingdom) and Japan (with a term until 2028) and applications pending in the United States; the second patent family has patents granted in Mexico, Canada and the United States (with a term until 2029) and an application pending in the United States; the third patent family has patents granted in Europe (validated in France, Germany, Ireland, Italy, Spain, Switzerland and the United Kingdom), China, India, Japan, Canada, Mexico and the United States (with a term until 2030) and applications pending in the United States); and the fourth patent family has patents granted in Canada, China, Israel, India, Mexico and the United States). We own pending patents for the formulation of our Twyneo® product in the United States (with a term until 2032), and patents granted in China, Japan, Canada, Mexico and Europe (validated in France, Germany, Ireland, Italy, Spain, Switzerland, United Kingdom) (with a term until 2032). We have pending patent applications in the United States for the composition of our Twyneo® product and one patent granted in the United States for the method of treatment of Twyneo® (with a term until 2038). We have five trademarks registered for our Twyneo® product in Israel, Europe, the United States and Canada.

For Epsolay®, we have obtained patents in China, Canada, Japan, Europe, Mexico and the United States (with a term until 2032) covering the composition for topical treatment of rosacea. We have further pending applications for this composition in the United States. There are two patent families directed to the process for encapsulation of the active agents of Epsolay® (one patent family has granted patents in Canada, India, Mexico, Europe (validated in France, Germany, Ireland, Italy, Spain, Switzerland and the United Kingdom) and Japan (with a term until 2028) and pending applications in the United States; and the second patent family has patents granted in Canada, China, Israel, India, Mexico and the United States). We also have 2 granted patents in the United States (with a term until 2040) and 14 patent applications pending covering the methods of use of Epsolay® for the treatment of rosacea.

We have one published international application and 3 pending applications in the United States covering the compositions of Epsolay® and Twyneo®, the processes for the encapsulation of the active agents of our Epsolay® and Twyneo®, and the methods of use.

We have four registered trademarks in Europe, Canada, the United States and Israel. These registrations cover potential brand names for our Epsolay® in Israel, Europe, Canada and the United States.

For SGT-210, we have 16 pending applications in China, Canada, Japan, Korea, Europe, Mexico and the United States, the refer to methods and compositions of use.

For SGT-310, we have 15 pending applications in China, Canada, Japan, Korea, Europe, Mexico and the United States, that refer to compositions per se, compositions for use, methods of treatments, regimens and kits.

For SGT-510, we have nine pending applications in China, Canada, Japan, Korea, Europe, Mexico and the United States, that refer to refer to compositions per se, dosage forms, methods of treatment, and regimens.

Competition

The pharmaceutical industry is subject to intense competition as well as rapid technological changes. Our ability to compete is based on a variety of factors, including product efficacy, safety, cost-effectiveness, patient compliance, patent position and effective product promotion. Competition is also based upon the ability of a company to offer a broad range of other product offerings, large direct sales forces and long-term customer relationships with target physicians.

There are numerous companies that have branded or generic products or product candidates in the dermatology market. Among them are Aclaris Therapeutics, Inc., Akorn, Inc., Almirall S.A., Aqua Pharmaceuticals LLC, Bayer HealthCare AG, Cassiopea SpA, Vyne Pharmaceuticals Ltd., Galderma Pharma S.A., Glenmark Pharmaceuticals Ltd., G&W Laboratories, Inc., LEO Pharma A/S, Mylan N.V., Novan, Inc., Novartis AG, Novum Pharma, LLC, Perrigo Company plc, Pfizer, Inc., Spear Therapeutics, Ltd., Sun Pharmaceutical Industries Ltd., Teligent, Inc., Teva Pharmaceutical Industries Ltd. and Bausch Health Companies Inc.

In order for our approved product candidates, if any, to compete successfully in the dermatology market, we will have to demonstrate that their efficacy, safety and cost-effectiveness provide an attractive alternative to existing therapies, some of which are widely known and accepted by physicians and patients, as well as to future new therapies. Such competition could lead to reduced market share for our product candidates and contribute to downward pressure on the pricing of our product candidates, which could harm our business, financial condition, operating results and prospects.

Many of the companies, academic research institutions, governmental agencies and other organizations involved in the field of dermatology have substantially greater financial, technical and human resources than we do, and may be better equipped to discover, develop, test and obtain regulatory approvals for products that compete with ours. They may also be better equipped to manufacture, market and sell products. These companies, institutions, agencies and organizations may develop and introduce products and drug delivery technologies competitive with or superior to ours which could inhibit our market penetration efforts.

Twyneo® and Epsolay® target the well-established acne and rosacea markets. We expect Twyneo®, and if approved by the FDA, Epsolay®, to compete with current standard-of-care treatments, whether branded, generic or over-the-counter, as well as with new treatments to be approved in the future. The current standard-of-care for acne includes topical anti-bacterial drugs such as benzoyl peroxide that are broadly available over-the-counter, prescription drug products that are based on single retinoid drug products such as Differin, Atralin, Retin-A, Retin-A Micro, Tazorac and Altreno, fixed-dose combinations of benzoyl peroxide and adapalene such as Epiduo and Epiduo Forte, fixed-dose combinations of benzoyl peroxide and clindamycin such as Duac, Benzaclin, Onexton and Acanya, fixed-dose combinations of tretinoin and clindamycin such as Ziana and Veltin, topical antiandrogen such as Winlevi and topical antibiotics such as Aczone and Amzeeq. The current standard of care for rosacea includes Metrogel, Finacea, Soolantra and the recently launched Zilxi, as well as oral Oracea (doxycycline embedded in a technology platform). As a fixed-dose combination product candidate, Twyneo® may also compete with drug products utilizing other technologies that can separate two drug substances, such as dual chamber tubes, dual pouches or dual sachets. In addition to these products, our generic drug product candidates are expected to face direct competition from branded drugs and authorized generics which are prescription drugs produced by the branded pharmaceutical companies and marketed under a private label, at generic prices.

Marketing, Sales and Distribution

We currently have limited sales, marketing and distribution capabilities. In June 2021, we entered into two five-year exclusive license agreements with Galderma pursuant to which Galderma has the exclusive right to, and is responsible for, all U.S. commercial activities for Twyneo®, and, if approved by the FDA, Epsolay®. Pursuant to the agreement, we are entitled to consideration of up to $11 million in upfront payments to us and regulatory approval milestone payments. We are also eligible to receive tiered double-digit royalties ranging from mid-teen to high-teen percentage of net sales as well as up to $9 million in sales milestone payments. We also expect to collaborate with third parties that have sales and marketing experience in order to commercialize our other investigational product candidates, if approved by the FDA for commercial sale, in lieu of our own sales force and distribution systems. If we are unable to enter into such arrangements for our other product candidates on acceptable terms or at all, we may not be able to successfully commercialize them. In other markets, we also expect to selectively pursue strategic collaborations with third parties in order to maximize the commercial potential of our product candidates.

Manufacturing

For the supply of current good manufacturing practice-grade, or cGMP-grade and clinical trial materials we rely on and expect to continue to rely on third-party contract manufacturing organizations, or CMOs, or on in-house manufacturing capabilities. As of August 2018, our in-house manufacturing operations have been audited for current good manufacturing, or cGMP, compliance, and were granted a cGMP certification by the Israel Ministry of Health. This certification allowed us to manufacture Twyneo® and its intermediates to support Phase 3 clinical trials. This cGMP certification expired in 2020, and since no other manufacturing for Phase 3 clinical trials is planned at the Company during 2021, the Company and the Israel Ministry of Health have mutually concluded that the cGMP certification will be reassessed and renewed for other products as they reach relevant stages of development. ISO 14001:2015 and ISO 45001:2018certifications continue to be maintained and are due for renewal in May 2024 and March 2021, respectively. For commercial manufacturing of our products, we intend to rely solely on CMOs. It is our policy to have multiple or alternative sources where possible for every service and material we use in our products.

Government Regulation

Regulation by governmental authorities in Israel, the United States and other countries is a significant factor in the development, manufacture and commercialization of our product candidates and in our ongoing research and development activities. Our business is subject to extensive government regulation in Israel for its manufacturing activities involving drug products, drug product intermediates, and drug product active substances to be used in Phase 1 and Phase 2 clinical trials.

Product Approval Process in the United States

Review and approval of drugs

In the United States, pharmaceutical products are subject to extensive regulation by the FDA. The Federal Food, Drug and Cosmetic Act, or FDCA, and other federal and state statutes and implementing regulations govern, among other things, the research, development, testing, manufacture, storage, recordkeeping, approval, labeling, promotion and marketing, distribution, post-approval monitoring and reporting, sampling, and import and export of pharmaceutical products. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval may subject an applicant to a variety of administrative or judicial sanctions and enforcement actions brought by the FDA, the Department of Justice or other governmental entities. Possible sanctions may include the FDA's refusal to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement and civil or criminal penalties.

FDA approval of a new drug application is required before any new unapproved drug or dosage form, can be marketed in the United States. Section 505 of the FDCA describes three types of new drug applications: (1) an application that contains full reports of investigations of safety and effectiveness (section 505(b)(1)); (2) an application that contains full reports of investigations of safety and effectiveness but where at least some of the information required for approval comes from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference (section 505(b)(2)); and (3) an application that contains information to show that the proposed product is identical in active ingredient, dosage form, strength, route of administration, labeling, quality, performance characteristics, and intended use, among other things, to a previously approved product (section 505(j)). Section 505(b)(1) and 505(b)(2) new drug applications are referred to as NDAs, and section 505(j) applications are referred to as ANDAs.

In general, the process required by the FDA prior to marketing and distributing a new drug, as opposed to a generic drug subject to section 505(j), in the United States usually involves the following:

- completion of pre-clinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practices, or GLP, requirements or other applicable regulations;

- submission to the FDA of an investigational new drug application, or IND, which must become effective before human clinical trials in the United States may begin;
- approval by an independent institutional review board, or IRB, or ethics committee at each clinical site before each trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practice, or GCP, requirements to establish the safety and efficacy of the proposed drug for its intended use;
- preparation and submission to the FDA of an NDA;
- satisfactory completion of an FDA advisory committee review, if applicable;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the product or components thereof are produced, to assess compliance with current good manufacturing practices, or cGMPs, and to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;
- satisfactory completion of FDA audits of clinical trial sites to assure compliance with GCPs and the integrity of the clinical data; and
- payment of user fees and FDA review and approval of the NDA.

Pre-clinical studies

Pre-clinical studies include laboratory evaluation or product chemistry, formulation and toxicity, as well as animal studies to assess the potential safety and efficacy of the product candidate. Pre-clinical safety tests must be conducted in compliance with the FDA regulations. The results of the pre-clinical studies, together with manufacturing information and analytical data, are submitted to the FDA as part of an investigational new drug application, or IND, which must become effective before clinical trials may commence. An IND is a request for authorization from the FDA to administer an investigational new drug product to humans. The central focus of an IND submission is on the general investigational plan and the protocol(s) for clinical studies. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30- day time period, raises safety concerns or questions about the proposed clinical trial. In such a case, the IND may be placed on clinical hold and the IND sponsor and the FDA must resolve any outstanding concerns or questions before the clinical trial can begin. Submission of an IND therefore may or may not result in FDA authorization to begin a clinical trial. Long-term pre-clinical studies, such as animal tests of reproductive toxicity and carcinogenicity, may continue after the IND application is submitted.

Clinical trials

Clinical trials involve the administration of an investigational product to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research subjects provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written trial protocols detailing, among other things, the objectives of the trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the local institutional review board, or IRB, and to the FDA as part of the IND.

An IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct continuing review at least annually. The IRB must review and approve, among other things, the trial protocol information to be provided to trial subjects. An IRB must operate in compliance with FDA regulations. Some studies also include oversight by an independent group of qualified experts organized by the clinical study sponsor, known as a data safety monitoring board, which provides authorization for whether or not a study may move forward at designated check points based on access to certain data from the study and may halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy. Depending on its charter, this group may determine whether a trial may move forward at designated check points based on access to certain data from the trial. The FDA or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. There are also requirements governing the reporting of ongoing clinical studies and clinical study results to public registries.

Clinical trials are typically conducted in three sequential phases, which may overlap or be combined:

- *Phase 1*: The drug is initially introduced into healthy human subjects or patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness and to determine optimal dosage.

- *Phase 2*: The drug is administered to a limited patient population to identify possible short-term adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.

- *Phase 3*: The drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product, and to provide adequate information for the labeling of the product.

In some cases, the FDA may require, or companies may voluntarily pursue, additional clinical trials after a product is approved to gain more information about the product. These so-called Phase 4 studies, may be conducted after initial marketing approval, and may be used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of an NDA.

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

While the IND is active and before approval, progress reports summarizing the results of the clinical trials and nonclinical studies performed since the last progress report must be submitted at least annually to the FDA, and written IND safety reports must be submitted to the FDA and investigators for serious and unexpected suspected adverse events, findings from other studies suggesting a significant risk to humans exposed to the same or similar drugs, findings from animal or *in vitro* testing suggesting a significant risk to humans, and any clinically important increased incidence of a serious suspected adverse reaction compared to that listed in the protocol or investigator brochure.

In addition, during the development of a new drug, sponsors are given opportunities to meet with the FDA at certain points. These points may be prior to submission of an IND, at the end of Phase 2, and before an NDA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date, for the FDA to provide advice, and for the sponsor and the FDA to reach agreement on the next phase of development. Sponsors typically use the meetings at the end of the Phase 2 trial to discuss Phase 2 clinical results and present plans for the pivotal Phase 3 clinical trials that they believe will support approval of the new drug.

Unlike NDA products which must be shown to be safe and effective for their intended use, ANDA products must be shown to be the same as, and bioequivalent to, a reference listed drug, or RLD. A product is considered bioequivalent if there is no significant difference in the rate and extent to which the active ingredient in the generic product and in the RLD becomes available at the site of drug action when administered at the same molar dose under similar conditions in an appropriately designed study. Accordingly, an applicant typically compares the systemic exposure profile of the generic test drug product to that of the RLD at the same regimen and exposure period as the RLD to demonstrate bioequivalence. For most ANDAs, bioequivalence must be shown in human clinical trials, but in some cases, FDA will accept in vitro data. Specific requirements are typically outlined by FDA in product-specific bioequivalence guidance.

Submission of an NDA to the FDA

Assuming successful completion of all required testing with all applicable regulatory requirements, the results of the pre-clinical studies and clinical trials, together with other detailed information, including information on the manufacture, control and composition of the product, are submitted to the FDA as part of an NDA requesting approval to market the product candidate for a proposed indication. Under the Prescription Drug User Fee Act, as amended, applicants are required to pay fees to the FDA for reviewing an NDA. These application user fees, as well as the annual program fees required for approved products, can be substantial. The NDA application review fee alone can exceed $2.5 million, subject to certain limited deferrals, waivers and reductions that may be available.

The FDA has 60 days from its receipt of an NDA to determine whether the application will be accepted for filing based on the agency's threshold determination that it is sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the NDA must be resubmitted with the additional information and is subject to payment of additional user fees. The resubmitted application is also subject to review before the FDA accepts it for filing. If found complete, the FDA will accept the NDA for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review.

Under the PDUFA, the FDA has agreed to certain performance goals in the review of NDAs through a two-tiered classification system, Standard Review and Priority Review. An NDA is eligible for Priority Review if the product candidate is designed to treat serious or life-threatening disease or condition, and if approved by the FDA, would provide a significant improvement in the treatment, diagnosis or prevention of a serious disease or condition compared to marketed products. For new molecular entities, or NMEs, such as those typically submitted in 505(b)(1) NDAs, the FDA endeavors to review applications subject to Standard Review within 10 months 60-day filing date, or within 6 months of the 60-day filing date for Priority Review. For non-NMEs, such as those typically submitted in 505(b)(2) NDAs, FDA's goal is to review applications subject to Standard Review within 10 months of receipt, and those subject to Priority Review within 6 months of receipt. The FDA, however, may not approve a drug within these established goals, as the review process is often significantly extended by FDA requests for additional information or clarification, and its review goals are subject to change from time to time.

Before approving an NDA, the FDA inspects the facilities at which the product is manufactured or facilities that are significantly involved in the product development and distribution process and will not approve the product unless cGMP compliance is satisfactory. Additionally, the FDA will typically inspect one or more clinical sites to assure compliance with GCP requirements. The FDA may also refer applications for novel drug products or drug products which present difficult questions of safety or efficacy to an advisory committee for review, evaluation and recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

After the FDA evaluates the NDA and the manufacturing facilities, it issues either an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A complete response letter indicates that the review cycle for an application is complete and that the application is not ready for approval. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing, or information, in order for the FDA to reconsider the application. Even with submission of this additional information, the FDA may ultimately decide that an application does not satisfy the regulatory criteria for approval. If, or when, the deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter.

If a product is approved, the approval will impose limitations on the indicated uses for which the product may be marketed, may require that warning statements be included in the product labeling, may require that additional studies or trials be conducted following approval as a condition of the approval, may impose restrictions and conditions on product distribution, prescribing or dispensing in the form of a risk management plan, or impose other limitations. For example, as a condition of NDA approval, the FDA may require a risk evaluation and mitigation strategy, or REMS, to ensure that the benefits of the drug outweigh the potential risks. If the FDA determines a REMS is necessary during review of the application, the drug sponsor must agree to the REMS plan at the time of approval. A REMS may be required to include various elements, such as a medication guide or patient package insert, a communication plan to educate healthcare providers of the drug's risks, limitations on who may prescribe or dispense the drug, or other elements to assure safe use, such as special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring and the use of patient registries. In addition, the REMS must include a timetable to periodically assess the strategy. The requirement for a REMS can materially affect the potential market and profitability of a drug.

Further changes to some of the conditions established in an approved application, including changes in indications, labeling, or manufacturing processes or facilities, require submission and FDA approval of a new NDA or NDA supplement before the change can be implemented, which may require manufacturers to develop additional data or conduct additional pre-clinical studies and clinical trials. An NDA supplement for a new indication typically requires clinical data similar to that in the original application, and the FDA uses the similar procedures in reviewing NDA supplements as it does in reviewing NDAs.

Any drug products receiving FDA approval will be subject to continuing regulation by the FDA. Certain requirements include, among other things, record-keeping requirements, reporting of adverse experiences with the product, providing the FDA with updated safety and efficacy information on an annual basis or more frequently for specific events, product sampling and distribution requirements, complying with certain electronic records and signature requirements and complying with FDA promotion and advertising requirements. These promotion and advertising requirements include standards for direct-to-consumer advertising, prohibitions against promoting drugs for uses or patient populations that are not described in the drug's approved labeling, known as "off-label use," and other promotional activities, such as those considered to be false or misleading.

Although physicians may prescribe legally available drugs for off-label uses, manufacturers may not encourage, market or promote such off-label uses. As a result, "off-label promotion" has formed the basis for litigation under the Federal False Claims Act, violations of which are subject to significant civil fines and penalties. In addition, manufacturers of prescription products are required to disclose annually to the Center for Medicaid and Medicare any payments made to physicians in the United States under the Sunshine Act of 2012. These payments could be in cash or kind, could be for any reason, and are required to be disclosed even if the payments are not related to the approved product. A failure to fully disclose or not report in time could lead to penalties of up to $1 million per year.

The manufacturing of any drug products must comply with applicable FDA manufacturing requirements contained in the FDA's cGMP regulations. The FDA's cGMP regulations require, among other things, quality control and quality assurance, as well as the corresponding maintenance of comprehensive records and documentation. Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are also required to register their establishments and list any products they make with the FDA and to comply with related requirements in certain states. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP requirements and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. These entities are further subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain cGMP compliance.

Discovery of problems with a product after approval may result in serious and extensive restrictions on a product, manufacturer or holder of an approved NDA, as well as lead to potential market disruptions. These restrictions may include recalls, suspension of a product until the FDA is assured that quality standards can be met, and continuing oversight of manufacturing by the FDA under a "consent decree," which frequently includes the imposition of costs and continuing inspections over a period of many years, as well as possible withdrawal of the product from the market. In addition, changes to the manufacturing process generally require prior FDA approval before being implemented. Other types of changes to the approved product, such as adding new indications and additional labeling claims, are also subject to further FDA review and approval. There also are continuing, annual program user fee requirements for any approved products, as well as new application fees for supplemental applications with clinical data.

The FDA also may require post-marketing testing, or Phase IV testing, as well as surveillance to monitor the effects of an approved product or place conditions on an approval that could otherwise restrict the distribution or use of our product candidates.

Once approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in mandatory revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

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

Pediatric trials and exclusivity

Even when not pursuing a pediatric indication, under the Pediatric Research Equity Act of 2003, an NDA or supplement thereto must contain data that is adequate to assess the safety and effectiveness of the drug product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. Sponsors must also submit pediatric study plans prior to the assessment data. Those plans must contain an outline of the proposed pediatric trials the applicant plans to conduct, including trial objectives and design, any deferral or waiver requests, and other information required by the statute. The applicant, the FDA, and the FDA's internal review committee must then review the information submitted, consult with each other, and agree upon a final plan. The FDA or the applicant may request an amendment to the plan at any time.

The FDA may also, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements.

Separately, in the event the FDA makes a written request for pediatric data relating to a drug product, an NDA sponsor who submits such data may be entitled to pediatric exclusivity. Pediatric exclusivity is a type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing non-patent exclusivity.

The Hatch-Waxman Amendments

ANDA Approval Process

The Hatch-Waxman Amendments established abbreviated FDA approval procedures for drugs that are shown to be equivalent to proprietary drugs previously approved by the FDA through the NDA process. Approval to market and distribute these drugs is obtained by submitting an ANDA to the FDA. An ANDA is a comprehensive submission that contains, among other things, data and information pertaining to the active pharmaceutical ingredient, drug product formulation, specifications and stability of the generic drug, as well as analytical methods, manufacturing process validation data, and quality control procedures. Premarket applications for generic drugs are termed abbreviated because they generally do not include pre-clinical and clinical data to demonstrate safety and effectiveness. Instead, a generic applicant must demonstrate that its product is bioequivalent to the innovator drug. In certain situations, an applicant may obtain ANDA approval of a generic product with a strength or dosage form that differs from a referenced innovator drug pursuant to the filing and approval of an ANDA Suitability Petition. The FDA will approve the generic product as suitable for an ANDA application if it finds that the generic product does not raise new questions of safety and effectiveness as compared to the innovator product. A product is not eligible for ANDA approval if the FDA determines that it is not bioequivalent to the referenced innovator drug, if it is intended for a different use, or if it is not subject to an approved Suitability Petition. However, such a product might be approved under an NDA, with supportive data from clinical trials.

505(b)(2) NDAs

Section 505(b)(2) was enacted as part of the Hatch-Waxman Amendments, and permits the filing of an NDA where at least some of the information required for approval comes from studies or trials not conducted by or for the applicant and for which the applicant has not obtained a right of reference. Section 505(b)(2) typically serves as an alternative path to FDA approval for modifications to formulations or uses of products previously approved by the FDA. If the 505(b)(2) applicant can establish that reliance on the FDA's previous findings of safety and effectiveness is scientifically appropriate, it may eliminate the need to conduct certain pre-clinical studies or clinical trials for the new product. The FDA may also require companies to perform additional studies or measurements, including clinical trials, to support the change from the approved branded reference drug. The FDA may then approve the new product candidate for all, or some, of the labeled indications for which the branded reference drug has been approved, as well as for any new indication sought by the 505(b)(2) applicant.

Orange Book Listing

In seeking approval for a drug through an NDA, including a 505(b)(1) and 505(b)(2) NDA, applicants are required to list with the FDA certain patents whose claims cover the applicant's product or method of using the product. Upon approval of an NDA, each of the patents listed in the application for the drug is then published in the FDA's publication of Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the "Orange Book." Any applicant who submits an ANDA seeking approval of a generic equivalent of a drug listed in the Orange Book or a Section 505(b)(2) NDA referencing a drug listed in the Orange Book must certify to the FDA (1) that no patent information on the drug product that is the subject of the application has been submitted to the FDA; (2) that such patent has expired; (3) the date on which such patent expires; or (4) that such patent is invalid or will not be infringed upon by the manufacture, use, or sale of the drug product for which the application is submitted. This last certification is known as a Paragraph IV certification. The applicant may also elect to submit a "section viii" statement certifying that its proposed label does not contain (or carves out) any language regarding a patented method-of-use rather than certify to a listed method-of-use patent.

If the applicant does not challenge one or more listed patents through a Paragraph IV certification, the FDA will not approve the ANDA or Section 505(b)(2) NDA until all the listed patents claiming the referenced product have expired. Further, the FDA will also not approve, as applicable, an ANDA or Section 505(b)(2) NDA until any non-patent exclusivity, as described in greater detail below, has expired.

If the ANDA or Section 505(b)(2) NDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the owner of the referenced NDA for the previously approved product and relevant patent holders within 20 days after the ANDA or Section 505(b)(2) NDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement suit against the ANDA or Section 505(b)(2) applicant. Under the FDCA, the filing of a patent infringement lawsuit within 45 days of receipt of the notification regarding a Paragraph IV certification automatically prevents the FDA from approving the ANDA or Section 505(b)(2) NDA until the earliest to occur of 30 months beginning on the date the patent holder receives notice, expiration of the patent, settlement of the lawsuit, or until a court deems the patent unenforceable, invalid or not infringed. Even if a patent infringement claim is not brought within the 45-day period, a patent infringement claim may be brought under traditional patent law, but it does not invoke the 30-month stay.

Moreover, in cases where an ANDA or Section 505(b)(2) application containing a Paragraph IV certification is submitted after the fourth year of a previously approved drug's five-year NCE exclusivity period, as described more fully below, and the patent holder brings suit within 45 days of notice of the Paragraph IV certification, the 30-month period is automatically extended to prevent approval of the Section 505(b)(2) application until the date that is seven and one-half years after approval of the previously approved reference product that has the five-year NCE exclusivity. The court also has the ability to shorten or lengthen either the 30-month or the seven and one-half year period if either party is found not to be reasonably cooperating in expediting the litigation.

Further, although applications submitted in a Section 505(b)(1) NDA are not subject to the same patent certification requirements as Section 505(b)(2) applications or ANDAs, and are not associated with litigation under the Hatch-Waxman Act, applicants may still face non-Hatch-Waxman patent litigation for products developed through the Section 505(b)(1) pathway.

Non-Patent Exclusivity

In addition to patent exclusivity, NDA holders may be entitled to a period of non-patent exclusivity, during which the FDA cannot approve an ANDA or 505(b)(2) application that relies on the listed drug. For example, a pharmaceutical manufacturer may obtain five years of non-patent exclusivity upon NDA approval of a new chemical entity, or NCE, which is a drug that contains an active moiety that has not been approved by FDA in any other NDA. An "active moiety" is defined as the molecule or ion responsible for the drug substance's physiological or pharmacologic action. During the five year exclusivity period, the FDA cannot accept for filing any ANDA seeking approval of a generic version of that drug or any 505(b)(2) NDA for the same active moiety and that relies on the FDA's findings regarding that drug, except that FDA may accept an application for filing after four years if the ANDA or 505(b)(2) applicant makes a Paragraph IV certification.

Another form of non-patent exclusivity is clinical investigation exclusivity. A drug, including one approved under Section 505(b)(2), may obtain a three-year period of exclusivity for a particular condition of approval, or change to a marketed product, such as a new formulation for a previously approved product, if one or more new clinical investigations (other than bioavailability or bioequivalence studies) was essential to the approval of the application and was conducted or sponsored by the applicant. Should this occur, the FDA would be precluded from approving any ANDA or 505(b)(2) application for the protected modification until after that three-year exclusivity period has run. However, unlike NCE exclusivity, the FDA can accept an application and begin the review process during the exclusivity period.

Review and Approval of Drug Products Outside the United States

In addition to regulations in the United States, if we target non-U.S. markets, we will be subject to a variety of foreign regulations governing manufacturing, clinical trials, commercial sales and distribution of our future product candidates. Whether or not we obtain FDA approval for a product candidate, we must obtain approval of the product by the comparable regulatory authorities of foreign countries before commencing clinical trials or marketing in those countries. The approval process varies from country to country, and the time may be longer or shorter than that required for FDA approval. The requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from country to country.

Under European Union regulatory systems, marketing authorizations may be submitted either under a centralized, decentralized or mutual recognition procedure. The centralized procedure provides for the grant of a single marketing authorization that is valid for all European Union member states. The decentralized procedure includes selecting one "reference member state," or RMS, and submitting to more than one-member state at the same time. The RMS National Competent Authority conducts a detailed review and prepares an assessment report, to which concerned member states provide comment. The mutual recognition procedure provides for mutual recognition of national approval decisions. Under this procedure, the holder of a national marketing authorization may submit an application to the remaining member states post-initial approval. Within 90 days of receiving the applications and assessment report, each member state must decide whether to recognize the approval.

Pharmaceutical Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any product candidates for which we obtain regulatory approval. In the United States and other markets, sales of any product candidates for which we receive regulatory approval for commercial sale will depend in part on the availability of coverage and reimbursement from third-party payors. Third-party payors include government health administrative authorities, managed care providers, private health insurers and other organizations. The process for determining whether a payor will provide coverage for a drug product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the drug product. Third-party payors may limit coverage to specific drug products on an approved list, or formulary, which might not include all of the FDA-approved drug products for a particular indication.

Third-party payors are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. We or Galderma may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of Epsolay® and Twyneo®. For example, Epsolay® and Twyneo® may not be considered medically necessary or cost-effective. A payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

In the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that drug products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies or trials that compare the cost-effectiveness of a particular product candidate to currently available therapies. For example, the European Union provides options for its member states to restrict the range of drug products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. European Union member states may approve a specific price for a drug product, or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the drug product on the market. Other member states allow companies to fix their own prices for drug products but monitor and control company profits. The downward pressure on health care costs in general, particularly prescription drugs, has become intense. As a result, there are increasingly high barriers to entry for new products. In addition, in some countries, cross-border imports from low-priced markets exert competitive pressure that may reduce pricing within a country. Any country that has price controls or reimbursement limitations for drug products may not allow favorable reimbursement and pricing arrangements.

Healthcare Reform

In March 2010, the President of the United States signed the ACA, one of the most significant healthcare reform measures in decades. The ACA substantially changed the way healthcare is financed by both governmental and private insurers, and significantly impacted the pharmaceutical industry. The ACA contained a number of provisions, including those governing enrollment in federal healthcare programs, reimbursement changes and fraud and abuse, which impacted existing government healthcare programs and will result in the development of new programs, including Medicare payment for performance initiatives and improvements to the physician quality reporting system and feedback program. Additionally, the ACA increased the minimum level of rebates payable by manufacturers of brand-name drugs from 15.1% to 23.1%, and imposed a non-deductible annual fee on pharmaceutical manufacturers or importers who sell "branded prescription drugs" to specified federal government programs.

Since its enactment, there have been judicial, executive and Congressional challenges to certain aspects of the ACA. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA without specifically ruling on the constitutionality of the ACA. Prior to the Supreme Court's decision, President Biden issued an executive order to initiate a special enrollment period from February 15, 2021 through August 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA.

In addition, other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. For example, the Budget Control Act of 2011 resulted in aggregate reductions to Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, will stay in effect through 2030, with the exception of a temporary suspension from May 1, 2020 through March 31, 2022 and a 1% reduction from April 1, 2022 through June 30, 2022, unless additional Congressional action is taken. Additionally, in January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. More recently, on March 11, 2021, the American Rescue Plan Act of 2021 was signed into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, beginning January 1, 2024.

The cost of prescription pharmaceuticals in the United States has also been the subject of considerable discussion. There have been several Congressional inquiries, as well as proposed and enacted legislation designed, among other things, to bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs and reform government program reimbursement methodologies for pharmaceutical products. For example, the Build Back Better Act, if enacted, would introduce substantial drug pricing reforms, including the establishment of a drug price negotiation program within the U.S. Department of Health and Human Services that would require manufacturers to charge a negotiated "maximum fair price" for certain selected drugs or pay an excise tax for noncompliance, and the establishment of rebate payment requirements on manufacturers under Medicare Parts B and D. If the Build Back Better Act is not enacted, similar or other drug pricing proposals could appear in future legislation. Individual states in the United States have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. We expect that additional state and federal healthcare initiatives will be adopted in the future, any of which could impact the coverage and reimbursement for drugs, including Twyneo®, and if approved by the FDA, Epsolay®.

Healthcare Laws and Regulations

Our current and future business operations may be subject to additional healthcare regulation and enforcement by the federal government and by authorities in the states and foreign jurisdictions in which we conduct our business. Such laws include, without limitation, state and federal anti-kickback, fraud and abuse, false claims, price reporting and physician and other healthcare provider payment transparency laws. Some of our pre-commercial activities are subject to some of these laws.

The federal Anti-Kickback Statute makes it illegal for any person or entity, including a prescription drug manufacturer or a party acting on its behalf to knowingly and willfully, directly or indirectly solicit, receive, offer, or pay any remuneration that is intended to induce the referral of business, including the purchase, order, lease of any good, facility, item or service for which payment may be made under a federal healthcare program, such as Medicare or Medicaid. The term "remuneration" has been broadly interpreted to include anything of value. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on one hand and prescribers, purchasers, formulary managers, and beneficiaries on the other. Although there are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution, the exceptions and safe harbors are drawn narrowly. Practices that involve remuneration that may be alleged to be intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exception or safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all its facts and circumstances. Several courts have interpreted the statute's intent requirement to mean that if any one purpose of an arrangement involving remuneration is to induce referrals of federal healthcare covered business, the Anti-Kickback Statute has been violated. In addition, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

The federal civil False Claims Act prohibits, among other things, any person or entity from knowingly presenting, or causing to be presented, for payment to, or approval by, federal programs, including Medicare and Medicaid, claims for items or services, including drugs, that are false or fraudulent or not provided as claimed, knowingly making, using or causing to be made or used, a false record or statement material to a false or fraudulent claim, or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to a federal program. Persons and entities can be held liable under these laws if they are deemed to "cause" the submission of false or fraudulent claims by, for example, providing inaccurate billing or coding information to customers or promoting a product off-label. In addition, our future activities relating to the reporting of wholesaler or estimated retail prices for our product candidates, the reporting of prices used to calculate Medicaid rebate information and other information affecting federal, state and third-party reimbursement for our product candidates, and the sale and marketing of our product candidates, are subject to scrutiny under this law. Moreover, 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.

HIPAA created new federal criminal statutes that prohibit among other actions, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Like 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.

The civil monetary penalties statute imposes penalties against any person or entity that, among other things, is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent.

The Affordable Care Act imposed, among other things, new annual reporting requirements for covered manufacturers for certain payments and other transfers of value provided to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain non-physician practitioners (nurse practitioners, certified nurse anesthetists, physician assistants, clinical nurse specialists, anesthesiology assistants and certified nurse midwives), and teaching hospitals, as well as certain ownership and investment interests held by physicians as defined by statute and their immediate family members.

Also, many states have similar fraud and abuse statutes or regulations that may be broader in scope and may apply regardless of payor, in addition to items and services reimbursed under Medicaid and other state programs. Additionally, to the extent that any of our product candidates are sold in a foreign country, we may be subject to similar foreign laws. Certain states also mandate implementation of compliance programs, impose restrictions on drug manufacturer marketing practices, require reporting of marketing expenditures and pricing information and/or require the tracking and reporting of gifts, compensation and other remuneration to physicians.

If our operations are found to be in violation of any of such laws or any other governmental regulations that apply to us, we may be subject to penalties, including, without limitation, administrative, civil and criminal penalties, damages, fines, disgorgement, contractual damages, reputational harm, diminished profits and future earnings, the curtailment or restructuring of our operations, exclusion from participation in federal and state healthcare programs or similar programs in other countries or jurisdictions, integrity oversight and reporting obligations, and imprisonment, any of which could adversely affect our ability to operate our business and our financial results.

Data Privacy and Security Laws

Numerous state, federal and foreign laws, regulations and standards govern the collection, use, access to, confidentiality and security of health-related and other personal information, and could apply now or in the future to our operations or the operations of our partners. In the United States, numerous federal and state laws and regulations, including data breach notification laws, health information privacy and security laws and consumer protection laws and regulations govern the collection, use, disclosure, and protection of health-related and other personal information. In addition, certain foreign laws govern the privacy and security of personal data, including health-related data. Privacy and security laws, regulations, and other obligations are constantly evolving, may conflict with each other to complicate compliance efforts, and can result in investigations, proceedings, or actions that lead to significant civil and/or criminal penalties and restrictions on data processing.

Innovation Authority

We have received royalty-bearing grants from the government of Israel through the IIA, for the financing of a portion of our research and development expenditures in Israel.

Under the Innovation Law and the IIA's rules and guidelines, recipients of grants, or Recipient Company(ies), are subject to certain obligations and restrictions with respect to the use of their IIA Funded Know-How, including, the following:

- **Royalty Payment Obligation**. In general, the Recipient Company is obligated to pay the IIA royalties from the revenues generated from the sale of products (and related services), whether received by the grant recipient or any affiliated entity, developed (in all or in part), directly or indirectly, as a result of, an Approved Program, or deriving therefrom, at rates which are determined under the IIA's rules and guidelines (currently a yearly rate of between 3% to 5% on sales of products or services developed under the Approved Programs, depending on the type of the Recipient Company — i.e., whether it is a "Small Company," or a "Large Company" as such terms are defined in the IIA's rules and guidelines), up to the aggregate amount of the total grants received by the IIA, plus annual interest based on LIBOR (as determined in the IIA's rules and guidelines);

- **Reporting Obligations**. The Innovation Law and the IIA's rules and guidelines impose on the Recipient Company certain reporting obligations (such as, periodic reports regarding the progress of the research and development activities under the Approved Program and the related research expenses, and regarding the scope of sales of the Recipient Company's products);

- **Local Manufacturing Obligation**. Products developed using the IIA grants must, as a general matter, be manufactured in Israel. The Recipient Company is prohibited from manufacturing products developed using these IIA grants outside of the State of Israel without receiving prior approval from the IIA (except for the transfer of less than 10% of the manufacturing capacity in the aggregate which requires only a notice, while the IIA has a right to deny such transfer within 30 days following the receipt of such notice). If the Recipient Company receives approval to manufacture products developed with IIA grants outside of Israel, it will be required (except for certain cases) to pay increased royalties to the IIA, up to 300% of the grant amount plus interest at annual rate based on LIBOR, depending on the manufacturing volume that is performed outside of Israel. The Recipient Company may also be subject to an accelerated royalty repayment rate. A Recipient Company also has the option of declaring in its IIA grant application its intention to exercise a portion of the manufacturing capacity abroad, thus avoiding the need to obtain additional approval following the receipt of the grant and avoiding the need to pay increased royalties to the IIA; and

- **IIA Funded Know-How transfer limitation**. Under the Innovation law and the IIA's rules and guidelines, a Recipient Company is prohibited from transferring the IIA Funded Know-How outside of Israel except under limited circumstances, and only with the approval of the Research Committee and in certain circumstances, subject to certain payments to the IIA calculated according to formulas provided under the IIA's rules and guidelines (which are capped to amounts specified under such rules and guidelines, generally up to 6 time the grants received plus interest). The scope of the support received, the royalties that have already paid to the IIA, the amount of time that has elapsed between the date on which the know-how was transferred and the date on which the IIA grants were received and the sale price and the form of transaction will be taken into account in calculating the amount of the payment to the IIA in the event of a transfer of IIA Funded Know-How outside of Israel. A transfer for the purpose of the Innovation Law and the IIA rules means an actual sale of the IIA-funded know-how, or any other transaction which in essence constitutes a transfer of the know-how (such as providing an exclusive license to a foreign entity for R&D purposes, which precludes the IIA funded company from further using such IIA Funded Know-How). A mere license solely to market products resulting from the IIA Funded Know-How would not be deemed a transfer for the purpose of the Innovation Law. Upon payment of such redemption fee, the IIA Funded Know-How and the manufacturing rights of the products supported by such IIA funding cease to be subject to the Innovation Law.

  Subject to the IIA's prior approval, a grant recipient may transfer IIA Funded Know-How to another Israeli company. If IIA Funded Know-How is transferred to another Israeli entity, the transfer would still require IIA approval but will not be subject to the payment of the redemption fee (we note that there will be an obligation to pay royalties to the IIA from the income of such sale transaction as part of the royalty payment obligation). In such case, the acquiring company would have to assume all of the selling company's responsibilities towards the IIA as a condition to IIA approval.

- **IIA Funded Know-How license limitation**. The IIA has published certain rules and guidelines with respect to the grant to a foreign entity of the right to use the IIA Funded Know-How for R&D purposes. According to these rules, the grant to a foreign entity of a right to use the IIA Funded Know-How (which does not entirely prevent the IIA funded company from using the Funded Know-How) is subject to receipt of the IIA's prior approval. This approval is subject to payment to the IIA in accordance with the formulas stipulated in these rules (such payment shall be no less than the amount of the IIA grants received (plus annual interest), and no more than the cap stated in the IIA rules and will generally be due only upon the receipt of the license fee from the licensee).

  The abovementioned rules include a mechanism with respect to the grant of a license by a Recipient Company (which is part of a multinational corporation) to its group entities to use its IIA Funded Know-How. Such license is subject to the IIA's prior approval and to the payment of 5% royalties from the income deriving from such license, with the cap of the royalties increasing to 150% of the grant amount. Such mechanism includes certain restrictions which must be met in order to be able to enjoy such lower royalty payment.

We have received grants from the IIA in connection with our research and development of a peripheral line of product candidates, which forms a negligible part of our activities, and therefore, we are subject to the aforementioned restrictions with respect to such product candidates. Such restrictions continue to apply even after payment of the full amount of royalties payable pursuant to the grants.

Even if our IIA funded know-how is transferred to another Israeli entity, the transfer would require the IIA's approval but will not be subject to the payment of a redemption fee (we note that there will be an obligation to pay royalties to the IIA from the income of such sale transaction as part of the royalty payment obligation). In such case, the acquiring company would have to assume all of our responsibilities towards the IIA as a condition to the IIA's approval.

The government of Israel does not own intellectual property rights in technology developed with IIA funding and there is no restriction on the export of products manufactured using technology developed with IIA funding. However, the IIA Funded Know-How is subject to transfer of know-how and manufacturing rights restrictions as described above. The IIA's approval is not required for the export of any products resulting from the IIA research or development grants.

We may not receive from the IIA the required approvals for any actual proposed transfer and, if received, we may be required to pay the IIA certain payments calculated according to formulas provided under the IIA's rules and guidelines.

Environmental, Health and Safety Matters

We are subject to extensive environmental, health and safety laws and regulations in a number of jurisdictions including Israel. These laws and regulations govern, among other things, (i) the use, storage, registration, handling, emission and disposal of chemicals, waste materials and sewage and (ii) chemical, air, water and ground contamination, air emissions and the cleanup of contaminated sites, including any contamination that results from spills due to our failure to properly dispose of chemicals, waste materials and sewage. Our operations at our Ness Ziona facility use chemicals and produce waste materials and sewage. Our activities require permits from various governmental authorities, including local municipal authorities, the Ministry of Environmental Protection and the Ministry of Health. The Ministry of Environmental Protection and the Ministry of Health, local authorities and the municipal water and sewage company conduct periodic inspections in order to review and ensure our compliance with the various regulations. Our business permit is currently in effect until December 31, 2026.

These laws, regulations and permits could potentially require the expenditure by us of significant amounts for compliance or remediation. If we fail to comply with such laws, regulations or permits, we may be subject to fines and other civil, administrative or criminal sanctions, including the revocation of permits and licenses necessary to continue our business activities. In addition, we may be required to pay damages or civil judgments in respect of third-party claims, including those relating to personal injury (including exposure to hazardous substances we use, store, handle, transport, manufacture or dispose of), property damage or contribution claims. Some environmental, health and safety laws allow for strict, joint and several liability for remediation costs, regardless of comparative fault. We may be identified as a responsible party under such laws. Such developments could have a material adverse effect on our business, financial condition and results of operations.

In addition, laws and regulations relating to environmental, health and safety matters are often subject to change. In the event of any changes or new laws or regulations, we could be subject to new compliance measures or to penalties for activities which were previously permitted.

The operations of our subcontractors and suppliers are also subject to various Israeli and foreign laws and regulations relating to environmental, health and safety matters, and their failure to comply with such laws and regulations could have a material adverse effect on our business and reputation, result in an interruption or delay in the development or manufacture of our product candidates, or increase the costs for the development or manufacture of our product candidates.

Properties

Our principal executive offices are located in a leased facility in Weizmann Science Park, Ness Ziona 7403650, Israel. The facility is 2,040 square meters, and houses our offices, warehouse, laboratories and production area. Our lease will expire on December 31, 2023.

Legal Proceedings

We are not subject to any material legal proceedings.

C. Organizational Structure

Not applicable.

D. Property, Plant and Equipment

See "Item 4. Information on the Company—B. Business Overview—Properties".

EXHIBIT INDEX

The exhibits filed with or incorporated into this Registration Statement are listed in the index of exhibits below.

Exhibit Number	Exhibit Description
1.1	Amended and Restated Memorandum of Association (incorporated by reference to Exhibit 3.1 of the Registration Statement on Form F-1/A filed with the Securities and Exchange Commission on January 23, 2018).
1.2	Amended and Restated Articles of Association (incorporated by reference to Exhibit 99.1 of Form 6-K/A filed with the Securities and Exchange Commission on August 20, 2018).
2.1	Form of Specimen Share Certificate (incorporated by reference to Exhibit 4.1 of the Registration Statement on Form F-1/A filed with the Securities and Exchange Commission on September 20, 2017).
2.2	Description of Share Capital (incorporated by reference to Exhibit 2.2 of the Annual Report on Form 20-F filed with the Securities and Exchange Commission on March 24, 2020).
4.1	Form of Indemnification Agreement (incorporated by reference to Exhibit 10.5 of the Registration Statement on Form F-1/A filed with the Securities and Exchange Commission on September 20, 2017).
4.2	2014 Share Incentive Plan (incorporated by reference to Exhibit 4.4 of the Annual Report on Form 20-F filed with the Securities and Exchange Commission on March 24, 2020).
4.3 **	Compensation Policy.
4.4	Registration Rights Agreement (incorporated by reference to Exhibit 99.2 of Form 6-K filed with the Securities and Exchange Commission on February 6, 2018).
4.5 ∞	Lease Agreement by and between the Registrant and Rachel Zacks, dated as of October 10, 2007 (incorporated by reference to Exhibit 10.7 of the Registration Statement on Form F-1/A filed with the Securities and Exchange Commission on August 29, 2017).
4.6∞	Lease Agreement by and between the Registrant and Rachel Zacks, dated as of September 29, 2014 (incorporated by reference to Exhibit 10.8 of the Registration Statement on Form F-1/A filed with the Securities and Exchange Commission on August 29, 2017).
4.7∞	Lease Agreement by and between the Registrant and Rachel Zacks, dated as of March 30, 2016 (incorporated by reference to Exhibit 10.9 of the Registration Statement on Form F-1/A filed with the Securities and Exchange Commission on August 29, 2017).
4.8∞	Lease Agreement by and between the Registrant and Rachel Zacks, dated as of September 20, 2016 (incorporated by reference to Exhibit 10.10 of the Registration Statement on Form F-1/A filed with the Securities and Exchange Commission on August 29, 2017).
4.9∞	Lease Agreement by and between the Registrant and Rachel Zacks, dated as of January 30, 2017 (incorporated by reference to Exhibit 10.11 of the Registration Statement on Form F-1/A filed with the Securities and Exchange Commission on August 29, 2017).

4.10∞	Lease Agreement by and between the Registrant and Rachel Zacks, dated as of September 25, 2017 (incorporated by reference to Exhibit 4.12 of the Annual on Form 20-F filed with the Securities and Exchange Commission on March 21, 2019).
4.11∞	Lease Agreement by and between the Registrant and Rachel Zacks, dated as of July 3, 2018 (incorporated by reference to Exhibit 4.13 of the Annual on Form 20-F filed with the Securities and Exchange Commission on March 21, 2019).
4.12∞	Lease Agreement by and between the Registrant and Rachel Zacks, dated as of August 14, 2018 (incorporated by reference to Exhibit 4.14 of the Annual on Form 20-F filed with the Securities and Exchange Commission on March 21, 2019).
4.13∞	Lease Agreement by and between the Registrant and Rachel Zacks, dated as of November 12, 2019 (incorporated by reference to Exhibit 4.15 of the Annual Report on Form 20-F filed with the Securities and Exchange Commission on March 24, 2020).
4.14	Promissory Note by and between the Registrant and Moshe Arkin, dated as of August 2, 2016 (incorporated by reference to Exhibit 10.12 of the Registration Statement on Form F-1/A filed with the Securities and Exchange Commission on August 29, 2017).
4.15	Schedule A, as amended, of Promissory Note by and between the Registrant and Moshe Arkin, dated as of June 28, 2017 (incorporated by reference to Exhibit 10.13 of the Registration Statement on Form F-1/A filed with the Securities and Exchange Commission on August 29, 2017).
4.16	Instrument of Conversion of Promissory Note by and between the Registrant and Moshe Arkin, dated as of August 22, 2017 (incorporated by reference to Exhibit 10.14 of the Registration Statement on Form F-1/A filed with the Securities and Exchange Commission on August 29, 2017).
4.17	Assignment Agreement between the Registrant and Medicis Pharmaceutical Corporation, dated August 16, 2013 (incorporated by reference to Exhibit 10.15 of the Registration Statement on Form F-1/A filed with the Securities and Exchange Commission on August 29, 2017).
4.18∞	Asset Transfer Agreement and Assignment Deed between Sol-Gel Technologies Ltd. and M. Arkin Dermatology Ltd., dated August 22, 2017 (incorporated by reference to Exhibit 10.16 of the Registration Statement on Form F-1/A filed with the Securities and Exchange Commission on January 30, 2017).
4.19† **	License Agreement between Sol-Gel Technologies Ltd. and Galderma Holding SA, dated June 21, 2021.
4.20† **	License Agreement between Sol-Gel Technologies Ltd. and Galderma Holding SA, dated June 21, 2021.
4.21† **	Supply Agreement between Sol-Gel Technologies Ltd., Galderma Holding SA, and Douglas Manufacturing Limited, dated June 21, 2021.
4.22† **	Termination Agreement between Padagis Israel Pharmaceuticals Ltd, and Sol-Gel Technologies Ltd., dated November 3, 2021.
4.23† **	Termination Agreement between Padagis Israel Pharmaceuticals Ltd, and Sol-Gel Technologies Ltd., dated November 3, 2021.

12.1 *	Certification by Chief Executive Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
12.2 *	Certification by Chief Financial Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
13.1 *	Certification by Chief Executive Officer pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
13.2 *	Certification by Chief Financial Officer pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
15.1 *	Consent of Independent Registered Public Accounting Firm
101	The following financial statements from the Company's 20-F for the fiscal year ended December 31, 2021, formatted in XBRL: (i) Consolidated Statements of Comprehensive Loss, (ii) Consolidated Statements of Financial Position, (iii) Consolidated Statements of Changes in Equity, (iv) Consolidated Statements of Cash Flows, and (v) Notes to the Consolidated Financial Statements.
*	Filed herewith.
**	Previously filed.
†	Certain confidential portions of this exhibit have been redacted from the publicly filed document because such portions are (i) not material and (ii) would be competitively harmful if publicly disclosed.
∞	Informal translation of the original Hebrew document.

SIGNATURE

The Registrant hereby certifies that it meets all of the requirements for filing on Form 20-F and that it has duly caused and authorized the undersigned to sign this annual report on its behalf.

SOL-GEL TECHNOLOGIES LTD.

By: /s/ Alon Seri-Levy
Name: Alon Seri-Levy
Title: Chief Executive Officer and Director

By: /s/ Gilad Mamlok
Name: Gilad Mamlok
Title: Chief Financial Officer

Date: April 7, 2022

SOL-GEL TECHNOLOGIES LTD.
CONSOLIDATED FINANCIAL STATEMENTS
AS OF DECEMBER 31, 2021

SOL-GEL TECHNOLOGIES LTD.
CONSOLIDATED FINANCIAL STATEMENTS
AS OF DECEMBER 31, 2021

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Report of Independent Registered Public Accounting Firm

To the board of directors and shareholders of Sol-Gel Technologies Ltd.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Sol-Gel Technologies Ltd**.** and its subsidiary (the "Company") as of December 31, 2021 and 2020, and the related consolidated statements of operations, of changes in shareholders' equity and of cash flows for each of the three years in the period ended December 31, 2021, including the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2021 and 2020, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2021 in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's consolidated financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits of these consolidated financial statements in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

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

Tel-Aviv, Israel
April 4, 2022

/s/ Kesselman & Kesselman
Certified Public Accountants (Isr.)
A member firm of PricewaterhouseCoopers International Limited

We have served as the Company's auditor since 2000.

Kesselman & Kesselman, 146 Derech Menachem Begin, Tel-Aviv 6492103, Israel,
P.O Box 7187 Tel-Aviv 6107120, Telephone: +972 -3- 7954555, Fax:+972 -3- 7954556, www.pwc.com/il

SOL-GEL TECHNOLOGIES LTD.
CONSOLIDATED BALANCE SHEETS
(U.S. dollars in thousands, except share and per share data)

	December 31	
	2020	2021
Assets		
CURRENT ASSETS:		
Cash and cash equivalents	$ 7,122	$ 20,085
Bank deposits	21,400	21,448
Marketable securities	21,652	1,709
Receivables from collaborative arrangements	2,153	13,065
Prepaid expenses and other current assets	1,074	800
TOTAL CURRENT ASSETS	53,401	57,107
NON-CURRENT ASSETS:		
Long-term receivables from collaborative arrangements	-	7,402
Restricted long-term deposits and cash	1,293	1,298
Property and equipment, net	1,817	1,051
Operating lease right-of-use assets	1,896	1,501
Funds in respect of employee rights upon retirement	754	830
TOTAL NON-CURRENT ASSETS	5,760	12,082
TOTAL ASSETS	$ 59,161	$ 69,189
Liabilities and shareholders' equity		
CURRENT LIABILITIES:		
Accounts payable	$ 1,203	$ 766
Other accounts payable	4,088	10,145
Current maturities of operating leases	673	781
TOTAL CURRENT LIABILITIES	5,964	11,692
LONG-TERM LIABILITIES:		
Operating leases liabilities	1,299	810
Liability for employee rights upon retirement	1,049	1,093
TOTAL LONG-TERM LIABILITIES	2,348	1,903
COMMITMENTS (Note 6)		
TOTAL LIABILITIES	8,312	13,595
SHAREHOLDERS' EQUITY:		
Ordinary shares, NIS 0.1 par value – authorized: 50,000,000 as of December 31, 2020 and 2021, respectively; issued and outstanding: 23,000,782 and 23,126,804 as of December 31, 2020 and December 31, 2021, respectively	635	638
Additional paid-in capital	231,577	233,098
Accumulated deficit	(181,363)	(178,142)
TOTAL SHAREHOLDERS' EQUITY	50,849	55,594
TOTAL LIABILITIES AND SHAREHOLDERS' EQUITY	$ 59,161	$ 69,189

The accompanying notes are an integral part of these consolidated financial statements.

SOL-GEL TECHNOLOGIES LTD.
CONSOLIDATED STATEMENTS OF OPERATIONS
(U.S. dollars in thousands, except share and per share data)

	Year ended December 31,		
	2019	**2020**	**2021**
COLLABORATION REVENUES	$ 22,904	$ 8,771	$ 23,772
LICENSE REVENUES	-	-	7,500
TOTAL REVENUES	22,904	8,771	31,272
RESEARCH AND DEVELOPMENT EXPENSES	40,578	27,913	20,381
GENERAL AND ADMINISTRATIVE EXPENSES	8,276	11,091	8,451
OTHER INCOME, net	-	-	524
TOTAL OPERATING INCOME (LOSS)	(25,950)	(30,233)	2,964
FINANCIAL INCOME, net	1,374	943	257
INCOME (LOSS) BEFORE INCOME TAXES	(24,576)	(29,290)	3,221
INCOME TAXES	(33)	-	-
NET INCOME (LOSS) FOR THE YEAR	$ (24,609)	$ (29,290)	$ 3,221
BASIC INCOME (LOSS) PER ORDINARY SHARE	$ (1.26)	$ (1.30)	$ 0.14
DILUTED INCOME (LOSS) PER ORDINARY SHARE	(1.26)	(1.30)	0.14
WEIGHTED AVERAGE NUMBER OF SHARES OUTSTANDING USED IN COMPUTATION OF BASIC AND DILUTED INCOME (LOSS) PER SHARE:			
BASIC	19,534,562	22,574,688	23,063,493
DILUTED	19,534,562	22,574,688	23,566,182

The accompanying notes are an integral part of these consolidated financial statements.

SOL-GEL TECHNOLOGIES LTD.
CONSOLIDATED STATEMENTS OF CHANGES IN SHAREHOLDERS' EQUITY
(U.S. dollars in thousands, except share data)

	Ordinary shares		Additional paid-in capital	Accumulated deficit	Total
	Number of shares	Amounts	Amounts		
BALANCE AS OF JANUARY 1, 2019	18,949,968	520	190,853	(127,464)	63,909
CHANGES DURING 2019:					
Net loss for the year				(24,609)	(24,609)
Vesting of restricted share units	15,332	*	*		-
Issuance of shares through public offering, net of issuance costs	1,437,500	41	10,572		10,613
Share-based compensation			2,552		2,552
BALANCE AS OF DECEMBER 31, 2019	20,402,800	561	203,977	(152,073)	52,465
CHANGES DURING 2020:					
Net loss for the year				(29,290)	(29,290)
Issuance of shares and warrants through public offering, net of issuance costs	2,091,907	61	21,245		21,306
Issuance of shares and warrants through private placement from the controlling shareholder	454,628	13	4,987		5,000
Vesting of restricted share units	23,000	*			
Exercise of options	28,447	*	151		151
Share-based compensation			1,217		1,217
BALANCE AS OF DECEMBER 31, 2020	23,000,782	635	231,577	(181,363)	50,849
CHANGES DURING 2021:					
Net income for the year				3,221	3,221
Issuance of shares through ATM, net of issuance costs	41,154	1	504		505
Vesting of restricted share units	19,170	*	*		
Exercise of options	65,698	2	330		332
Share-based compensation			687		687
BALANCE AS OF DECEMBER 31, 2021	23,126,804	638	233,098	(178,142)	55,594

* Less than 1,000.

The accompanying notes are an integral part of these consolidated financial statements.

SOL-GEL TECHNOLOGIES LTD.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(U.S. dollars in thousands)

	Year ended December 31,		
	2019	**2020**	**2021**
CASH FLOWS FROM OPERATING ACTIVITIES:			
Net income (loss) for the year	$ (24,609)	$ (29,290)	$ 3,221
Adjustments required to reconcile net income (loss) to net cash used in operating activities:			
Depreciation	887	946	880
Loss from disposal of property and equipment	-	-	29
Changes in accrued liability for employee rights upon retirement	38	21	(32)
Share-based compensation expenses	2,552	1,217	687
Net changes in operating leases	5	71	14
Changes in fair value of marketable securities	65	138	(125)
Finance expenses, net	50	12	55
Changes in operating asset and liabilities:			
Receivables from collaborative arrangements	(4,120)	1,967	(10,912)
Prepaid expenses and other current assets	1,694	219	274
Accounts payable, accrued expenses and other	938	(542)	5,620
Long-term receivables from collaborative arrangements	-	-	(7,402)
Net cash used in operating activities	(22,500)	(25,241)	(7,691)
CASH FLOWS FROM INVESTING ACTIVITIES:			
Purchase of property and equipment	(597)	(449)	(143)
Bank deposits	1,000	(21,400)	(48)
Restricted long-term deposits	(10)	(21)	(5)
Investments in marketable securities	(38,702)	(32,322)	(6,716)
Proceeds from sales and maturity of marketable securities	54,333	51,498	26,784
Net cash provided by (used in) investing activities	16,024	(2,694)	19,872
CASH FLOWS FROM FINANCING ACTIVITIES:			
Proceeds from issuance of shares through ATM, net of issuance costs	-	-	505
Proceeds from exercise of options granted to employees	-	151	332
Proceeds from issuance of shares and warrants through public offering, net of issuance costs	10,613	21,306	-
Net proceeds from issuance of shares and warrants to the controlling shareholder through private placement	-	5,000	-
Net cash provided by financing activities	10,613	26,457	837
EFFECT OF EXCHANGE RATE ON CASH AND CASH EQUIVALENTS	(50)	(12)	(55)
INCREASE (DECREASE) IN CASH AND CASH EQUIVALENTS	4,087	(1,490)	12,963
CASH AND CASH EQUIVALENTS AND RESRICTED CASH AT BEGINNING OF THE YEAR	5,675	9,762	8,272
CASH AND CASH EQUIVALENTS AND RESTRICTED CASH AT END OF THE YEAR	$ 9,762	$ 8,272	$ 21,235
Cash and Cash equivalents	9,412	7,122	20,085
Restricted cash	350	1,150	1,150
CASH AND CASH EQUIVALENTS AND RESTRICTED CASH SHOWN IN STATEMENT OF CASH FLOWS	$ 9,762	$ 8,272	$ 21,235
SUPPLEMENTARY INFORMATION ON INVESTING AND FINANCING ACTIVITIES NOT INVOLVING CASH FLOWS:			
Recognition of new operating lease ROU and liabilities	$ 1,329	$ 378	$ 253
SUPPLEMENTARY INFORMATION:			
Income taxes paid	$ -	$ 7	$ 34
Interest received	$ 1,600	$ 770	$ 774

The accompanying notes are an integral part of these consolidated financial statements.

NOTE 1 — NATURE OF OPERATIONS

Sol-Gel Technologies Ltd. (collectively with its subsidiary, the Company) is an Israeli Company incorporated in 1997.

The Company is a clinical stage specialty pharmaceutical company focused on developing and commercializing topical dermatological drug products. The Company's lead product candidates are based upon its proprietary microencapsulation delivery system, consisting of microcapsules made of precipitated silica. The most advanced investigational drugs in the Company's product pipeline are: (i) Twyneo®, which is developed for the treatment of acne vulgaris and (ii) Epsolay®, a potential treatment for subtype II rosacea. The New Drug Application ("NDA") for Twyneo® was accepted by the U.S. Food and Drug Administration (the "FDA"), which assigned a Prescription Drug User Fee Act ("PDUFA") goal date of August 1, 2021. The NDA for Epsolay® was accepted by the FDA, which assigned a PDUFA goal date of April 26, 2021. On such PDUFA goal date, the Company received confirmation from the FDA that action on the NDA could not be taken since a pre-approval inspection of the production site of Epsolay® still needs to be conducted. On February 18,2022 the FDA conducted a pre-approval inspection of the production site for Epsolay®, currently pending approval by the FDA. In June 2021, the Company entered into two exclusive license agreements with Galderma for the commercialization of Twyneo® and Epsolay®, in the United States, see note 8. On July 27, 2021, the Company announced that the FDA approved the drug product, Twyneo®. In addition to the novel product candidates, the Company's products included the generic products Acyclovir, Ivermectin and other generic product candidates. In November 2021, the company entered into an agreement with Padagis, to sell its rights in relation to ten generic collaborative agreements between the parties, including the agreements for two approved generic drug products. Under the new agreement, the company has retained collaboration rights to two generic programs related to four generic drug candidates, see note 7b.

The Company has a wholly owned U.S. subsidiary - Sol-Gel Technologies Inc. (the "Subsidiary"). The Subsidiary supports the Company with regard to marketing, regulatory affairs and business development relating to its products and technology in the U.S.

Since incorporation through December 31, 2021, the Company has an accumulated deficit of approximately $178,142 and its activities have been funded mainly by its shareholders, collaboration revenues and license agreements, see also Notes 7 and 8. The Company expects to continue to incur significant research and development and other costs related to its ongoing operations.

In addition, management is continuing to analyze cash resources and considering raising additional funding from different sources, such as corporate collaborations, public or private equity offerings and/or debt financings, and/or selling shares under the Company's Open Market Sale Agreement with Jefferies LLC. Management expects that the Company's cash and cash equivalents, deposits and marketable securities as of December 31, 2021 will allow the Company to fund its operating plan through at least the next 12 months from the financial statement issuance date.

The Company is subject to risks and uncertainties as a result of the COVID-19 pandemic. To date, the impact of COVID-19 pandemic has been limited and resulted in delays with respect to pre-approval inspections.

The full extent to which the COVID-19 pandemic will directly or indirectly impact the Company's business, results of operations and financial condition, including revenues from collaboration arrangements, expenses, reserves and allowances, manufacturing, supply, regulatory approvals, clinical trials, commercial launch of branded and generic product candidates, research and development costs and employee-related amounts, will depend on future developments that are highly uncertain and cannot be predicted. The Company continues to monitor and assess new information related to the COVID-19 pandemic, the actions taken to contain or treat COVID-19, as well as the economic impact on various markets.

NOTE 1 — NATURE OF OPERATIONS (continued)**:**

Furthermore, the estimation process required to prepare the Company's consolidated financial statements requires assumptions to be made about future events and conditions and the impact of COVID-19 on its financial results, and while management believes such assumptions are reasonable, they are inherently subjective and uncertain. The Company's actual results could differ materially from those estimates.

NOTE 2 — SIGNIFICANT ACCOUNTING POLICIES

Basis of presentation

The Company's financial statements have been prepared in accordance with generally accepted accounting principles in the United States of America ("U.S. GAAP").

a. Use of estimates in the preparation of financial statements

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

As applicable to these consolidated financial statements, the most significant estimates and assumptions relate to the fair value of share-based compensation and the incremental borrowing rate for leases.

b. Functional and presentation currency

The U.S. dollar ("dollar") is the currency of the primary economic environment in which the operations of the Company and its subsidiary are conducted. The Company's financing has been provided in dollars, revenues are primarily in dollars and a significant part of expenses are incurred in dollars. The financial statements are presented in dollars, which is the Company's functional and presentation currency.

Transactions and balances originally denominated in dollars are presented at their original amounts. Balances in non-dollar currencies are translated into dollars using historical and current exchange rates for non-monetary and monetary balances, respectively. For non-dollar transactions and other items in the statements of operations (indicated below), the following exchange rates are used: (I) for transactions — exchange rates at transaction dates or average rates; and (ii) for other items (derived from non-monetary balance sheet items such as depreciation) — historical exchange rates. Currency transaction gains and losses are presented in financial income or expenses, as appropriate.

c. Cash and cash equivalents

The Company considers as cash equivalents all short-term, highly liquid investments, which include short-term bank deposits with original maturities of three months or less from the date of purchase that are not restricted as to withdrawal or use and are readily convertible to known amounts of cash.

d. Bank deposits

Bank deposits with original maturity dates of more than three months but less than one year are included in short-term deposits. Such short-term deposits bear interest at an average annual rate of approximately 0.46%-0.82% in 2021. Interest accrued on bank deposits was recorded as interest receivable as part of "Prepaid expenses and other current assets" in the company's balance sheet.

Bank deposits with maturity of more than one year are considered long-term.

(U.S. dollars in thousands, except share and per share amounts)

NOTE 2 - SIGNIFICANT ACCOUNTING POLICIES (continued)**:**

e. Marketable securities

Marketable securities consist of debt securities. The Company elected the fair value option to measure and recognize its investments in debt securities in accordance with ASC 825, Financial Instruments as the Company manages its portfolio and evaluates the performance on a fair value basis. Changes in fair value, realized gains and losses on sales of marketable securities, are reflected in the statements of operation as finance expense (income), net.

f. Derivatives and hedging

The Company carries out transactions involving foreign currency exchange derivative financial instruments. The transactions are designed to hedge the Company's exposure in currencies other than the U.S. dollar. The derivative does not qualify for hedge accounting, therefore the changes in the fair value are included in financial expense (income), net.
The currency hedged items are denominated in New Israeli Shekel (NIS). The counterparties to the derivatives are major banks in Israel.

As of December 31, 2021, the Company has $1,150 on the Company's bank account that is restricted in order to secure the hedging transactions. This amount is presented among Restricted long-term deposits and cash.

g. Trade receivables

Trade receivables are initially recognized at the transaction price and subsequently measured at amortized cost less any allowance for expected credit losses.
Starting from January 1, 2020, the Company applies ASU 2016-13 "Financial Instruments Credit Losses Measurement of Credit Losses on Financial Instruments" ("the Standard").

h. Property and equipment

1) Property and equipment are stated at cost, net of accumulated depreciation and amortization.

2) The Company's property and equipment are depreciated utilizing the straight-line method on the basis of their estimated useful life.

Annual rates of depreciation are as follows:

	%
Laboratory equipment	10 – 33 (mainly 15 – 25)
Office equipment and furniture	7 – 15
Computers and related equipment	33

Leasehold improvements are amortized utilizing the straight-line method over the shorter of the expected lease term or the estimated useful life of the improvements.

NOTE 2 - SIGNIFICANT ACCOUNTING POLICIES (continued)**:**

i. Impairment of long-lived assets

The Company tests long-lived assets for impairment whenever events or circumstances present an indication of impairment. If the sum of expected future cash flows (undiscounted and without interest charges) of the assets is less than the carrying amount of such assets, an impairment loss would be recognized. The assets would then be written down to their estimated fair values.

For the three years ended December 31, 2021, the Company did not recognize an impairment loss for its long-lived assets.

j. Share-based compensation

The Company accounts for employees' and non-employees' share-based payment awards classified as equity awards using the grant-date fair value method. The fair value of share-based payment transactions is recognized as an expense over the requisite service period.

The Company elected to recognize compensation costs for awards conditioned only on continued service that have a graded vesting schedule using the accelerated method based on the multiple-option award approach.

The Company measures share-based compensation to non-employees in the same manner (except for certain exceptions) as share-based compensation to employees.

The Company has elected to recognize forfeitures as they occur.

k. Research and development expenses

Research and development expenses include costs directly attributable to the conduct of research and development programs, including the cost of salaries, share-based compensation expenses, payroll taxes and other employee benefits, lab expenses, consumable equipment and consulting fees. All costs associated with research and developments are expensed as incurred.

Acquisitions of in-process research and development product candidate, which are not part of business combination, are recognized as an expense as research and development expenses as incurred.

Grants received from Israel Innovation Authority (hereafter — "IIA"), formerly known as the Office of the Chief Scientist of the Ministry of Economy and Industry, or the OCS are recognized when the grant becomes receivable, provided there is reasonable assurance that the Company will comply with the conditions attached to the grant and there is reasonable assurance the grant will be received. The grant is deducted from the research and development expenses as the applicable costs are incurred. See note 6a(1).

Clinical trial costs are a significant component of research and development expenses and include costs associated with third-party contractors. The Company outsources its clinical trial activities utilizing external entities such as clinical research organizations, independent clinical investigators, and other third-party service providers to assist the Company with the execution of its clinical trials. Clinical trial costs are expensed as incurred.

NOTE 2 - SIGNIFICANT ACCOUNTING POLICIES (continued)**:**

l. Revenue recognition

The Company applies ASC 606, Revenue from Contracts with Customers. According to the standard, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration that the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of Topic 606, the entity performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the performance obligation is satisfied.

An entity only applies the five-step model to contracts when it is probable that the entity will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer, after considering any price concession expected to be provided to the customer, when applicable. At contract inception, the entity assesses the goods or services promised within each contract and determines those that are performance obligations and assesses whether each promised good or service is distinct. A good or service promised to a customer is distinct if the customer can benefit from the good or service either on its own or together with other resources that are readily available to the customer and the entity's promise to transfer the good or service to the customer is separately identifiable from other promises in the contract. The entity then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

Collaborative Arrangements

The Company entered into collaborative arrangements with partners that fall under the scope of Topic 808, Collaborative Arrangements ("ASC 808"). While these arrangements are in the scope of ASC 808, the Company may analogize to ASC 606 for some aspects of the arrangements. The Company analogizes to ASC 606 for certain activities within the collaborative arrangement for the delivery of a good or service (i.e., a unit of account) that is part of its ongoing major or central operations. Revenue recognized by analogizing to ASC 606 is recorded as "collaboration revenues".

The terms of the Company's collaborative arrangements typically include one or more of the following: (i) royalties on net sales of licensed products; (ii) reimbursements or cost-sharing of R&D expenses. Each of these payments results in collaboration revenues or an offset against R&D expense.

Royalties: For arrangements that include sales-based royalties and the license is deemed to be the predominant item to which the royalties relate, the Company recognizes collaboration revenues at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied).

Under certain collaborative arrangements, the Company has been reimbursed for a portion of its R&D expenses or participates in the cost-sharing of such R&D expenses. Such reimbursements and cost-sharing arrangements have been reflected as a reduction of R&D expense in the Company's consolidated statements of operations, as
the Company does not consider performing research and development services for reimbursement to be a part of its ongoing major or central operations.

For arrangements that include a significant financing component, the company separates the significant financing component from the revenue and interest income is recorded when payments are received. See note 7.

NOTE 2 - SIGNIFICANT ACCOUNTING POLICIES (continued)**:**

l. Revenue recognition (continued):

Licensing agreements

The Company has identified one performance obligation in The License Agreements: Grant of the license and use of its IP. The Grant of the license and use of its IP performance obligation considered to be a right to use IP in accordance with ASC 606. Therefore, revenue is recognized at a point in time, upon transfer of control over the license to the licensee.

ASC 606 defines the 'Transaction Price' as the amount of consideration to which the entity expects to be entitled in exchange for transferring the promised goods or services to a customer. The transaction price contains variable consideration contingent upon the licensee achieving certain milestones, as well as sales-based royalties, in accordance with the relevant agreement. Variable payments, contingent on achieving additional milestones, are included in the transaction price based on most likely amount method. Amounts included in the transaction price are recognized only when it is probable that a significant reversal of cumulative revenues will not occur, usually upon achievement of the specific milestone, in accordance with the relevant agreement. Sales-based royalties are not included in the transaction price. Rather, they are recognized as the related sale occurs, due to the specific exception of ASC 606 for sales-based royalties in licensing of intellectual properties.

m. Income taxes

1) Deferred taxes

The Company accounts for income taxes in accordance with ASC 740, "Income Taxes" ("ASC 740"). ASC 740 prescribes the use of the liability method whereby deferred tax asset and liability account balances are determined based on differences between the financial reporting and tax bases of assets and liabilities and are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse. The Company provides a valuation allowance, if necessary, to reduce deferred tax assets to their estimated realizable value if it is more likely than not that a portion or all of the deferred tax assets will not be realized, based on the weight of available positive and negative evidence. Deferred tax liabilities and assets are classified as non-current.

2) Uncertainty in income taxes

The Company follows a two-step approach in recognizing and measuring uncertain tax positions. The first step is to evaluate the tax position for recognition by determining if the available evidence indicates that it is more likely than not that the position will be sustained based on technical merits. If this threshold is met, the second step is to measure the tax position as the largest amount that has more than a 50% likelihood of being realized upon ultimate settlement.

NOTE 2 - SIGNIFICANT ACCOUNTING POLICIES (continued)**:**

n. Leases

Right of Use ("ROU") assets represent the Company's right to use an underlying asset for the lease term and lease liabilities represent the Company's obligation to make lease payments arising from the lease. Operating lease ROU assets and liabilities are recognized at commencement date based on the present value of lease payments over the lease term. The Company's lease terms may include options to extend or terminate the lease when it is reasonably certain that the Company will exercise that option.

The Company uses the implicit rate when readily determinable. As the Company's leases do not provide an implicit rate, the Company uses its estimated incremental borrowing rate based on the information available at commencement date in determining the present value of lease payments. Lease expense for lease payments is recognized on a straight-line basis over the lease term. The Company elected to not separate lease and non-lease components for the leases. The Company elected the practical expedient of the short-term lease recognition exemption for all leases with a term shorter than 12 months.

Additionally, the company applies the portfolio approach to account for operating lease ROU asset and liabilities for certain car leases and incremental borrowing rates.

o. Concentration of credit risks

Financial instruments that potentially subject the Company to concentration of credit risk consist principally of cash and cash equivalents, bank deposits and marketable securities and certain receivables. The Company deposits cash and cash equivalents with highly rated financial institutions (Israeli banks). In addition, all marketable securities carry a high rating or are government insured. The Company has not experienced any material credit losses in these accounts and does not believe it is exposed to significant credit risk on these instruments.

p. Income (loss) per share

Basic income (loss) per share is computed on the basis of the net income (loss) for the period divided by the weighted average number of ordinary shares outstanding during the period. Diluted income (loss) per share is based upon the weighted average number of ordinary shares and of ordinary shares equivalents outstanding when dilutive. Ordinary share equivalents include outstanding stock options, restricted shares and warrants, which are included under the treasury stock method when dilutive. The calculation of diluted income (loss) per share does not include 1,260,984, 3,271,507 and 3,397,834 options, restricted shares and warrants for the years ended December 31, 2019, 2020 and 2021, respectively, because their effect would be anti-dilutive.

NOTE 2 - SIGNIFICANT ACCOUNTING POLICIES (continued)**:**

q. Fair value measurement

Fair value is based on the price that would be received from the sale of an asset or that would be paid to transfer a liability in an orderly transaction between market participants at the measurement date. In order to increase consistency and comparability in fair value measurements, the guidance establishes a fair value hierarchy that prioritizes observable and unobservable inputs used to measure fair value into three broad levels, which are described as follows:

Level 1: Quoted prices (unadjusted) in active markets that are accessible at the measurement date for assets or liabilities. The fair value hierarchy gives the highest priority to Level 1 inputs.

Level 2: Observable prices that are based on inputs not quoted on active markets but corroborated by market data.

Level 3: Unobservable inputs are used when little or no market data is available. The fair value hierarchy gives the lowest priority to Level 3 inputs.

In determining fair value, the Company utilizes valuation techniques that maximize the use of observable inputs and minimize the use of unobservable inputs to the extent possible and considers counterparty credit risk in its assessment of fair value.

Due to the short term nature and/or low-risk nature of the Company's cash and cash equivalents, bank deposits, restricted cash, receivables from collaborative arrangements, restricted long-term deposits, accrued expenses (under other account payable), operating leases liabilities and other liabilities, their carrying amounts approximates their fair value.

(U.S. dollars in thousands, except share and per share amounts)

NOTE 3 — MARKETABLE SECURITIES

The following table sets forth the Company's marketable securities for the indicated period:

	December 31,	
	2020	2021
Level 2 securities:		
U.S government and agency bonds	$ 4,192	275
Other foreign government bonds	2,006	-
Corporate bonds*	15,454	1,434
Total	$ 21,652	$ 1,709

* Investments in Corporate bonds rated A or higher.

The Company's debt securities are classified within Level 2 because it uses quoted market prices or alternative pricing sources and models utilizing market observable inputs to determine their fair value.
The cost of marketable securities As of December 31, 2021 is $1,734.

The table below sets forth a summary of the changes in the fair value of the Company's marketable securities for the years ended December 31, 2020 and 2021:

	December 31,	
	2020	2021
Balance at beginning of the year	$ 40,966	21,652
Additions	32,322	6,716
Sale or maturity	(51,498)	(26,784)
Changes in fair value during the year	(138)	125
Balance at end of the year	$ 21,652	1,709

As of December 31, 2021, all the Company's debt securities are due within one year.

(U.S. dollars in thousands, except share and per share amounts)

NOTE 4 — PROPERTY AND EQUIPMENT

	December 31	
	2020	2021
Cost:		
Laboratory equipment	$ 3,644	$ 3,588
Office equipment and furniture	265	265
Computers and software	530	357
Leasehold improvements	1,953	1,993
	6,392	6,203
Less:		
Accumulated depreciation and amortization	(4,575)	(5,152)
Property and equipment, net	$ 1,817	$ 1,051

Depreciation and amortization expense totaled $887, $946 and $880 for the years ended December 31, 2019, 2020 and 2021, respectively.

NOTE 5 — EMPLOYEE SEVERANCE BENEFITS

The Company is required to make severance payments upon dismissal of an employee or upon termination of employment in certain circumstances. The severance payment liability to the employees (based upon length of service and the latest monthly salary — one month's salary for each year employed) is recorded on the Company's balance sheet under "Liability for employee rights upon retirement." The liability is recorded as if it was payable at each balance sheet date on an undiscounted basis.

In accordance with the current employment terms starting in August 2014 with all of its employees (Section 14 of the Israeli Severance Pay Law, 1963), the Company makes regular deposits with certain insurance companies for accounts controlled by each applicable employee in order to secure the employee's retirement benefit obligation. The Company is fully relieved from any severance pay liability with respect to each such employee after it makes the payments on behalf of the employee. The liability accrued in respect of these employees and the amounts funded, as of the respective agreement dates, are not reflected in the Company balance sheet, as the amounts
funded are not under the control and management of the Company and the pension or severance pay risks have been irrevocably transferred to the applicable insurance companies (the "Contribution Plan").

With regard to the period before August 2014, the liability is funded in part from the purchase of insurance policies or by the establishment of pension funds with dedicated deposits in the funds. The amounts used to fund these liabilities are included in the balance sheets under "Funds in respect of employee rights upon retirement." These policies are the Company's assets.

The amounts of severance payment expenses were $402, $428 and $445 for the years ended December 31, 2019, 2020 and 2021, respectively, of which $363, $408 and $404 in the years ended December 2019, 2020 and 2021, respectively, were in respect of the Contribution Plan.

The Company expects to contribute approximately $404 in the year ending December 31, 2022 to insurance companies in connection with its expected severance liabilities for that year.

NOTE 6 — COMMITMENTS :

a. **Royalty Commitments:**

1) The Company is obligated to pay royalties to the IIA on proceeds from the sale of products developed from research and development activities that were funded, partially, by grants from the IIA.

Under the specific terms of the funding arrangements with the IIA, royalties of 3.5% to 25% are payable on the sale of products developed with funding received from the IIA, which payments shall not exceed, in the aggregate, 300% of the amount of the grant received (dollar linked), plus interest at annual rate based on LIBOR.

Up to December 31, 2021, the Company had recognized and received grants from the IIA in the aggregate amount of $1,430 (no grants were received in the years ended December 31, 2019, 2020 and 2021). Through December 31, 2021, the Company recorded an accumulated royalty expense of $2,109 as royalties to the IIA with respect to revenue recognized through December 31, 2021($32, $25 and $23 were recorded in 2019, 2020 and 2021 accordingly, as an expense in the consolidated statements of operations).

2) The Company has an agreement, that was amended several times (hereafter — the agreements) with Yissum Research Development Company (hereafter — "Yissum"), the technology-licensing arm of the Hebrew University of Jerusalem.

According to the agreements, the Company received from Yissum an exclusive and a non-exclusive license for the commercialization of certain Yissum patents. According to the agreements the Company shall pay Yissum:
Royalties of 1.5% of net sales related to certain patents. 1.5% – 8% of proceeds received by the Company for the sub-license or license of certain patents.

Royalty expenses in immaterial amounts were recorded in 2019, 2020 and 2021 in respect of these agreements.

According to the agreements, the Company may continue commercial use of certain Yissum's patents in connection with the products and subject to the obligation to pay Yissum the royalties and the sub-license fees.

The Company granted rights to a third party for use and commercialization of certain Yissum patents.

b. **Lease Agreements**

The Company leases offices and vehicles under operating leases. For leases with terms greater than 12 months, the Company records right of use assets and lease liabilities at the present value of lease payments over the leases term.

Offices
The Company leases office spaces and research and development facilities under several agreements. These agreements are linked to the change in the Israeli consumer price index and expire in December 2023. These agreements are classified as operating leases and presented under operating lease right-of-use assets and operating leases liabilities. A restricted deposit of $136 has been deposited in order to secure the agreement.

(U.S. dollars in thousands, except share and per share amounts)

NOTE 6 — COMMITMENTS (continued):

Vehicles

The Company has entered into operating lease agreements for vehicles used by its employees for a period of 3 years. These contracts are classified as operating leases and presented under operating lease right-of-use assets and operating leases liabilities.

Lease Position

The table below presents the lease-related assets and liabilities recorded on the consolidated balance sheet:

	As of December 31,	
	2020	2021
Assets		
Operating Leases		
Operating lease right-of-use assets	$ 1,896	$ 1,501
Liabilities		
Current liabilities		
Current maturities of operating leases	$ 673	$ 781
Long-term liabilities		
Non-current operating leases	$ 1,299	$ 810
Weighted Average Remaining Lease Term		
Operating leases	1.29	0.87
Weighted Average Discount Rate		
Operating leases	6.25%	6.13%

Lease Costs

The table below presents certain information related to lease costs of operating leases for the year ended December 31, 2021:

	Year Ended December 31,	
	2020	2021
Operating lease cost:	$ 685	$ 872

(U.S. dollars in thousands, except share and per share amounts)

NOTE 6 — COMMITMENTS (continued):

The table below presents supplemental cash flow information related to leases for the year ended December 31, 2021:

	Year Ended December 31,	
	2020	2021
Cash paid for amounts included in the measurement of leases liabilities:		
Operating cash flows from operating leases	$ 735	$ 843

Undiscounted Cash Flows

The table below reconciles the undiscounted cash flows for each of the first five years and total of the remaining years to the operating lease liabilities recorded on the consolidated balance sheet:

	Operating Leases
For the year ending December 31, 2021	
2022	$ 858
2023	789
2024	30
Total minimum lease payments	1,677
Less: amount of lease payments representing interest	(86)
Present value of future minimum lease payments	1,591
Less: Current maturities of operating leases	781
Long-term operating leases liabilities	810
	$ 1,591

c. In June 2008, the Company entered into a Master Clinical Trial Services Agreement with a third party, which was later amended in April 2017, to retain its services as a clinical research organization for certain product candidate subject to task work orders to be issued by the Company. During 2018, the Company entered into six additional task orders. As consideration for its services the Company will pay a total amount of approximately $14,425 during the term of the engagement and based on achievement of certain milestones, out of which $12,710 were recognized as an expense until December 31, 2021.

d. In 2016 through 2020, the Company entered into several collaboration agreements mainly with one third party (the "Partner") for the development, manufacturing and commercialization of several product candidates (including an agreement assumed by the Company in August 2018, following the transfer of an in-process research and development product candidate from a related party). In November 2021, the Company entered into a new agreement (the "New Agreement") with the Partner, to sell its rights to the Partner in relation to ten generic collaborative agreements between the parties. Under the New Agreement, the Company has retained collaboration rights to two generic programs related to four generic drug candidates. See detailed information in note 7b.

e. In October 2017, the Company entered into a Clinical Development Master Services Agreement with a third party, to retain it as clinical research organization for certain product candidate, subject to task work orders to be issued by the Company. As consideration for its services the Company will pay a total amount of approximately $13,955 during the term of the engagement and based on achievement of certain milestones, out of which $13,430 were recognized as an expense until December 31, 2021.

NOTE 7 — COLLABORATION AGREEMENTS

a. In 2007, the Company granted rights to a third party for use and commercialization of a product for skin protection. Under this agreement, the Company is entitled to royalties during the years 2016 to 2024. Based on current sales, royalties are not material.

b. In 2016 through 2020, the Company entered into several collaboration agreements mainly with one Partner for the development, manufacturing and commercialization of several generic product candidates. Under the agreements, the Partner is obligated to conduct regulatory, scientific, clinical and technical activities necessary to develop the product and prepare and file ANDA, with the FDA and gain regulatory approval. The Company participates in the development of the product candidates, including participation in joint steering committees and is obligated for sourcing the active pharmaceutical ingredient (API) during the development phase.

Upon FDA approval, the Partner has exclusive rights and is required to use diligent efforts to commercialize these products in territories defined under the agreements, including all required sales, marketing and distributing activities associated with the agreements. The Company is entitled to a share of the Partner's gross profits related to the sale of the products, as such term is defined in each of the agreements.

During the years ended December 31, 2019, 2020 and 2021, the Company recognized collaboration revenues related to sales of products in the U.S. under these agreements in the amounts of $22,775, $8,673 and $3,303, respectively.

These Agreements are considered to be within the scope of ASC 808, as the parties are active participants and exposed to the risks and rewards of the collaborative activity. The Company recognizes collaboration revenues when the related sales occur.

In November 2021, the Company entered into a New Agreement with the Partner, to sell its rights in relation to ten generic collaborative agreements between the parties, including the agreements for two approved generic drug products. Under the New Agreement, the Company has retained collaboration rights to two generic programs related to four generic drug candidates. Following the signing of the New Agreement, the Company is no longer entitled to receive its share in profit as detailed above.

Under the terms of the New Agreement, effective as of November 1, 2021, the Company will unconditionally receive $21.5 million over 24 months, in lieu of its share in future gross profits for the two approved generic drug products and its potential gross profits for eight unapproved generic programs. The Company received $1,250 as an upfront payment and $20,250 in eight equal quarterly instalments. The New Agreement also provides that effective as of November 1, 2021, the Company will cease paying any outstanding and future operational costs related to these collaborative agreements.

NOTE 8 – LICENSE AGREEMENTS:

In June 2021, the Company entered into two exclusive license agreements with Galderma for the commercialization of two of the Company most advanced investigational drug products (Twyneo® and Epsolay®) in the United States. The Company is entitled to up to $7.5 million per product in upfront payments and regulatory approval milestone payments assuming 2021 approval of each respective product. The Company is also eligible to receive tiered double-digit royalties ranging from mid-teen to high-teen percentage of net sales as well as up to $9 million in sales milestone payments.

NOTE 8 – LICENSE AGREEMENTS (continued):

According to the agreement, the Company has an option to regain commercialization rights five years following first commercialization. In the third quarter of 2021, the Company received $7.5 million for Twyneo® and $4 million for Epsolay® of upfront payments, which are refundable if FDA approval for each respective product is not received by December 31, 2021. On July 27, 2021, the Company announced that the FDA approved the Company's first proprietary drug product, Twyneo®. See note 1. Since FDA approval for Epsolay® had not been received as of December 31, 2021, the Company is required to refund the $4 million upfront payment, which is recorded under " Other accounts payable" in the Company's balance sheet. In March 2022, the Company has refunded the $4 million upfront payment to Galderma.

NOTE 9— SHARE CAPITAL

a. Ordinary shares

Rights of the Company's ordinary shares

Each ordinary share is entitled to one vote. The holder of the ordinary shares is also entitled to receive dividends whenever funds are legally available, when and if declared by the Board of Directors. Since its inception, the Company has not declared any dividends.

1) On August 12, 2019, the Company completed an underwritten follow-on public offering, in which it issued 1,437,500 ordinary shares, including the full exercise by the underwriters of their option to purchase 187,500 additional ordinary shares, at a public offering price of $8.00 per ordinary share.
The total proceeds received from the offering, net of issuance costs, were approximately $10,613.

2) On February 19, 2020, the Company completed an underwritten public offering, in which it issued 2,091,907 ordinary shares and 2,091,907 warrants to purchase up to 1,673,525 ordinary shares, at a public offering price of $11.00 per ordinary shares. The warrants are exercisable over a three-year period from the date of issuance at a per share exercise price of $14, subject to certain adjustments as defined in the agreement. The total proceeds received from the offering, net of issuance costs, were approximately $21,306.

   In addition, and in parallel to the public offering, the Company signed an agreement for a private placement with its controlling shareholder for an additional investment of approximately $5,000 in consideration of 454,628 ordinary shares and 454,628 warrants to purchase up to 363,702 ordinary shares, at the same terms of the underwritten public offering mentioned above. The private placement agreement was contingent on certain conditions and was approved by the company's shareholders on April 8, 2020. The total proceeds of $5,000 were received in April 2020.

3) In July 2021, the Company entered into an ATM sales agreement with Jefferies LLC ("Jefferies"), pursuant to which the Company is entitled, at its sole discretion, to offer and sell through Jefferies, acting as sales agent, Shares having an aggregate offering price of up to $25.0 million throughout the period during which the ATM facility remains in effect. The Company agreed to pay Jefferies a commission of 3.0% of the gross proceeds from the sale of shares under the facility.

   From the effective date of the agreement through the issuance date of this report, 41,154 shares were sold under the program for total gross proceeds of approximately $0.5 million, leaving an available balance under the facility of approximately $24.5 million as of the issuance date of this report.

NOTE 9— SHARE CAPITAL (continued):

b. Share-based compensation:

1) **Option plan**

In December, 2014, the Company's Board of Directors approved a Share Incentive Plan (hereafter — the Plan) and reserved a pool of 629,025 ordinary shares, par value NIS 0.1 each, or such other number as the Board may determine, subject to certain terms and conditions as defined in the Plan. According to the Plan, the Company may issue shares or restricted shares, may grant options or restricted share units and other share-based awards (hereafter — the awards) to the Company's employees, consultants, directors and other service providers.

The Plan is designed to enable the Company to grant awards to purchase Ordinary Shares under various and different tax regimes including, without limitation: pursuant and subject to Section 102 of the Israeli Tax Ordinance and pursuant and subject to Section 3(i) of the Israeli Tax Ordinance and under Internal revenue Code Section 422.

The awards may be exercised after vesting and in accordance with vesting schedules which will be determined by the Board of Directors for each grant. The maximum term of the awards is 10 years. The fair value of each option granted under this Plan is estimated using the Black-Scholes option pricing method. Expected volatility is based on the historical volatility of the company and of comparable peer companies.

The risk-free interest rate assumption is based on observed interest rates appropriate for the expected term of the options granted in dollar terms. The expected term of the options is estimated based on the simplified method, as its historical experience for options grants as a public company is insufficient.

In December 2019, the Company's Board of Directors approved an increase of the ordinary shares that may be issued under the Company's Plan by reserving an additional amount of 912,230 ordinary shares.
As of December 31, 2021, 753,578 ordinary shares remain available for future grants under the Plan.

2) **Options grants**

a. Option granted to employees and directors

During the twelve months ended December 31, 2021, the Company granted 248,600 options to employees and directors:

i. In January 2021 and March 2021, the Company granted a total of 20,000 options and 3,600 options, respectively, to several employees to purchase ordinary shares at an exercise price of $10.44 and $9.93 per share, respectively.

The options vest over a period of 4 years; one quarter of the options vest on the first anniversary of the vesting commencement date (as described in each agreement) and the rest vest quarterly over the following three years. The options expire on the tenth anniversary of their grant date.

ii. In February 2021, the Company granted a total of 225,000 options to several directors to purchase ordinary shares at an exercise price of $10.02 per share.

The options vest over a period of 3 years; one third of the options vest on the first anniversary of the vesting commencement date (as described in each agreement) and the rest vest quarterly over the following two years. The options expire on the tenth anniversary of their grant date.

(U.S. dollars in thousands, except share and per share amounts)

NOTE 9 — SHARE CAPITAL (continued):

The fair value of options granted in 2019 and 2021 was $485 and $1,061, respectively. No options were granted in 2020. The underlying data used for computing the fair value of the options are as follows:

	2019	2021
Value of one ordinary share	$6.08-$8.59	$9.56-$10.44
Dividend yield	0%	0%
Expected volatility	74.87%-77.83%	59.52%-70.48%
Risk-free interest rate	1.82%-2.75%	0.55%-1.14%
Expected term	6.11 years	3.25-7 years

The total unrecognized compensation cost of employee options at December 31, 2021 is $376, which is expected to be recognized over a period of 3.17 years.

The following table summarizes the number of options granted to employees under the Plan for the year ended December 31, 2021, and related information:

	Year ended December 31		
	2021		
	Number of options	Weighted average exercise price	Weighted average remaining contractual life
Options outstanding at the beginning of the year	1,000,894	$ 4.63	6.05
Granted	248,600	$ 10.05	-
Exercised	(65,702)	$ 5.05	-
Expired	(1,350)	$ 5.57	-
Forfeited	(51,413)	$ 7.73	-
Options outstanding at the end of the year	1,131,029	$ 5.64	5.73
Options exercisable at the end of the year	1,030,267	$ 4.42	4.37

b. Option granted to non-employees

The total unrecognized compensation cost of non-employees' options at December 31, 2021 is $1, which is expected to be recognized over a period of 0.23 years.

(U.S. dollars in thousands, except share and per share amounts)

NOTE 9— SHARE CAPITAL (continued)

The following table summarizes the number of options granted to non-employees under the Plan for the year ended December 31, 2021, and related information:

	Year ended December 31		
	2021		
	Number of options	Weighted average exercise price	Weighted average remaining contractual life
Options outstanding at the beginning of the year	198,575	$ 7.70	6.84
Granted			
Options outstanding at the end of the year	198,575	$ 7.70	5.84
Options exercisable at the end of the year	173,465	$ 7.60	5.83

c. The aggregate intrinsic value of the total outstanding and of total exercisable options as of December 31, 2021 is approximately $3,313 and $3,312, respectively.

d. Restricted Share Units (RSUs) granted to Directors

In February 2018 and September 2018, the board of directors approved and recommended the Company shareholders to approve a total grant of 46,000 and 11,500 RSUs, respectively, to its independent and external directors that vest annually in equal portions over a three-year period. The fair value of shares as of the date of grant was $495 and $105 respectively. As of December 31, 2021, 57,500 RSUs were vested.

e. The following table illustrates the effect of share-based compensation on the statements of operations:

	Year ended December 31		
	2019	2020	2021
Research and development expenses	$ 1,028	$ 431	$ 33
General and administrative expenses	$ 1,524	$ 786	$ 654
	$ 2,552	$ 1,217	$ 687

NOTE 10 - TAXES ON INCOME

a. Tax rates in Israel

The Company is taxed in accordance with Israeli tax laws. The corporate tax rates applicable to 2019, 2020 and 2021 is 23%. Capital gain is subject to capital gain tax according to the corporate tax rate in the year the assets are sold.

b. Tax rates for the U.S Subsidiary

The subsidiary is taxed according to U.S. tax laws. The Company's income is taxed in the United States at the federal rate of 21%.

c. Tax benefits under the Law for the Encouragement of Capital Investments, 1959 (the "Investment Law")

Under the Investment Law, including Amendment No. 60 to the Investment Law that was published in April 2005, by virtue of the Benefited Enterprise program for certain of its facilities; the Company may be entitled to various tax benefits.

The main benefit arising from such status is the reduction in tax rates on income derived from a Benefited Enterprise. The extent of such benefits depends on the location of the enterprise. Since the Company's facilities are not located in "national development zone A," income derived from Benefited Enterprises will be tax exempt for a period of two years and then have a reduced tax rate for a period of up to an additional eight years.

The period of tax benefits, as described above, is limited to 12 years from the beginning of the Benefited Enterprise election year (2012). As of December 31, 2021, the period of benefits has not yet commenced.

In the event of distribution of cash dividends from income, which was tax exempt as above, the amount distributed will be subject to the tax rate it was exempted from. The Company is entitled to claim accelerated depreciation in respect of equipment used by the approved enterprises during five tax years.

Entitlement to the above benefits is conditioned upon the Company fulfilling the conditions stipulated by the Investment Law and regulations published thereunder.

In the event of failure to comply with these conditions, the benefits may be canceled and the Company may be required to refund the amount of the benefits, in whole or in part, with the addition of linkage differences to the Israeli consumer price index and interest.

The Investment Law was amended as part of the Economic Policy Law for the years 2011 – 2012 (the "Amendment"), which became effective on January 1, 2011 and was further amended in August 2013 and January 2017.

Under the 2017 Amendment, and provided the conditions stipulated therein are met, income derived by Preferred Companies from 'Preferred Technological Enterprises' ("PTE") (as defined in the 2017 Amendment), would be subject to reduced corporate tax rates of 7.5% in Development Zone "A" and 12% elsewhere, or 6% in case of a 'Special Preferred Technological Enterprise' ("SPTE") as defined in the 2017 Amendment) regardless of the company's geographical location within Israel. A Preferred Company distributing dividends from income derived from its PTE or SPTE, would subject the recipient to a 20% tax (or lower, if so provided under an applicable tax treaty). The 2017 Amendment further provides that, in certain circumstances, a dividend distributed to a corporate shareholder who is not an Israeli resident for tax purposes would be subject to a 4% tax (inter alia, if the amount of foreign investors in the distributing company exceeds 90%). Such taxes would generally be withheld at source by the distributing company.

NOTE 10- TAXES ON INCOME (continued)

On June 14, 2017, the Encouragement of Capital Investments Regulations (Preferred Technology Income and Capital Profits for a Technological Enterprise), 2017 (the "Regulations") were published, which adopted Action 5 under the base erosion and profit shifting ("BEPS") regulations. The Regulations describe, inter alia, the mechanism used to determine the calculation of the benefits under the PTE and under the SPTE Regime and determine certain requirements relating to documentation of intellectual property for the purpose of the PTE. According to these provisions, a company that complies with the terms under the PTE regime may be entitled to certain tax benefits with respect to income generated during the company's regular course of business and derived from the preferred intangible asset (as determined in the Investments Law), excluding income derived from intangible assets used for marketing and income attributed to production activity. In the event that intangible assets used for marketing purposes generate over 10% of the PTE's income, the relevant portion, calculated using a transfer pricing study, would be subject to regular corporate income tax. If such income does not exceed 10%, the PTE will not be required to exclude the marketing income from the PTE's total income. The Regulations set a presumption of direct production expenses plus 10% with respect to income related to production, which can be countered by the results of a supporting transfer pricing study. Tax rates applicable to such production income expenses will be similar to the tax rates under the Preferred Enterprise regime, to the extent such income would be considered as eligible. In order to calculate the preferred income, the PTE is required to take into account the income and the research and development expenses that are attributed to each single preferred intangible asset. Nevertheless, it should be noted that the transitional provisions allow companies to take into account the income and research and development expenses attributed to all of the preferred intangible assets they have.

Under the transitional provisions of the law, a company is allowed to continue to enjoy the tax benefits available under the law prior to its amendment until the end of the period of benefits, as defined in the law. In each year during the period of benefits as a Benefited Enterprise, the Company will be able to opt for application of the amendment, thereby making available the tax rates discussed above. The Company's election to apply the amendment is irrecoverable.

As of December 31, 2021, the Company's management decided not to adopt the application of the Amendment.

There is no assurance that future taxable income of the Company will qualify as Benefited or Preferred income or that the benefits described above will be available to the Company in the future.

d. Tax assessments

Tax assessments filed by the Company through the year 2016 are considered to be final.

(U.S. dollars in thousands, except share and per share amounts)

NOTE 10 - TAXES ON INCOME (continued)

e. Losses for tax purposes carried forward to future years

As of December 31, 2021, the Company had approximately $170.8 million of net carry forward tax losses which are available to reduce future taxable income with no limited period of use.

f. Deferred income taxes:

	December, 31	
	2020	**2021**
In respect of:		
Net operating loss carry forward	$ 34,835	$ 39,280
Research and development expenses	7,133	5,153
Other	1,085	875
Less – valuation allowance	(43,053)	(45,308)
Net deferred tax assets	$ -	$ -

g. Reconciliation of theoretical tax expenses to actual expenses

Actual tax expenses are in respect of the U.S. subsidiary. The primary reconciling items between the statutory tax rate of the Company and the effective rate are the full valuation allowance of deferred tax assets and nondeductible expenses in relation to the operations in Israel.

h. Roll forward of valuation allowance

Balance at January 1, 2019	$ 26,166
Additions	8,781
Balance at December 31, 2019	$ 34,947
Additions	8,106
Balance at December 31, 2020	$ 43,053
Additions	2,255
Balance at December 31, 2021	$ 45,308

i. Provision for uncertain tax positions

As of December 31, 2020, and 2021, the Company does not have a provision for uncertain tax positions.

(U.S. dollars in thousands, except share and per share amounts)

NOTE 11 — SUPPLEMENTARY FINANCIAL STATEMENT INFORMATION

Other accounts payables and accruals

	December, 31	
	2020	2021
Accrued expenses	$ 3,250	1,685
Employees payables	812	754
Institutions	26	3,625
Refundable upfront payment	-	4,000
Other	-	81
	$ 4,088	$ 10,145

NOTE 12 — RELATED PARTIES

a. Related parties include the Controlling Shareholder and companies under his control, the Board of Directors and the Executive Officers of the Company.

b. As to options and restricted shares granted to directors and executive officers, see note 9d.

NOTE 13 — SUBSEQUENT EVENTS

In March 2022, the Company has refunded the $4 million upfront payment to Galderma, See detailed information in note 8.

Exhibit 12.1

CERTIFICATION BY CHIEF EXECUTIVE OFFICER PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Alon Seri-Levy, certify that:

1. I have reviewed this annual report on Form 20-F of Sol-Gel Technologies Ltd.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the company as of, and for, the periods presented in this report;

4. The company's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the company and have:

    a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the company, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

    b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

    c) Evaluated the effectiveness of the company's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

    d) Disclosed in this report any change in the company's internal control over financial reporting that occurred during the period covered by the annual report that has materially affected, or is reasonably likely to materially affect, the company's internal control over financial reporting;

5. The company's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the company's auditors and the audit committee of the company's board of directors (or persons performing the equivalent functions):

    a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the company's ability to record, process, summarize and report financial information; and

    b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the company's internal control over financial reporting.

Date: April 7, 2022

/s/ Alon Seri-Levy
Alon Seri-Levy
Chief Executive Officer

Exhibit 12.2

CERTIFICATION BY CHIEF FINANCIAL OFFICER PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Gilad Mamlok, certify that:

1. I have reviewed this annual report on Form 20-F of Sol-Gel Technologies Ltd.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the company as of, and for, the periods presented in this report;

4. The company's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the company and have:

    e) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the company, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

    f) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

    g) Evaluated the effectiveness of the company's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

    h) Disclosed in this report any change in the company's internal control over financial reporting that occurred during the period covered by the annual report that has materially affected, or is reasonably likely to materially affect, the company's internal control over financial reporting;

5. The company's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the company's auditors and the audit committee of the company's board of directors (or persons performing the equivalent functions):

    c) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the company's ability to record, process, summarize and report financial information; and

    d) Any fraud, whether or not material, that involves management or other employees who have a significant role in the company's internal control over financial reporting.

Date: April 7, 2022

/s/ Gilad Mamlok
Gilad Mamlok
Chief Financial Officer

Exhibit 13.1

CERTIFICATION BY CHIEF EXECUTIVE OFFICER PURSUAN TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report of Sol-Gel Technologies Ltd. (the "Company") on Form 20-F for the period ended December 31, 2021 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned officer of the Company certifies, pursuant to 18 U.S.C. §1350, as adopted pursuant to §906 of the Sarbanes-Oxley Act of 2002, that to such officer's knowledge:

(1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: April 7, 2022

/s/ Alon Seri-Levy
Alon Seri-Levy
Chief Executive Officer

Exhibit 13.2

CERTIFICATION BY CHIEF FINANCIAL OFFICER PURSUAN TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report of Sol-Gel Technologies Ltd. (the "Company") on Form 20-F for the period ended December 31, 2021 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned officer of the Company certifies, pursuant to 18 U.S.C. §1350, as adopted pursuant to §906 of the Sarbanes-Oxley Act of 2002, that to such officer's knowledge:

(1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: April 7, 2022

/s/ Gilad Mamlok
Gilad Mamlok
Chief Financial Officer

Exhibit 15.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statements on Form S-8 (No. 333-223915) and Form F-3 (No. 333-230564) of Sol-Gel Technologies Ltd. of our report dated April 4, 2022 relating to the financial statements, which appears in this Amendment No. 1 to Form 20-F.

Tel-Aviv, Israel
April 7, 2022

/s/Kesselman & Kesselman
Certified Public Accountants (Isr.)
A member firm of PricewaterhouseCoopers International Limited