SOLIGENIX, INC.
Form 10-K
March 26, 2019

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

þ ANNUAL REPORT UNDER SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934.

For the Fiscal Year Ended **December 31, 2018**

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

For the transition period from _____ to _____

Commission File No. 000-16929

SOLIGENIX, INC.

(Exact name of registrant as specified in its charter)

Delaware	**41-1505029**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification Number)

29 EMMONS DRIVE, SUITE B-10

PRINCETON, NJ **08540**
(Address of principal executive offices) (Zip Code)

(609) 538-8200
(Registrant's telephone number, including area code)

Securities registered under Section 12 (b) of the Exchange Act:

Title of Each Class	Name of Each Exchange on Which Registered
Common Stock, par value $.001 per share	**The Nasdaq Capital Market**
Common Stock Purchase Warrants	

Securities registered under Section 12(g) of the Exchange Act: **None**

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes No þ

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes No þ

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 þ No

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted and posted 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 and post such files). Yes þ No

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this 10-K or any amendments to this Form 10-K. þ

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

Large accelerated filer	Accelerated filer
Non-accelerated filer	Smaller reporting company þ
	Emerging growth company

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

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes No þ

The aggregate market value of the common stock held by non-affiliates of the registrant was approximately $8,437,036 (assuming, for this purpose, that executive officers, directors and holders of 10% or more of the common stock are affiliates), based on the closing price of the registrant’s common stock as reported on The Nasdaq Capital Market on June 30, 2018, 8,750,801 shares of the registrant’s Common Stock, par value $0.001 per share, were outstanding.

DOCUMENTS INCORPORATED BY REFERENCE: None.

SOLIGENIX, INC.

ANNUAL REPORT ON FORM 10-K

For the Year Ended December 31, 2018

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PART I

Item 1. Business

This Annual Report on Form 10-K contains statements of a forward-looking nature relating to future events or our future financial performance. These statements are only predictions and actual events or results may differ materially. In evaluating such statements, you should carefully consider the various factors identified in this report that could cause actual results to differ materially from those indicated in any forward-looking statements, including those set forth in "Risk Factors" in this Annual Report on Form 10-K. See "Cautionary Note Regarding Forward Looking Statements."

Our Business Overview

We are a late-stage biopharmaceutical company focused on developing and commercializing products to treat rare diseases where there is an unmet medical need. We maintain two active business segments: BioTherapeutics and Vaccines/BioDefense.

Our BioTherapeutics business segment is developing a novel photodynamic therapy (SGX301) utilizing topical synthetic hypericin activated with safe visible fluorescent light for the treatment of cutaneous T-cell lymphoma ("CTCL"), our first-in-class innate defense regulator technology, dusquetide (SGX942) for the treatment of oral mucositis in head and neck cancer, and proprietary formulations of oral beclomethasone 17,21-dipropionate ("BDP") for the prevention/treatment of gastrointestinal ("GI") disorders characterized by severe inflammation, including pediatric Crohn's disease (SGX203) and acute radiation enteritis (SGX201).

Our Vaccines/BioDefense business segment includes active development programs for RiVax®, our ricin toxin vaccine candidate and SGX943, our therapeutic candidate for antibiotic resistant and emerging infectious disease. The development of our vaccine programs currently is supported by our heat stabilization technology, known as ThermoVax®, under existing and on-going government contract funding. With the government contract from the National Institute of Allergy and Infectious Diseases ("NIAID"), we will attempt to advance the development of RiVax® to protect against exposure to ricin toxin..

An outline of our business strategy follows:

Following positive interim analysis, complete enrollment and report final results in our pivotal Phase 3 clinical trial of SGX301 for the treatment of CTCL;

Continue enrollment of the pivotal Phase 3 clinical trial of SGX942 for the treatment of oral mucositis in head and neck cancer;

Continue development of RiVax® in combination with our ThermoVax® technology to develop a new heat stable vaccine in biodefense with NIAID funding support;

Continue to apply for and secure additional government funding for each of our BioTherapeutics and Vaccines/BioDefense programs through grants, contracts and/or procurements;

Pursue business development opportunities for our pipeline programs, as well as explore merger/acquisition strategies; and

Acquire or in-license new clinical-stage compounds for development.

Corporate Information

We were incorporated in Delaware in 1987 under the name Biological Therapeutics, Inc. In 1987, we merged with Biological Therapeutics, Inc., a North Dakota corporation, pursuant to which we changed our name to "Immunotherapeutics, Inc." We changed our name to "Endorex Corp." in 1996, to "Endorex Corporation" in 1998, to "DOR BioPharma, Inc." in 2001, and finally to "Soligenix, Inc." in 2009. Our principal executive offices are located at 29 Emmons Drive, Suite B-10, Princeton, New Jersey 08540 and our telephone number is (609) 538-8200.

Our Product Candidates in Development

The following tables summarize our product candidates under development:

BioTherapeutic Product Candidates

Soligenix Product Candidate	Therapeutic Indication	Stage of Development
SGX301	Cutaneous T-Cell Lymphoma	Phase 2 trial completed; demonstrated significantly higher response rate compared to placebo; Phase 3 clinical trial enrolled first patient in December 2015, with positive interim analysis received in October 2018, and final results expected in the first quarter of 2020
SGX942	Oral Mucositis in Head and Neck Cancer	Phase 2 trial completed; demonstrated significant response compared to placebo with positive long-term (12 month) safety also reported; Phase 3 clinical trial enrolled first patient in December 2017, with interim analysis enrollment completion expected in the first half of 2019 and the interim analysis anticipated in the third quarter of 2019; final results expected in the first half of 2020
SGX203**	Pediatric Crohn's disease	Phase 1/2 clinical trial completed; efficacy data, pharmacokinetic (PK)/pharmacodynamic (PD) profile and safety profile demonstrated; Phase 3 clinical trial initiation contingent upon additional funding, such as through partnership
SGX201**	Acute Radiation Enteritis	Phase 1/2 clinical trial completed; safety profile and preliminary efficacy demonstrated; further clinical development contingent upon additional funding, such as through partnership

Vaccine Thermostability Platform**

Soligenix Product Candidate	Indication	Stage of Development
ThermoVax®	Thermostability of aluminum adjuvanted vaccine for ricin	Pre-clinical

BioDefense Products**

Soligenix Product Candidate	Indication	Stage of Development
RiVax®	Vaccine against Ricin Toxin Poisoning	Phase 1a and 1b trials completed, safety and neutralizing antibodies for protection demonstrated; Phase 2 trial planned for the second half of 2019
OrbeShield®	Therapeutic against GI ARS	Pre-clinical
SGX943	Therapeutic against Emerging Infectious Diseases	Pre-clinical

** *Contingent upon continued government contract/grant funding or other funding source.*

BioTherapeutics Overview

SGX301 – for Treating Cutaneous T-Cell Lymphoma

SGX301 is a novel, first-in-class, photodynamic therapy that utilizes safe visible light for activation. The active ingredient in SGX301 is synthetic hypericin, a photosensitizer which is topically applied to skin lesions and then activated by fluorescent light 16 to 24 hours later. Hypericin is also found in several species of *Hypericum* plants, although the drug used in SGX301 is chemically synthesized by a proprietary manufacturing process and not extracted from plants. Importantly, hypericin is optimally activated with visible light thereby avoiding the negative consequences of ultraviolet light. Other light therapies using UVA light result in serious adverse effects including secondary skin cancers.

Combined with photoactivation, in clinical trials synthetic hypericin has demonstrated significant anti-proliferative effects on activated normal human lymphoid cells and inhibited growth of malignant T-cells isolated from CTCL patients. In both settings, it appears that the mode of action is an induction of cell death in a concentration as well as a light dose-dependent fashion. These effects appear to result, in part, from the generation of singlet oxygen during photoactivation of hypericin.

Hypericin is one of the most efficient known generators of singlet oxygen, the key component for phototherapy. The generation of singlet oxygen induces necrosis and apoptosis in adjacent cells. The use of topical synthetic hypericin coupled with directed visible light results in generation of singlet oxygen only at the treated site. We believe that the use of visible light (as opposed to cancer-causing ultraviolet light) is a major advance in photodynamic therapy. In a published Phase 2 clinical study in CTCL, after six weeks of twice weekly therapy, a majority of patients experienced a statistically significant ($p \leq 0.04$) improvement with SGX301 whereas the placebo was ineffective: 58.3% compared to 8.3%, respectively.

SGX301 has received Orphan Drug designation as well as Fast Track designation from the U.S. Food and Drug Administration (“FDA”). The Orphan Drug Act is intended to assist and encourage companies to develop safe and effective therapies for the treatment of rare diseases and disorders. In addition to providing a seven-year term of market exclusivity for SGX301 upon final FDA approval, Orphan Drug designation also positions us to be able to leverage a wide range of financial and regulatory benefits, including government grants for conducting clinical trials, waiver of FDA user fees for the potential submission of a New Drug Application (“NDA”) for SGX301, and certain tax credits. In addition, Fast Track is a designation that the FDA reserves for a drug intended to treat a serious or life-threatening condition and one that demonstrates the potential to address an unmet medical need for the condition. Fast Track designation is designed to facilitate the development and expedite the review of new drugs. For instance, should events warrant, we will be eligible to submit a NDA for SGX301 on a rolling basis, permitting the FDA to review sections of the NDA prior to receiving the complete submission. Additionally, NDAs for Fast Track

development programs ordinarily will be eligible for priority review. SGX301 for the treatment of CTCL also was granted Orphan Drug designation from the European Medicines Agency ("EMA") Committee for Orphan Medical Products and Promising Innovative Medicine ("PIM") designation from the Medicines and Healthcare Products Regulatory Agency ("MHRA") in the United Kingdom ("UK").

In August 2018, the United States Patent Office granted us a patent titled "Systems and Methods for Producing Synthetic Hypericin" for the unique proprietary process manufacturing the highly purified form of synthetic hypericin, the active pharmaceutical ingredient in SGX301.

We initiated our pivotal Phase 3 clinical study of SGX301 for the treatment of CTCL during December 2015. This trial, referred to as the "FLASH" study (Fluorescent Light Activated Synthetic Hypericin), aims to evaluate the response to SGX301 as a skin directed therapy to treat early stage CTCL. We are actively enrolling patients with approximately 35 CTCL centers across the United States ("U.S.") participating in this pivotal trial. The Phase 3 protocol is a highly powered, double-blind, randomized, placebo-controlled, multicenter trial and seeks to enroll approximately 120 evaluable subjects. The trial consists of three treatment cycles, each of eight weeks duration. Treatments are administered twice weekly for the first six weeks and treatment response is determined at the end of the eighth week. In the first treatment cycle, approximately 80 subjects receive SGX301 and 40 receive placebo treatment of their index lesions. In the second cycle, all subjects receive SGX301 treatment of their index lesions, and in the third cycle all subjects receive SGX301 treatment of all of their lesions. The majority of subjects enrolled to date have elected to continue into the third optional, open-label cycle of the study. We continue to work closely with the Cutaneous Lymphoma Foundation, as well as the National Organization for Rare Disorders. Subjects are followed for an additional six months after their last evaluation visit. The primary efficacy endpoint is assessed on the percentage of patients in each of the two treatment groups (i.e., SGX301 and placebo) achieving a partial or complete response of the treated lesions, defined as a ≥ 50% reduction in the total Composite Assessment of Index Lesion Disease Severity ("CAILS") score for three index lesions at the Cycle 1 evaluation visit (Week 8) compared to the total CAILS score at baseline. Other secondary measures assess treatment response including duration, degree of improvement, time to relapse and safety.

During September 2017, the National Cancer Institute ("NCI"), part of the National Institutes of Health ("NIH") awarded us a Small Business Innovation Research ("SBIR") grant of approximately $1.5 million over two years to support the conduct of our pivotal, Phase 3, randomized, double-blind, placebo-controlled study evaluating SGX301 (synthetic hypericin) as a treatment for CTCL.

During October 2018, an Independent Data Monitoring Committee ("DMC") completed an unblinded interim analysis with data from approximately 100 subjects, including an assessment of the Phase 3 FLASH study's primary efficacy endpoint. The DMC provided a positive recommendation to randomize approximately 40 additional subjects into the trial to maintain the rigorous assumption of 90% statistical power for the primary efficacy endpoint. No safety concerns were reported by the DMC based on the interim analysis.

We estimate the potential worldwide market for SGX301 is in excess of $250 million for all applications, including the treatment of CTCL. This potential market information is a forward-looking statement, and investors are urged not to place undue reliance on this statement. While we have determined this potential market size based on assumptions that we believe are reasonable, there are a number of factors that could cause our expectations to change or not be realized.

Cutaneous T-Cell Lymphoma

CTCL is a class of non-Hodgkin's lymphoma ("NHL"), a type of cancer of the white blood cells that are an integral part of the immune system. Unlike most NHLs, which generally involve B-cell lymphocytes (involved in producing antibodies), CTCL is caused by an expansion of malignant T-cell lymphocytes (involved in cell-mediated immunity) normally programmed to migrate to the skin. These skin-trafficking malignant T-cells migrate to the skin, causing various lesions to appear that may change shape as the disease progresses, typically beginning as a rash and eventually forming plaques and tumors. Mycosis fungoides ("MF") is the most common form of CTCL. It generally presents with skin involvement only, manifested as scaly, erythematous patches. Advanced disease with diffuse lymph node and visceral organ involvement is usually associated with a poorer response rate to standard therapies. A relatively uncommon sub-group of CTCL patients present with extensive skin involvement and circulating malignant cerebriform T-cells, referred to as Sézary syndrome. These patients have substantially graver prognoses (expected five-year survival rate of 24%), than those with MF (expected five-year survival rate of 88%).

CTCL mortality is related to stage of disease, with median survival generally ranging from about 12 years in the early stages to only 2.5 years when the disease has advanced. There is currently no FDA-approved drug for front-line treatment of early stage CTCL. Treatment of early-stage disease generally involves skin-directed therapies. One of the most common unapproved therapies used for early-stage disease is oral 5 or 8-methoxypsoralen ("Psoralen") given with ultraviolet A ("UVA") light, referred to as PUVA, which is approved for dermatological conditions such as disabling psoriasis not adequately responsive to other forms of therapy, idiopathic vitiligo and skin manifestations of CTCL in

persons who have not been responsive to other forms of treatment. Psoralen is a mutagenic chemical that interferes with DNA causing mutations and other malignancies. Moreover, UVA is a carcinogenic light source that when combined with the Psoralen, results in serious adverse effects including secondary skin cancers; therefore, the FDA requires a Black Box warning for PUVA.

CTCL constitutes a rare group of NHLs, occurring in about 4% of the approximate 500,000 individuals living with NHL. We estimate, based upon review of historic published studies and reports and an interpolation of data on the incidence of CTCL, that it affects over 20,000 individuals in the U.S., with approximately 2,800 new cases seen annually.

Dusquetide

Dusquetide (research name: SGX94) is an innate defense regulator ("IDR") that regulates the innate immune system to simultaneously reduce inflammation, eliminate infection and enhance tissue healing.

Dusquetide is based on a new class of short, synthetic peptides known as IDRs. It has a novel mechanism of action in that it modulates the body's reaction to both injury and infection and is both simultaneously anti-inflammatory and anti-infective. IDRs have no direct antibiotic activity but modulate host responses, increasing survival after infections with a broad range of bacterial Gram-negative and Gram-positive pathogens including both antibiotic sensitive and resistant strains, as well as accelerating resolution of tissue damage following exposure to a variety of agents including bacterial pathogens, trauma and chemo- or radiation-therapy. IDRs represent a novel approach to the control of infection and tissue damage via highly selective binding to an intracellular adaptor protein, sequestosome-1, also known as p62, which has a pivotal function in signal transduction during activation and control of the innate defense system. Preclinical data indicate that IDRs may be active in models of a wide range of therapeutic indications including life-threatening bacterial infections as well as the severe side-effects of chemo- and radiation-therapy. Additionally, due to selective binding to p62, dusquetide may have potential anti-tumor action.

Dusquetide has demonstrated efficacy in numerous animal disease models including mucositis, colitis, skin infection and other bacterial infections and has been evaluated in a double-blind, placebo-controlled Phase 1 clinical trial in 84 healthy volunteers with both single ascending dose and multiple ascending dose components. Dusquetide was shown to have a good safety profile and be well-tolerated in all dose groups when administered by IV over 7 days and was consistent with safety results seen in pre-clinical studies. We believe that market opportunities for dusquetide include, but are not limited to, oral and gastrointestinal mucositis, acute Gram-positive bacterial infections (e.g., methicillin resistant *Staphylococcus aureus* (MRSA)), acute Gram-negative infections (e.g., acinetobacter, melioidosis), and acute radiation syndrome.

SGX942 – for Treating Oral Mucositis in Head and Neck Cancer

SGX942 is our product candidate containing our IDR technology, dusquetide, targeting the treatment of oral mucositis in head and neck cancer patients. Oral mucositis in this patient population is an area of unmet medical need where there are currently no approved drug therapies. Accordingly, we received Fast Track designation for the treatment of oral mucositis as a result of radiation and/or chemotherapy treatment in head and neck cancer patients from the FDA. In addition, dusquetide has been granted PIM designation in the UK by the MHRA for the treatment of severe oral mucositis in head and neck cancer patients receiving chemoradiation therapy. The U.S. Patent and Trademark Office and the European Patent Office granted us the patent titled "Novel Peptides and Analogs for Use in the Treatment of Oral Mucositis" on August 16, 2016 and January 23, 2019, respectively. The newly issued patent claims therapeutic use of dusquetide and related IDR analogs, and adds to composition of matter claims for dusquetide and related

analogs that have been granted in the U.S. and worldwide.

We initiated a Phase 2 clinical study of SGX942 for the treatment of oral mucositis in head and neck cancer patients in December of 2013. We completed enrollment in this trial in the second half of 2015, and in December 2015 released positive preliminary results. In this Phase 2 proof-of-concept clinical study that enrolled 111 patients, SGX942, at a dose of 1.5 mg/kg, successfully reduced the median duration of severe oral mucositis by 50%, from 18 days to 9 days ($p=0.099$) in all patients and by 67%, from 30 days to 10 days ($p=0.040$) in patients receiving the most aggressive chemoradiation therapy for treatment of their head and neck cancer. The p-values met the prospectively defined statistical threshold of $p<0.1$ in the study protocol. A less severe occurrence of oral mucositis, ulcerative oral mucositis (defined as oral mucositis with a WHO score ≥2 corresponding to the occurrence of overt ulceration in the mouth), was also monitored during the study. In the patients receiving the most aggressive chemoradiation therapy, the median duration of oral mucositis was found to decrease from 65 days in the placebo treated patients to 51 days in the patients treated with SGX942 1.5 mg/kg ($p=0.099$).

In addition to identifying the best dose of 1.5 mg/kg, this study achieved all objectives, including increased incidence of “complete response” of tumor at the one month follow-up visit (47% in placebo vs. 63% in SGX942 at 1.5 mg/kg). Decreases in mortality and decreases in infection rate were also observed with SGX942 treatment, consistent with the preclinical results observed in animal models.

SGX942 was found to be generally safe and well tolerated, consistent with the safety profile observed in the prior Phase 1 study conducted in 84 healthy volunteers. The long-term (12 month) follow-up data was consistent with the preliminary positive safety and efficacy findings. While the placebo population experienced the expected 12-month survival rate of approximately 80%, as defined in the Surveillance, Epidemiology, and End Results statistics 1975-2012 from the National Cancer Institute, the SGX942 1.5 mg/kg treatment group reported a 12-month survival rate of 93% (7% mortality in the SGX942 1.5 mg/kg group compared to 19% in the placebo group). Similarly, tumor resolution (complete response) at 12 months was better in the SGX942 1.5 mg/kg treatment group relative to the placebo population (80% in the 1.5 mg/kg group compared to 74% in the placebo group). Moreover, in the patients receiving chemotherapy every third week, the SGX942 1.5 mg/kg treatment group had a tumor resolution rate (complete response) of 82% throughout the 12 months following chemoradiation therapy, while the placebo group experienced a 64% complete response rate. The long-term follow-up results from the Phase 2 study are reviewed in "Dusquetide: Reduction in Oral Mucositis associated with Enduring Ancillary Benefits in Tumor Resolution and Decreased Mortality in Head and Neck Cancer Patients" published online in Biotechnology Reports and available at the following link: https://doi.org/10.1016/j.btre.2017.05.002. In addition to safety, evaluations of other secondary efficacy endpoints, such as the utilization of opioid pain medication, indicated that the SGX942 1.5mg/kg treatment group had a 40% decrease in the use of opioids at the later stage of the treatment phase of the trial, when oral mucositis is usually most severe and expected to increase pain medication use. This was in contrast to the placebo group, which demonstrated a 10% increase in use of opioids over this same period. Data from this Phase 2 trial was published online in the Journal of Biotechnology. The publication also delineates the supportive nonclinical data in this indication, demonstrating consistency in the qualitative and quantitative biological response, including dose response, across the nonclinical and clinical data sets. The results are available at the following link: http://authors.elservier.com/sd/article/S01681656116315668.

On September 9, 2016, we and SciClone Pharmaceuticals, Inc. ("SciClone") entered into an exclusive license agreement, pursuant to which we granted rights to SciClone to develop, promote, market, distribute and sell SGX942 in defined territories. Under the terms of the license agreement, SciClone will be responsible for all aspects of development, product registration and commercialization in the territories, having access to data generated by us. In exchange for exclusive rights, SciClone will pay us royalties on net sales, and we will supply commercial drug product to SciClone on a cost-plus basis, while maintaining worldwide manufacturing rights.

We have received clearance from the FDA to advance the pivotal Phase 3 protocol for SGX942 in the treatment of oral mucositis in patients with head and neck cancer receiving chemoradiation therapy. Additionally, we have received positive Scientific Advice from the EMA for the development of SGX942 as a treatment for oral mucositis in patients with head and neck cancer. The Scientific Advice from the EMA indicates that a single, double-blind, placebo-controlled, multinational, Phase 3 pivotal study, if successful, in conjunction with the Phase 2 dose-ranging study, is generally considered sufficient to support a marketing authorization application ("MAA") to the EMA for potential licensure in Europe. The advice also provided several suggestions to strengthen the study design and data collection that were integrated into the final protocol. Scientific Advice is offered by the EMA to stakeholders for clarification of questions arising during development of medicinal products. The scope of Scientific Advice is limited to scientific issues and focuses on development strategies rather than pre-evaluation of data to support an MAA. Scientific Advice is legally non-binding and is based on the current scientific knowledge which may be subject to future changes.

We are working with leading oncology centers, a number of which participated in the Phase 2 study, to advance this Phase 3 clinical trial referred to as the "DOM–INNATE" study (Dusquetide treatment in Oral Mucositis – by modulating INNATE immunity). Based on the positive and previously published Phase 2 results (Study IDR-OM-01), the pivotal Phase 3 clinical trial (Study IDR-OM-02) is a highly powered, double-blind, randomized, placebo-controlled, multinational trial that will seek to enroll approximately 190 subjects with squamous cell carcinoma of the oral cavity and oropharynx who are scheduled to receive a minimum total cumulative radiation dose of 55 Gy fractionated as 2.0-2.2 Gy per day with concomitant cisplatin chemotherapy given as a dose of 80-100 mg/m^2 every third week. Subjects are randomized to receive either 1.5 mg/kg SGX942 or placebo given twice a week during and for two weeks following completion of chemoradiation therapy ("CRT"). The primary endpoint for the study is the median duration of severe oral mucositis, which is assessed by oral examination at each treatment visit and then through six weeks following completion of CRT. Oral mucositis is evaluated using the WHO Grading system. Severe oral mucositis is defined as a WHO Grade of ≥3. Subjects are followed for an additional 12 months after the completion of treatment.

During July 2017, we initiated our pivotal Phase 3 study with a controlled roll-out of U.S. study sites, followed by the addition of European centers in 2018. We anticipate that approximately fifty U.S. and European oncology centers will be participating in this pivotal Phase 3 study. We anticipate an interim analysis report from an independent data monitoring committee to be available in the third quarter of 2019.

During September 2017, the National Institute of Dental and Craniofacial Research ("NIDCR"), part of the NIH, awarded us a SBIR grant of approximately $1.5 million over two years to support the conduct of our Phase 3, multinational, randomized, double-blind, placebo-controlled study evaluating SGX942 (dusquetide) as a treatment for severe oral mucositis in patients with head and neck cancer receiving CRT.

We estimate the potential worldwide market for SGX942 is in excess of $500 million for all applications, including the treatment of oral mucositis. This potential market information is a forward-looking statement, and investors are urged not to place undue reliance on this statement. While we have determined this potential market size based on assumptions that we believe are reasonable, there are a number of factors that could cause our expectations to change or not be realized.

Oral Mucositis

Mucositis is the clinical term for damage done to the mucosa by anticancer therapies. It can occur in any mucosal region, but is most commonly associated with the mouth, followed by the small intestine. We estimate, based upon our review of historic studies and reports, and an interpolation of data on the incidence of mucositis, that mucositis affects approximately 500,000 people in the U.S. per year and occurs in 40% of patients receiving chemotherapy. Mucositis can be severely debilitating and can lead to infection, sepsis, the need for parenteral nutrition and narcotic analgesia. The GI damage causes severe diarrhea. These symptoms can limit the doses and duration of cancer treatment, leading to sub-optimal treatment outcomes.

The mechanisms of mucositis have been extensively studied and have been linked to the interaction of chemotherapy and/or radiation therapy with the innate defense system. Bacterial infection of the ulcerative lesions is regarded as a secondary consequence of dysregulated local inflammation triggered by therapy-induced cell death, rather than as the primary cause of the lesions.

We estimate, based upon our review of historic studies and reports, and an interpolation of data on the incidence of oral mucositis, that oral mucositis is a subpopulation of approximately 90,000 patients in the U.S., with a comparable number in Europe. Oral mucositis almost always occurs in patients with head and neck cancer treated with radiation therapy (greater than 80% incidence of severe mucositis) and is common in patients undergoing high dose

chemotherapy and hematopoietic cell transplantation, where the incidence and severity of oral mucositis depends greatly on the nature of the conditioning regimen used for myeloablation.

Oral BDP

Oral BDP (beclomethasone 17,21-dipropionate) represents a first-of-its-kind oral, locally acting therapy tailored to treat GI inflammation. BDP has been marketed in the U.S. and worldwide since the early 1970s as the active pharmaceutical ingredient in a nasal spray and in a metered-dose inhaler for the treatment of patients with allergic rhinitis and asthma. Oral BDP is specifically formulated for oral administration as a single product consisting of two tablets. One tablet is intended to release BDP in the upper sections of the GI tract and the other tablet is intended to release BDP in the lower sections of the GI tract.

Based on its pharmacological characteristics, oral BDP may have utility in treating other conditions of the gastrointestinal tract having an inflammatory component. We are planning to pursue development programs for the treatment of pediatric Crohn’s disease, acute radiation enteritis and GI ARS pending further grant funding. We are also exploring the possibility of testing oral BDP for local inflammation associated with ulcerative colitis, among other indications.

We estimate the potential worldwide market for oral BDP is in excess of $500 million for all applications, including the treatment of pediatric Crohn's disease. This potential market information is a forward-looking statement, and investors are urged not to place undue reliance on this statement. While we have determined this potential market size based on assumptions that we believe are reasonable, there are a number of factors that could cause our expectations to change or not be realized.

SGX203 – for Treating Pediatric Crohn's Disease

SGX203 is a two tablet delivery system of BDP specifically designed for oral use that allows for administration of immediate and delayed release BDP throughout the small bowel and the colon. The FDA has given SGX203 Orphan Drug designation as well as Fast Track designation for the treatment of pediatric Crohn's disease. We will pursue a pivotal Phase 3 clinical trial of SGX203 for the treatment of pediatric Crohn's disease contingent upon additional funding, such as through partnership funding support.

Pediatric Crohn's Disease

Crohn's disease causes inflammation of the GI tract. Crohn's disease can affect any area of the GI tract, from the mouth to the anus, but it most commonly affects the lower part of the small intestine, called the ileum. The swelling caused by the disease extends deep into the lining of the affected organ. The swelling can induce pain and can make the intestines empty frequently, resulting in diarrhea. Because the symptoms of Crohn's disease are similar to other intestinal disorders, such as irritable bowel syndrome and ulcerative colitis, it can be difficult to diagnose. People of Ashkenazi Jewish heritage have an increased risk of developing Crohn's disease.

Crohn's disease can appear at any age, but it is most often diagnosed in adults in their 20s and 30s. However, approximately 30% of people with Crohn's disease develop symptoms before 20 years of age. We estimate, based upon our review of historic published studies and reports, and an interpolation of data on the incidence of pediatric Crohn's disease, that pediatric Crohn's disease is a subpopulation of approximately 80,000 patients in the U.S. with a comparable number in Europe. Crohn's disease tends to be both severe and extensive in the pediatric population and a relatively high proportion (approximately 40%) of pediatric Crohn's patients have involvement of their upper gastrointestinal tract.

Crohn's disease presents special challenges for children and teens. In addition to bothersome and often painful symptoms, the disease can stunt growth, delay puberty, and weaken bones. Crohn's disease symptoms may sometimes prevent a child from participating in enjoyable activities. The emotional and psychological issues of living with a chronic disease can be especially difficult for young people.

SGX201 – for Preventing Acute Radiation Enteritis

SGX201 is a delayed-release formulation of BDP specifically designed for oral use. In 2012, we completed a Phase 1/2 clinical trial testing SGX201 in prevention of acute radiation enteritis. Patients with rectal cancer scheduled to undergo concurrent radiation and chemotherapy prior to surgery were randomized to one of four dose groups. The objectives of the study were to evaluate the safety and maximal tolerated dose of escalating doses of SGX201, as well as the preliminary efficacy of SGX201 for prevention of signs and symptoms of acute radiation enteritis. The study demonstrated that oral administration of SGX201 was safe and well tolerated across all four dose groups. There was also evidence of a potential dose response with respect to diarrhea, nausea and vomiting and the assessment of enteritis according to National Cancer Institute Common Terminology Criteria for Adverse Events for selected gastrointestinal events. In addition, the incidence of diarrhea was lower than that seen in published historical control data in this patient population. This program was supported in part by a $500,000 two-year SBIR grant awarded by the NIH. We continue to work with our Radiation Enteritis medical advisors to identify additional funding opportunities to support the clinical development program.

We have received Fast Track designation from the FDA for SGX201 for acute radiation enteritis.

Acute Radiation Enteritis

External radiation therapy is used to treat most types of cancer, including cancer of the bladder, uterine, cervix, rectum, prostate, and vagina. During delivery of treatment, some level of radiation will also be delivered to healthy tissue, including the bowel, leading to acute and chronic toxicities. The large and small bowels are very sensitive to radiation and the larger the dose of radiation the greater the damage to normal bowel tissue. Radiation enteritis is a condition in which the lining of the bowel becomes swollen and inflamed during or after radiation therapy to the abdomen, pelvis, or rectum. Most tumors in the abdomen and pelvis need large doses, and almost all patients receiving radiation to the abdomen, pelvis, or rectum will show signs of acute enteritis.

Patients with acute enteritis may have nausea, vomiting, abdominal pain and bleeding, among other symptoms. Some patients may develop dehydration and require hospitalization. With diarrhea, the gastrointestinal tract does not function normally, and nutrients such as fat, lactose, bile salts, and vitamin B12 are not well absorbed.

Symptoms will usually resolve within two to six weeks after therapy has ceased. Radiation enteritis is often not a self-limited illness, as over 80% of patients who receive abdominal radiation therapy complain of a persistent change in bowel habits. Moreover, acute radiation injury increases the risk of development of chronic radiation enteropathy, and overall 5% to 15% of the patients who receive abdominal or pelvic irradiation will develop chronic radiation enteritis.

We estimate, based upon our review of historic published studies and reports, and an interpolation of data on the treatment courses and incidence of cancers occurring in the abdominal and pelvic regions, there to be over 100,000 patients annually in the U.S., with a comparable number in Europe, who receive abdominal or pelvic external beam radiation treatment for cancer, and these patients are at risk of developing acute and chronic radiation enteritis.

Vaccines/BioDefense Overview

ThermoVax® – Thermostability Technology

ThermoVax® is a novel method of rendering aluminum salt, (known colloquially as Alum), adjuvanted vaccines stable at elevated temperatures. Alum is the most widely employed adjuvant technology in the vaccine industry. The value of ThermoVax® lies in its potential ability to eliminate the need for cold chain production, transportation, and storage for Alum adjuvanted vaccines. This would relieve the high costs of producing and maintaining vaccines under

refrigerated conditions. Based on historical reports from the World Health Organization and other scientific reports, we believe that a meaningful proportion of vaccine doses globally are wasted due to excursions from required cold chain temperature ranges. This is due to the fact that most Alum adjuvanted vaccines need to be maintained at between 2 and 8 degrees Celsius (“C”) and even brief excursions from this temperature range (especially below freezing) usually necessitates the destruction of the product or the initiation of costly stability programs specific for the vaccine lots in question. ThermoVax® has the potential to facilitate easier storage and distribution of strategic national stockpile vaccines for ricin exposure in emergency settings.

ThermoVax® development was supported pursuant to our $9.4 million NIAID grant enabling development of thermo-stable ricin (RiVax®) and anthrax (VeloThrax®) vaccines. Proof-of-concept preclinical studies with ThermoVax® indicate that it is able to produce stable vaccine formulations using adjuvants, protein immunogens, and other components that ordinarily would not withstand long temperature variations exceeding customary refrigerated storage conditions. These studies were conducted with our aluminum-adjuvanted ricin toxin vaccine, RiVax® and our aluminum-adjuvanted anthrax vaccine, VeloThrax®. Each vaccine was manufactured under precise lyophilization conditions using excipients that aid in maintaining native protein structure of the key antigen. When RiVax® was kept at 40 degrees C (104 degrees Fahrenheit) for up to one year, all of the animals vaccinated with the lyophilized RiVax® vaccine developed potent and high titer neutralizing antibodies. In contrast, animals that were vaccinated with the liquid RiVax® vaccine kept at 40 degrees C did not develop neutralizing antibodies and were not protected against ricin exposure. The ricin A chain is extremely sensitive to temperature and rapidly loses the ability to induce neutralizing antibodies when exposed to temperatures higher than 8 degrees C. When VeloThrax® was kept for up to 16 weeks at 70 degrees C, it was able to develop a potent antibody response, unlike the liquid formulation kept at the same temperature. Moreover, we also have demonstrated the compatibility of our thermostabilization technology with other secondary adjuvants such as TLR-4 agonists.

We also entered into a collaboration agreement with Axel Lehrer, PhD of the Department of Tropical Medicine, Medical Microbiology and Pharmacology, John A. Burns School of Medicine, University of Hawai i at Manoa ("UH Manoa") and Hawaii Biotech, Inc. ("HBI") to develop a heat stable subunit Ebola vaccine. Dr. Lehrer, a co-inventor of the Ebola vaccine with HBI, has shown proof of concept efficacy with subunit Ebola vaccines in non-human primates. The most advanced Ebola vaccines involve the use of vesicular stomatitis virus and adenovirus vectors – live, viral vectors which complicate the manufacturing, stability and storage requirements. Dr. Lehrer's vaccine candidate is based on highly purified recombinant protein antigens, circumventing many of these manufacturing difficulties. Dr. Lehrer and HBI have developed a robust manufacturing process for the required proteins. Application of ThermoVax® may allow for a product that can avoid the need for cold chain distribution and storage, yielding a vaccine ideal for use in both the developed and developing world. This agreement has expired in accordance with its terms.

On February 7, 2019, European Journal of Pharmaceutics and Biopharmaceutics published a scientific article demonstrating the successful thermostabilization of an Ebola subunit vaccine candidate.

During September 2017, we announced we will be participating in a NIAID Research Project (R01) grant awarded to UH Manoa for the development of a trivalent thermostabilized Ebola vaccine, with our awarded funding of approximately $700,000 over five years. Previous collaborations demonstrated the feasibility of developing a heat stable subunit Ebola vaccine. Under the terms of the subaward, we will continue to support vaccine formulation development with our proprietary vaccine thermostabilization technology, ThermoVax®. Ultimately, the objective is to produce a thermostable trivalent filovirus vaccine for protection against Ebola and related diseases, allowing worldwide distribution without the need for cold storage.

On December 21, 2010, we executed a worldwide exclusive license agreement with the University of Colorado ("UC") for certain patents relating to ThermoVax® in all fields of use. In April 2018, the UC delivered a notice of termination of our license agreement based upon our failure to achieve one of the development milestones: initiation of the Phase 1 clinical trial of the heat stabilization technology by March 31, 2018. After negotiating with the UC, we and the UC agreed to extend the termination date to October 31, 2018 in order to allow us time to agree upon a potential agreement that would allow us to keep the rights to, and to continue to develop, the heat stabilization technology or a product candidate containing the heat stabilization technology in our field of use.

On October 31, 2018, in a series of related transactions, (a) we and the UC agreed to terminate the original license agreement, (b) the UC and VitriVax, Inc. ("VitriVax") executed a worldwide exclusive license agreement for the heat stabilization technology for all fields of use, and (c) we and VitriVax executed a worldwide exclusive sublicense agreement for the heat stabilization technology for use in the fields of ricin and Ebola vaccines. We paid a $100,000 sublicense fee on the effective date of the sublicense agreement. To maintain the sublicense we are obliged to pay a minimum annual royalty of $20,000 until first commercial sale of a sublicensed product, upon which point, we shall pay an earned royalty of 2% of net sales subject to a minimum royalty of $50,000 each year. We are also required to pay royalty on any sub-sublicense income based on a declining percentage of all sub-sublicense income calculated within the contractual period until reaching a minimum of 15% after two years. In addition, we are required to pay

VitriVax milestone fees of: (a) $50,000 upon initiation of a Phase II clinical trial of the sublicensed product, (b) $200,000 upon regulatory approval of a sublicensed product, and (c) $1 million upon achieving $10 million in aggregate net sales of a sublicensed product in the U.S. or equivalent. To date none of these milestones have been met.

RiVax® – Ricin Toxin Vaccine

RiVax® is our proprietary vaccine candidate being developed to protect against exposure to ricin toxin and if approved, would be the first ricin vaccine. The immunogen in RiVax® induces a protective immune response in animal models of ricin exposure and functionally active antibodies in humans. The immunogen consists of a genetically inactivated ricin A chain subunit that is enzymatically inactive and lacks residual toxicity of the holotoxin. RiVax® has demonstrated statistically significant ($p < 0.0001$) preclinical survival results, providing 100% protection against acute lethality in an aerosol exposure non-human primate model (Roy et al, 2015, Thermostable ricin vaccine protects rhesus macaques against aerosolized ricin: Epitope-specific neutralizing antibodies correlate with protection, PNAS USA 112:3782-3787), and has also been shown to be well tolerated and immunogenic in two Phase 1 clinical trials in healthy volunteers. Results of the first Phase 1 human trial of RiVax® established that the immunogen was safe and induced antibodies that we believe may protect humans from ricin exposure. The antibodies generated from vaccination, concentrated and purified, were capable of conferring immunity passively to recipient animals, indicating that the vaccine was capable of inducing functionally active antibodies in humans. The outcome of this study was published in the Proceedings of the National Academy of Sciences (Vitetta et al., 2006, A Pilot Clinical Trial of a Recombinant Ricin Vaccine in Normal Humans, PNAS, 103:2268-2273). The second trial which was completed in September 2012 and was sponsored by University of Texas Southwestern Medical Center ("UTSW"), evaluated a more potent formulation of RiVax® that contained an aluminum adjuvant (Alum). The results of the Phase 1b study indicated that Alum-adjuvanted RiVax® was safe and well tolerated, and induced greater ricin neutralizing antibody levels in humans than adjuvant-free RiVax®. The outcomes of this second study were published in the Clinical and Vaccine Immunology (Vitetta et al., 2012, Recombinant Ricin Vaccine Phase 1b Clinical Trial, Clin. Vaccine Immunol. 10:1697-1699). We have adapted the original manufacturing process for the immunogen contained in RiVax® for thermostability and large scale manufacturing and recent studies have confirmed that the thermostabilized RiVax® formulation enhances the stability of the RiVax® antigen, enabling storage for at least 1 year at temperatures up to 40°C (104 °F). The program will pursue approval via the FDA "Animal Rule" since it is not possible to test the efficacy of the vaccine in a clinical study which would expose humans to ricin. Uniform, easily measured and species-neutral immune correlates of protection that can be measured in humans and animals, and are indicative of animal survival to subsequent ricin challenge, are central to the application of the "Animal Rule". Recent work has identified such potential correlates of immune protection in animals and work to qualify and validate these approaches is continuing, with the goal of utilizing these assays in a planned Phase 1/2 clinical trial with the thermostable RiVax® formulation. During September 2018, we published an extended stability study of RiVax®, showing up to 100% protection in mice after 12 months storage at 40°C (104 °F) as well as identification of a potential in vitro stability indicating assay, critical to adequately confirming the long-term shelf life of the vaccine. We have entered into a collaboration with IDT Biologika GmbH to scale-up the formulation/filling process and continue development and validation of analytical methods established at IDT to advance the program. We also have initiated a development agreement with Emergent BioSolutions, Inc. to implement a commercially viable, scalable production technology for the RiVax® drug substance protein antigen.

The development of RiVax® has been sponsored through a series of overlapping challenge grants, UC1, and cooperative grants, U01, from the NIH, granted to us and to UTSW where the vaccine originated. The second clinical trial was supported by a grant from the FDA's Office of Orphan Products to UTSW. To date, we and UTSW have collectively received approximately $25 million in grant funding from the NIH for the development of RiVax®. In September 2014, we entered into a contract with the NIH for the development of RiVax® that would provide up to an

additional $24.7 million of funding in the aggregate if options to extend the contract are exercised by the NIH. The development agreements with Emergent BioSolutions and IDT are specifically funded under this NIH contract.

During June 2017 NIAID exercised an option for the evaluation of RiVax® to fund additional animal efficacy studies. The exercised option will provide us with approximately $2.0 million in additional funding. Additionally, during August 2017 NIAID exercised an option to fund good manufacturing practices compliant RiVax® bulk drug substance and finished drug product manufacturing, which is required for the conduct of future preclinical and clinical safety and efficacy studies. The exercised option will provide us with approximately $2.5 million in additional non-dilutive funding, bringing the total amount awarded to date under this contract to $21.2 million, of which $13.5 million is still available. If all contract options are exercised, the total award of up to $24.7 million will support the preclinical, manufacturing and clinical development activities necessary to advance heat stable RiVax® with the FDA. In addition to the ongoing funding of up to $24.7 million for the development of RiVax®, biomarkers for RiVax® testing have been successfully identified, facilitating potential approval under the FDA Animal Rule.

RiVax® has been granted Orphan Drug designation by the FDA for the prevention of ricin intoxication. In addition, RiVax® has also been granted Orphan Drug designation in the EU from the EMA Committee for Orphan Medical Products.

Assuming development efforts are successful for RiVax®, we believe potential government procurement contract(s) could reach as much as $200 million. This potential procurement contract information is a forward-looking statement, and investors are urged not to place undue reliance on this statement. While we have determined this potential procurement contract value based on assumptions that we believe are reasonable, there are a number of factors that could cause our expectations to change or not be realized.

As a new chemical entity, an FDA approved RiVax® vaccine has the potential to qualify for a biodefense Priority Review Voucher ("PRV"). Approved under the 21st Century Cures Act in late 2016, the biodefense PRV is awarded upon approval as a medical countermeasure when the active ingredient(s) have not been otherwise approved for use in any context. PRVs are transferable and can be sold, with sales in recent years of up to $350 million. When redeemed, PRVs entitle the user to an accelerated review period of nine months, saving a median of seven months review time as calculated in 2009. However, FDA must be advised 90 days in advance of the use of the PRV and the use of a PRV is associated with an additional user fee ($2.7 million in 2017).

Ricin Toxin

Ricin toxin can be cheaply and easily produced, is stable over long periods of time, is toxic by several routes of exposure and thus has the potential to be used as a biological weapon against military and/or civilian targets. As a bioterrorism agent, ricin could be disseminated as an aerosol, by injection, or as a food supply contaminant. The potential use of ricin toxin as a biological weapon of mass destruction has been highlighted in a Federal Bureau of Investigation Bioterror report released in November 2007 titled Terrorism 2002-2005, which states that "Ricin and the bacterial agent anthrax are emerging as the most prevalent agents involved in WMD investigations" (http://www.fbi.gov/stats-services/publications/terrorism-2002-2005/terror02_05.pdf). In recent years, Al Qaeda in the Arabian Peninsula has threatened the use of ricin toxin to poison food and water supplies and in connection with explosive devices. Domestically, the threat from ricin remains a concern for security agencies. In April 2013, letters addressed to the President of the United States, a U.S. Senator and a judge tested positive for ricin. As recently as October 2018, an envelope addressed to President Trump was suspected to contain this potent and potentially lethal toxin, which was subsequently confirmed to contain pieces of castor beans used to make ricin.

The Centers for Disease Control and Prevention has classified ricin toxin as a Category B biological agent. Ricin works by first binding to glycoproteins found on the exterior of a cell, and then entering the cell and inhibiting protein synthesis leading to cell death. Once exposed to ricin toxin, there is no effective therapy available to reverse the course of the toxin. The recent ricin threat to government officials has heightened the awareness of this toxic threat. Currently, there is no FDA approved vaccine to protect against the possibility of ricin toxin being used in a terrorist attack, or its use as a weapon on the battlefield nor is there a known antidote for ricin toxin exposure.

OrbeShield® – for Treating GI Acute Radiation Syndrome

OrbeShield® is an oral immediate and delayed release formulation of the topically active corticosteroid BDP and is being developed for the treatment of GI ARS. Corticosteroids are a widely used class of anti-inflammatory drugs. BDP is a corticosteroid with predominantly topical activity that is approved for use in asthma, psoriasis and allergic rhinitis.

OrbeShield® has demonstrated positive preclinical results in a canine GI ARS model which indicate that dogs treated with OrbeShield® demonstrated statistically significant (p=0.04) improvement in survival with dosing at either two hours or 24 hours after exposure to lethal doses of total body irradiation ("TBI") when compared to control dogs. OrbeShield® appears to significantly mitigate the damage to the GI epithelium caused by exposure to high doses of radiation using a well-established canine model of GI ARS.

The GI tract is highly sensitive to ionizing radiation and the destruction of epithelial tissue is one of the first effects of radiation exposure. The rapid loss of epithelial cells leads to inflammation and infection that are often the primary cause of death in acute radiation injury. This concept of GI damage also applies to the clinical setting of oncology, where high doses of radiation cannot be administered effectively to the abdomen because radiation is very toxic to the intestines. We are seeking to treat the same type of toxicity in our acute radiation enteritis clinical program with SGX201. As a result, we believe that OrbeShield® has the potential to be a "dual use" compound, a desirable characteristic which is a specific priority for ARS and other medical countermeasure indications.

In September 2013, we received two government contracts from the Biomedical Advanced Research and Development Authority ("BARDA") and NIAID for the advanced preclinical and manufacturing development of OrbeShield® leading to FDA approval to treat GI ARS. The BARDA contract contained a two year base period with two contract options, exercisable by BARDA, for a total of five years and up to $26.3 million. The NIAID contract consisted of a one year base period and two contract options, exercisable by NIAID, for a total of three years and up to $6.4 million. We received a combined approximate $18 million in contract funding from both BARDA and NIAID which includes combined supplemental funding of $634,000, extending the programs through the first quarter of 2017. The NIAID contract was completed during the first quarter of 2017 along with the