

SOLIGENIX, INC.  
Form 10-K  
March 24, 2016

**UNITED STATES SECURITIES AND EXCHANGE COMMISSION**

**Washington, D.C. 20549**

**FORM 10-K**

(Mark One)

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

For the Fiscal Year Ended **December 31, 2015**

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**

(State or other jurisdiction of

incorporation or organization)

**41-1505029**

(I.R.S. Employer

Identification Number)

**29 EMMONS DRIVE, SUITE C-10**

**PRINCETON, NJ**

(Address of principal executive offices)

**08540**

(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
<b>Common Stock, par value \$.001 per share</b>	<b>OTCQB</b>

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 ☒

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

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Website, if any, 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 ☒ 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. ☒

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

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company” in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer Accelerated filer Non-accelerated filer Smaller reporting company ☐

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

The aggregate market value of the common stock held by non-affiliates of the registrant was approximately \$22,060,000 (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 Over-the-Counter Bulletin Board on March 18, 2016.

As of March 18, 2016, 31,269,522 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, 2015**

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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 first-in-class photodynamic therapy (SGX301) utilizing topical synthetic hypericin activated with safe visible light for the treatment of cutaneous T-cell lymphoma (“CTCL”), 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), and our novel innate defense regulator (“IDR”) technology, dusquetide (SGX942) for the treatment of oral mucositis in head and neck cancer.

Our Vaccines/BioDefense business segment includes active development programs for RiVax™, our ricin toxin vaccine candidate, OrbeShield®, our GI acute radiation syndrome (“GI ARS”) therapeutic candidate and SGX943, our melioidosis therapeutic candidate. 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. We plan to use the funds received under our government contracts with the Biomedical Advanced Research and Development Authority (“BARDA”) and NIAID to advance the development of OrbeShield® for the treatment of GI ARS.

An outline for our business strategy follows:

Complete enrollment and report preliminary results in our pivotal Phase 3 clinical trial of SGX301 for the treatment of CTCL;

Initiate a Phase 3 clinical trial of SGX203, for the treatment of pediatric Crohn's disease;

Continue to collect the long-term follow-up safety data from the SGX942 Phase 2 proof-of-concept study in the treatment of oral mucositis in head and neck cancer patients and publish the findings from this study;

Obtain FDA agreement on a pivotal Phase 2b/3 protocol of SGX942 in the treatment of oral mucositis in head and neck cancer patients;

Continue development of RiVax™ in combination with our ThermoVax® technology, to develop new heat stable vaccines in biodefense and infectious diseases with the potential to collaborate and/or partner with other companies in these areas;

Advance the preclinical and manufacturing development of OrbeShield® as a biodefense medical countermeasure for the treatment of GI ARS;

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

Acquire or in-license new clinical-stage compounds for development; and

Explore other business development and merger/acquisition strategies.

### Corporate Information

We were incorporated in Delaware in 1987 under the name Biological Therapeutics, Inc. In 1987, the Company 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 C-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 initiated in the second half of 2015, with data expected in the second half of 2016
SGX942	Oral Mucositis in Head and Neck Cancer	Phase 2 trial initiated in the second half of 2013, with positive preliminary results reported in the second half of 2015; seek to obtain FDA agreement on the Phase 2b/3 protocol in the second half of 2016
SGX203**	Pediatric Crohn's disease	Phase 1/2 clinical trial completed June 2013, efficacy data, pharmacokinetic (PK)/pharmacodynamic (PD) profile and safety confirmed; Phase 3 clinical trial planned for the second half of 2016, with data expected in the first half of 2018
SGX201**	Acute Radiation Enteritis	Phase 1/2 clinical trial complete; safety and preliminary efficacy demonstrated; Phase 2 trial planned for the first half of 2017

### Vaccine Thermostability Platform\*\*

Soligenix Product Candidate	Indication	Stage of Development
ThermoVax®	Thermostability of aluminum adjuvanted vaccines	Pre-clinical

BioDefense Products\*\*

Soligenix Product Candidate	Indication	Stage of Development
RiVax™	Vaccine against Ricin Toxin Poisoning	Phase 1B trial complete, safety and neutralizing antibodies for protection demonstrated; Phase 1/2 trial planned for the second half of 2016
OrbeShield®	Therapeutic against GI ARS	Pre-clinical program initiated
SGX943	Melioidosis	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 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 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 improvement with topical hypericin treatment 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 United States Food and Drug Administration (the “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 also was granted orphan drug designation from the European Medicines Agency Committee for Orphan Medical Products.

We initiated our pivotal Phase 3 clinical study of SGX301 in the treatment of CTCL during December 2015 and anticipate data in the second half of 2016.

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 than those with MF.

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.

## SGX94

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

SGX94 is based on a new class of short, synthetic peptides known as IDRs that have a novel mechanism of action in that it is 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.

SGX94 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. SGX94 was shown to be safe and well-tolerated in all dose groups when administered by IV over 7 days and was consistent with safety results seen in pre-clinical studies. SGX94 is the subject of an open Investigational New Drug (“IND”) application which has been cleared by the FDA. We believe that market opportunities for SGX94 include mucositis, acute methicillin resistant *Staphylococcus aureus* (MRSA) bacterial infections, acinetobacter, melioidosis, acute radiation syndrome and as a vaccine adjuvant, with potential opportunities for non-dilutive funding to support the development.

#### SGX942 – for Treating Oral Mucositis in Head and Neck Cancer

SGX942 is our product candidate containing our IDR technology platform, SGX94, 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.

We initiated a Phase 2 clinical study of SGX942 in the treatment of oral mucositis in head and neck cancer patients in the second half 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 (CRT) for treatment of their head and neck cancer. In addition to identifying the optimal dose of 1.5 mg/kg, this study achieved all objectives, including a trend towards 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 significant decreases in infection rate were also observed with SGX942 treatment, consistent with the preclinical results observed in animal models, and are being further evaluated. 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. Long-term follow-up evaluations are ongoing with final results expected in the fourth quarter of 2016. Data from this Phase 2 trial is expected to be submitted for future presentation and publication.

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 recently 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 in 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 are pursuing orphan drug designations for relevant indications as appropriate in both the U.S. and Europe. An orphan drug designation provides for seven years and ten years of market exclusivity upon approval in the U.S. and Europe, respectively.

#### 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 anticipate initiating a Phase 3 clinical study of SGX203 in the treatment of pediatric Crohn's disease in the second half of 2016.

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.

#### 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 recent published historical control data in this patient population. This program was supported in part by a \$500,000 two-year Small Business Innovation and Research ("SBIR") grant awarded by the National Institutes of Health ("NIH"). We are currently working with our Radiation Enteritis medical advisory board in pursuing additional funding from the NIH to support the clinical development program.

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

We estimate the potential worldwide market for oral BDP is in excess of \$500 million for all applications, including the treatment of acute radiation enteritis. 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.

#### 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 B 12 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

Our 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 companies of 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. We believe that the savings realized from the elimination of cold chain costs and related product losses would significantly increase the profitability of vaccine products. We believe that elimination of the cold chain could further facilitate the use of these vaccines in the lesser developed parts of the world. ThermoVax® has the potential to facilitate easier storage and distribution of strategic national stockpile vaccines in emergency settings.

ThermoVax<sup>®</sup> development was supported pursuant to our \$9.4 million NIAID grant enabling development of thermo-stable ricin (RiVax<sup>™</sup>) and anthrax (VeloThrax<sup>®</sup>) vaccines. Proof-of-concept preclinical studies with ThermoVax<sup>®</sup> 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<sup>™</sup> and our aluminum-adjuvanted anthrax vaccine, VeloThrax<sup>®</sup>. Each vaccine was manufactured under precise lyophilization conditions using excipients that aid in maintaining native protein structure of the key antigen. When RiVax<sup>™</sup> was kept at 40 degrees C (104 degrees Fahrenheit) for up to one year, all of the animals vaccinated with the lyophilized RiVax<sup>™</sup> vaccine developed potent and high titer neutralizing antibodies. In contrast, animals that were vaccinated with the liquid RiVax<sup>™</sup> 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<sup>®</sup> 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 have also demonstrated the compatibility of our thermostabilization technology with other secondary adjuvants such as TLR-4 agonists. Additionally, the University of Colorado conducted a study that demonstrated a heat stable vaccine formulation of a human papillomavirus (HPV) vaccine. The work was conducted by Drs. Randolph and Garcea and demonstrated the successful conversion of a commercial virus-like particle (VLP) based vaccine requiring cold chain storage to a subunit, alum-adjuvanted, vaccine which is stable at ambient temperatures. This work, funded by a University of Colorado Seed grant and the Specialized Program of Research Excellence (SPORE) in cervical cancer, is the first demonstration of the utility of ThermoVax<sup>®</sup> technology for the development of a subunit based commercial vaccine. The HPV vaccine formulation was found to be stable for at least 12 weeks at 50 degrees C. In the study, mice immunized with the ThermoVax<sup>®</sup>-stabilized HPV subunit vaccine were also found to achieve immune responses similar to the commercial HPV vaccine, Cervarix<sup>®</sup>, as measured by either total antibody levels or neutralizing antibody levels. Moreover, whereas the immune responses to Cervarix<sup>®</sup> were reduced after storage for 12 weeks at 50 degrees C, the ThermoVax<sup>®</sup> formulated vaccine retained its efficacy. The results were published online in the European Journal of Pharmaceutics and Biopharmaceutic. See <http://www.sciencedirect.com/science/article/pii/S0939641115002416>.

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 Mānoa 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<sup>®</sup> 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.

We intend to seek out potential partnerships with companies marketing FDA/ex-U.S. health authority approved Alum adjuvanted vaccines and currently developing Alum adjuvanted vaccines that are interested in eliminating the need for cold chain for their products. We believe that ThermoVax<sup>®</sup> also will enable us to expand our vaccine development expertise beyond biodefense into the infectious disease space and also has the potential to allow for the development

of multivalent vaccines (e.g., combination ricin-anthrax vaccine).

#### 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 subunit ricin A chain that is enzymatically inactive and lacks residual toxicity of the holotoxin. RiVax™ has demonstrated statistically significant ( $p < 0.0001$ ) preclinical survival results in a lethal 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 March 24, 2015), 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 completed in September 2012, 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. 10:1697-9). We have adapted the original manufacturing process for the immunogen contained in RiVax™ for large scale manufacturing and are further establishing correlates of the human immune response in non-human primates. We have initiated a development agreement with Emergent BioSolutions 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 Soligenix 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.

RiVax™ has been granted orphan drug designation by the FDA for the prevention of ricin intoxication.

Assuming development efforts are successful for RiVax™, we believe potential government procurement contract(s) could reach \$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.

## 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 Investigations 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](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. As recently as April 2013, letters addressed to the President, a U.S. Senator and a judge tested positive for ricin.

The Center for Disease Control 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 of BARDA for ARS and other medical countermeasure indications. The FDA has cleared the IND application for OrbeShield® for the mitigation of morbidity and mortality associated with GI ARS.

In September 2013, we received two government contracts from BARDA and NIAID for the advanced preclinical and manufacturing development of OrbeShield® leading to FDA approval to treat GI ARS. The BARDA contract contains 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 consists 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. Previously, development of OrbeShield® had been largely supported by a \$1 million NIH grant to Soligenix’s academic partner, the Fred Hutchinson Cancer Research Center. In July 2012, we received an SBIR grant from NIAID of approximately \$600,000 to support further preclinical development of OrbeShield® for the treatment of acute GI ARS. The FDA has given OrbeShield® orphan drug designation and Fast Track designation for the prevention of death following a potentially lethal dose of total body irradiation during or after a radiation disaster.

Assuming development efforts are successful for OrbeShield®, we believe potential government procurement contracts could reach as much as \$450 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.

## GI Acute Radiation Syndrome

ARS occurs after toxic radiation exposure and involves several organ systems, notably the bone marrow, the GI tract and, later, the lungs. In the event of a nuclear disaster or terrorist detonation of a nuclear bomb, casualties exposed to

greater than 2 grays (“Gy”) of absorbed radiation are at high risk for development of clinically significant ARS. Exposure to high doses of radiation exceeding 10-12 Gy causes acute GI injury which can result in death. The GI tract is highly sensitive due to the continuous need for crypt stem cells and production of mucosal epithelium. The extent of injury to the bone marrow and the GI tract are the principal determinants of survival after exposure to TBI. Although the hematopoietic syndrome can be rescued by bone marrow transplantation or growth factor administration, there is no established treatment or preventive measure for the GI damage that occurs after high-dose radiation. As a result, we believe there is an urgent medical need for specific medical counter measures against the lethal pathophysiological manifestations of radiation-induced GI injury.

#### SGX943 – for Treating Melioidosis

SGX943 uses the same active ingredient as SGX94 and is being developed in preclinical studies as a potential treatment for melioidosis. Because SGX943 directly targets the innate immune system (and does not attempt to kill the bacteria directly), we believe it is particularly relevant for antibiotic-resistant bacteria. The bacteria which causes melioidosis, *Burkholderia pseudomallei*, is known to be resistant to most antibiotics and to require prolonged treatment with the few antibiotics that do work. In February 2014, we were awarded a one-year NIAID SBIR award of approximately \$300,000 to further evaluate SGX943 as a potential treatment for melioidosis. Preclinical results to date have demonstrated that SGX943 treatment, in combination with standard of care antibiotics such as doxycycline, can statistically significantly enhance survival in a lethal murine pneumonic melioidosis model ( $p < 0.001$ ).

## Melioidosis

Melioidosis is a potentially fatal infection caused by the Gram-negative bacillus, *Burkholderia pseudomallei* (“Bp”). Highly resistant to many antibiotics, Bp can cause an acute disease characterized by a fulminant pneumonia and a chronic condition that can recrudesce. There is no preventive vaccine or effective immunotherapy for melioidosis. We believe that there is an unmet medical need for improved prevention and therapy.

Bp infection (melioidosis) is a major public health concern in the endemic regions of Southeast Asia and Northern Australia. In Northeast Thailand, which has the highest incidence of melioidosis, the mortality rate associated with Bp infection is over 40 percent, making it the third most common cause of death from infectious disease in that region after HIV/AIDS and tuberculosis. Bp activity is seen in Southeast Asia, South America, Africa, the Middle East, India, and Australia. The highest pockets of disease activity occur in Northern Australia and Northeast Thailand with increasing recognition of disease activity in coastal regions of India.

Beyond its public health significance, Bp and the closely-related *Burkholderia mallei* (“Bm”) are considered possible biological warfare agents by the DHHS because of the potential for widespread dissemination through aerosol. Bp like its relative Bm, the cause of Glanders, was studied by the U.S. as a potential biological warfare agent, but was never weaponized. It has been reported that the Soviet Union was also experimenting with Bp as a biological warfare agent. Both Bp and Bm have been designated high priority threats by the DHHS in its PHEMCE Strategy released in 2012 and are classified as Category B Priority Pathogens by NIAID.

## The Drug Approval Process

The FDA and comparable regulatory agencies in state, local and foreign jurisdictions impose substantial requirements on the clinical development, manufacture and marketing of new drug and biologic products. The FDA, through regulations that implement the Federal Food, Drug, and Cosmetic Act, as amended, or FDCA, and other laws and comparable regulations for other agencies, regulate research and development activities and the testing, manufacture, labeling, storage, shipping, approval, recordkeeping, advertising, promotion, sale, export, import and distribution of such products. The regulatory approval process is generally lengthy, expensive and uncertain. Failure to comply with applicable FDA and other regulatory requirements can result in sanctions being imposed on us or the manufacturers of our products, including holds on clinical research, civil or criminal fines or other penalties, product recalls, or seizures, or total or partial suspension of production or injunctions, refusals to permit products to be imported into or exported out of the United States, refusals of the FDA to grant approval of drugs or to allow us to enter into government supply contracts, withdrawals of previously approved marketing applications and criminal prosecutions.

Before human clinical testing in the U.S. of a new drug compound or biological product can commence, an Investigational New Drug, or IND, application is required to be submitted to the FDA. The IND application includes results of pre-clinical animal studies evaluating the safety and efficacy of the drug and a detailed description of the clinical investigations to be undertaken.

Clinical trials are normally done in three phases, although the phases may overlap. Phase 1 trials are smaller trials concerned primarily with metabolism and pharmacologic actions of the drug and with the safety of the product. Phase 2 trials are designed primarily to demonstrate effectiveness and safety in treating the disease or condition for which the product is indicated. These trials typically explore various doses and regimens. Phase 3 trials are expanded clinical trials intended to gather additional information on safety and effectiveness needed to clarify the product's benefit-risk relationship and generate information for proper labeling of the drug, among other things. The FDA receives reports on the progress of each phase of clinical testing and may require the modification, suspension or termination of clinical trials if an unwarranted risk is presented to patients. When data is required from long-term use of a drug following its approval and initial marketing, the FDA can require Phase 4, or post-marketing, studies to be conducted.

With certain exceptions, once successful clinical testing is completed, the sponsor can submit a New Drug Application, or NDA, for approval of a drug, or a Biologic License Application, or BLA, for biologics such as vaccines, which will be reviewed, and if successful, approved by the FDA, allowing the product to be marketed. The process of completing clinical trials for a new drug is likely to take a number of years and require the expenditure of substantial resources. Furthermore, the FDA or any foreign health authority may not grant an approval on a timely basis, if at all. The FDA may deny the approval of an NDA or BLA, in its sole discretion, if it determines that its regulatory criteria have not been satisfied or may require additional testing or information. Among the conditions for marketing approval is the requirement that the prospective manufacturer's quality control and manufacturing procedures conform to good manufacturing practice regulations. In complying with standards contained in these regulations, manufacturers must continue to expend time, money and effort in the area of production, quality control and quality assurance to ensure full technical compliance. Manufacturing facilities, both foreign and domestic, also are subject to inspections by, or under the authority of, the FDA and by other federal, state, local or foreign agencies.

Even after initial FDA or foreign health authority approval has been obtained, further studies, including Phase 4 post-marketing studies, may be required to provide additional data on safety and will be required to gain approval for the marketing of a product as a treatment for clinical indications other than those for which the product was initially tested. For certain drugs intended to treat serious, life-threatening conditions that show great promise in earlier testing, the FDA can also grant conditional approval. However, drug developers are required to study the drug further and verify clinical benefit as part of the conditional approval provision, and the FDA can revoke approval if later testing does not reproduce previous findings. The FDA may also condition approval of a product on the sponsor agreeing to certain mitigation strategies that can limit the unfettered marketing of a drug. Also, the FDA or foreign regulatory authority will require post-marketing reporting to monitor the side effects of the drug. Results of post-marketing programs may limit or expand the further marketing of the product. Further, if there are any modifications to the drug, including any change in indication, manufacturing process, labeling or manufacturing facility, an application seeking approval of such changes will likely be required to be submitted to the FDA or foreign regulatory authority.

In the U.S., the FDCA, the Public Health Service Act, the Federal Trade Commission Act, and other federal and state statutes and regulations govern, or influen