

SOLIGENIX, INC.  
Form 10-K  
March 25, 2015

**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, 2014**

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

**41-1505029**  
(I.R.S. Employer

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incorporation or organization)

Identification Number)

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

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 ☒ R

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 ☒ R

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 ☒ R 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 ☒ R 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

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incorporated by reference in Part III of this 10-K or any amendments to this Form 10-K. R

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 ☒ R

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

The aggregate market value of the common stock held by non-affiliates of the registrant was approximately \$26,533,000 (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 June 30, 2014.

As of March 17, 2015, 25,168,354 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, 2014**

**Table of Contents**

<b>Item</b>	<b>Description</b>	<b>Page</b>
	<b><u>Part I</u></b>	
1.	<u>Business</u>	3
1A.	<u>Risk Factors</u>	25
1B.	<u>Unresolved Staff Comments</u>	41
2.	<u>Properties</u>	41
3.	<u>Legal Proceedings</u>	41
	<b><u>Part II</u></b>	
5.	<u>Market for Registrant’s Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities</u>	42
6.	<u>Selected Financial Data</u>	42
7.	<u>Management’s Discussion and Analysis of Financial Condition and Results of Operations</u>	43
8.	<u>Financial Statements and Supplementary Data</u>	50
9.	<u>Changes in and Disagreements with Accountants on Accounting and Financial Disclosure</u>	50
9A.	<u>Controls and Procedures</u>	50
9B.	<u>Other Information</u>	51
	<b><u>Part III</u></b>	
10.	<u>Directors, Executive Officers and Corporate Governance</u>	52
11.	<u>Executive Compensation</u>	57
12.	<u>Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters</u>	60
13.	<u>Certain Relationships and Related Transactions and Director Independence</u>	62
14.	<u>Principal Accountant Fees and Services</u>	63
	<b><u>Part IV</u></b>	
15.	<u>Exhibits and Financial Statement Schedules</u>	64
	<u>Signatures</u>	68
	<u>Consolidated Financial Statements</u>	F-1

## 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 developing product candidates intended to address unmet medical needs in areas of inflammation, oncology, and biodefense. We maintain two active business segments: BioTherapeutics and Vaccines/BioDefense.

Our BioTherapeutics business segment is developing a first-in-class photo-dynamic therapy (SGX301) utilizing 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 (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, VeloThrax™, our anthrax vaccine candidate, OrbeShield™, our GI acute radiation syndrome (“GI ARS”) therapeutic candidate and SGX943, our melioidosis therapeutic candidate. The development of our vaccine programs is supported by our heat stabilization technology, known as ThermoVax™, under existing and on-going government contract funding. With the recently awarded 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. Additionally, we have entered into a global and exclusive channel collaboration with Intrexon Corporation (“Intrexon”) through which we intend to develop and commercialize a human monoclonal antibody therapy (SGX101) to treat melioidosis.

An outline for our business strategy follows:

- Conduct a Phase 3 clinical trial for SGX301 for the treatment of CTCL;
- Conduct a Phase 2 clinical trial of SGX942 for the treatment of oral mucositis in head and neck cancer;
- Initiate a Phase 3 clinical trial of oral BDP, known as SGX203, for the treatment of pediatric Crohn's disease;
- Evaluate the effectiveness of oral BDP in other therapeutic indications involving inflammatory conditions of the GI tract such as prevention of acute radiation enteritis;
- Develop RiVax™ and VeloThrax™ 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, an example of which is our collaboration with Intrexon.

## **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 C-10, Princeton, New Jersey 08540 and our telephone number is (609) 538-8200.

## **Our Products in Development**

The following tables summarize our products under development:

### **BioTherapeutic Product Candidates**

<b>Soligenix Product Candidate</b>	<b>Therapeutic Indication</b>	<b>Stage of Development</b>
SGX301	Cutaneous T-Cell Lymphoma	Phase 2 trial completed; demonstrated significantly higher response rate ( $p \leq 0.04$ ) compared to placebo;
		Phase 3 clinical trial planned for the first 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 data expected in the second half of 2015
		Phase 1/2 clinical trial completed June 2013, efficacy data, pharmacokinetic (PK)/pharmacodynamic (PD) profile and safety confirmed;
SGX203**	Pediatric Crohn’s disease	Phase 3 clinical trial planned for the second half of 2015, with data expected in the first half of 2017
		Phase 1/2 clinical trial complete; safety and preliminary efficacy demonstrated;
SGX201**	Acute Radiation Enteritis	Phase 1/2 clinical trial complete;
		safety and preliminary efficacy demonstrated;

Phase 2 trial planned for the second half of 2015,  
with data expected in the second half of 2016

**Vaccine Thermostability Platform\*\***

<b>Soligenix Product</b>	<b>Indication</b>	<b>Stage of Development</b>
ThermoVax™	Thermostability of aluminum adjuvanted vaccines	Pre-clinical

**BioDefense Products\*\***

<b>Soligenix Product</b>	<b>Indication</b>	<b>Stage of Development</b>
RiVax™	Vaccine against	Phase 1B trial complete, safety and neutralizing antibodies for protection demonstrated;
	Ricin Toxin Poisoning	Phase 1/2 trial planned for the second half of 2015
VeloThrax™	Vaccine against Anthrax Poisoning	Pre-clinical;
		Phase 1 clinical trial planned for second half of 2016
OrbeShield™	Therapeutic against GI ARS	Pre-clinical program initiated
SGX943/SGX101	Melioidosis	Pre-clinical program initiated

\*\* 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 ( $p\text{-value} \leq 0.04$ ) improvement with topical hypericin treatment whereas the placebo was ineffective: 58.3% compared to 8.3%, respectively.

SGX301 has received orphan drug designation from 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.

We anticipate initiating a Phase 3 clinical study of SGX301 in the treatment of CTCL in the first half of 2015.

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. See “Risk Factors” and “Cautionary Note Regarding Forward-Looking Statements – Industry Data and Market Information.”

### **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 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 innate defense regulators (“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 United States Food and Drug Administration (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 in the first half of 2013. 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 SGX942 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.

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 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. See “Risk Factors” and “Cautionary Note Regarding Forward-Looking Statements – Industry Data and Market Information.”

### **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 designations for relevant indications as appropriate in both the US and Europe. An orphan drug designation in the US enables seven years of market exclusivity upon approval, while the EU approval provides with ten years of market exclusivity.

### 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 2015.

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. See “Risk Factors” and “Cautionary Note Regarding Forward-Looking Statements – Industry Data and Market Information.”

### **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 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. See “Risk Factors” and “Cautionary Note Regarding Forward-Looking Statements – Industry Data and Market Information.”

### **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-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™ 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 have also demonstrated the compatibility of our thermostabilization technology with other secondary adjuvants such as TLR-4 agonists.

We intend to seek out potential partnerships with companies marketing FDA/ex-U.S. health authority approved Alum adjuvanted vaccines that are interested in eliminating the need for cold chain for their products. We believe that ThermoVax™ also will enable us to expand our vaccine development expertise beyond biodefense into the infectious disease space and 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 ( $p < 0.001$ ) 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 Epub ahead of print March 9, 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.

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. See “Risk Factors” and “Cautionary Note Regarding Forward-Looking Statements – Industry Data and Market Information.”

## **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 Centers 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 ricin vaccine, nor is there a known antidote for ricin toxin exposure.

## ***VeloThrax™ – Anthrax Vaccine***

VeloThrax™ is our proprietary vaccine candidate based on a recombinant protective antigen (“rPA”) derivative intended for use against anthrax. We have entered into an exclusive license option with Harvard College to license VeloThrax™ (also known as DNI for dominant negative inhibitor) for a vaccine directed at the prevention of anthrax infection of humans. VeloThrax™ is a translocation-deficient mutant of a protective antigen with double mutations of K397D and D425K that impede the conformational changes necessary for endosomal membrane translocation into the cell cytoplasm. In the absence of that protective antigen translocation step, anthrax toxin trafficking and function cease.

We believe that VeloThrax™ is a more immunogenic candidate than native rPA. This apparent increase in immunogenicity suggests that the DNI rPA is processed and presented to the immune system more efficiently by cellular antigen processing pathways, which is consistent with known properties of the molecule.

DNI versions of rPA such as VeloThrax™ are also capable of inducing antibodies that neutralize the activity of the anthrax toxin complex. Unlike fully-functional rPA, VeloThrax™ might be given to a patient post-exposure without risk of enhancing intoxication during an infection, although clinical tests involving intravenous administration of potentially therapeutic levels of DNI rPA resulted in serious adverse events and so further development of this product as a therapeutic biological for blocking the effects of infection by *B. anthracis* was discontinued. Our studies of VeloThrax™ will be at a dose 1,000 times lower than the dose previously tested for an intramuscular or intradermal vaccine.

We believe that VeloThrax™'s greater immunogenicity could lead to a vaccine that can be administered in the fewest possible doses to induce the highest level of toxin neutralizing antibodies. Utilizing ThermoVax™, we believe that we will be able to develop VeloThrax™ into a vaccine with an improved stability profile, an issue that has proven challenging in the development of other anthrax vaccines. Extended stability at ambient temperatures would be a significant improvement for stockpiled vaccines and one which is not expected from conventional vaccines. Assuming long-term stability can be met, VeloThrax™ could be stockpiled for general prophylactic as well as a post exposure use.