Soligenix Investor Relations

Soligenix Receives Hong Kong Patent for Improved Production of Synthetic Hypericin

Active Ingredient in HyBryte™ for the Treatment ofCutaneous T-Cell Lymphoma and SGX302 for the Treatment of Psoriasis

PRINCETON, N.J., Oct. 22, 2024 /PRNewswire/ -- Soligenix, Inc. (Nasdaq: SNGX) (Soligenix or the Company), a late-stage biopharmaceutical company focused on developing and commercializing products to treat rare diseases where there is an unmet medical need, announced today that the Hong Kong Patent Office has granted the patent entitled "Systems and Methods for Producing Synthetic Hypericin". The newly issued patent's claims are directed to a novel, highly purified form of synthetic hypericin manufactured through a unique proprietary process. Synthetic hypericin is the active pharmaceutical ingredient in HyBryte™, the Company's photodynamic therapy for the treatment of cutaneous T-cell lymphoma (CTCL), set to initiate a confirmatory Phase 3 clinical trial before the end of the year. The same active ingredient is also used in SGX302, a potential topical treatment for plaque psoriasis. This new granted patent (HK1260757) is a related patent to US Pat. Nos. 10,053,413 and 10,526,268, previously issued in the United States (U.S.), and is in the same family as another patentgranted in Europe. These patents are expected to expire in 2036, and form part of a larger collection of different patent families, including previously granted foreign patents covering liquid formulations and methods of use (EP Pat. No. 2,571,507) and issued U.S. patents for methods of synthesis (US Pat. No. 8,629,302), as well as other granted patents throughout the world.

HyBryte™ is a novel, first-in-class, photodynamic therapy that combines synthetic hypericin, a highly potent photosensitizer that is applied to the cancerous CTCL skin lesions and activated using a safe, visible light treatment. This treatment approach avoids the risk of secondary malignancies (including melanoma) inherent with the frequently employed DNA-damaging chemotherapeutic drugs and other photodynamic therapies that are dependent on ultraviolet exposure.

HyBryte™ has shown statistically significant efficacy in aPhase 3 randomized, placebo-controlled trial (FLASH trial, Fluorescent Light Activated Synthetic Hypericin) and will be initiating a second confirmatory Phase 3 placebo-controlled study (FLASH2) in 4Q 2024. Additional supportive studies have demonstrated the utility of longer treatment times (Study RW-HPN-MF-01), the lack of significant systemic exposure to hypericin after topical application (Study HPN-CTCL-02) and its relative efficacy and tolerability compared to Valchlor® (Study HPN-CTCL-04).

SGX302 leverages the same mechanism of action as HyBryte™, and is focused on the treatment of mild to moderate plaque psoriasis. Previous and ongoing Phase 2 studies have indicated efficacy in psoriasis, with biological effectiveness demonstrated.

"This recently issued patent continues to expand, strengthen and protect our synthetic hypericin patent estate," stated Christopher J. Schaber, PhD, President and Chief Executive Officer of Soligenix. "With this broad worldwide patent coverage in place, we look forward to completing the confirmatory Phase 3 CTCL study to potentially address the unmet medical need that currently exists in this orphan disease, while also completing our ongoing Phase 2a study in psoriasis that has a much larger patient population but remains an underserved market."

About HyBryte™

HyBryte™ (research name SGX301) is a novel, first-in-class, photodynamic therapy utilizing safe, visible light for activation. The active ingredient in HyBryte™ is synthetic hypericin, a potent photosensitizer that is topically applied to skin lesions that is taken up by the malignant T-cells, and then activated by safe, visible light approximately 24 hours later. The use of visible light in the red-yellow spectrum has the advantage of penetrating more deeply into the skin (much more so than ultraviolet light) and therefore potentially treating deeper skin disease and thicker plaques and lesions. This treatment approach avoids the risk of secondary malignancies (including melanoma) inherent with the frequently employed DNA-damaging drugs and other phototherapy that are dependent on ultraviolet exposure. Combined with photoactivation, 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 a published Phase 2 clinical study in CTCL, patients experienced a statistically significant (p=0.04) improvement with topical hypericin treatment whereas the placebo was ineffective. HyBryte™ has received orphan drug and fast track designations from the U.S. Food and Drug Administration (FDA), as well as orphan designation from the European Medicines Agency (EMA).

The published Phase 3 FLASH trial enrolled a total of 169 patients (166 evaluable) with Stage IA, IB or IIA CTCL. The trial consisted of three treatment cycles. Treatments were administered twice weekly for the first 6 weeks and treatment response was determined at the end of the 8th week of each cycle. In the first double-blind treatment cycle (Cycle 1), 116 patients received HyBryte™ treatment (0.25% synthetic hypericin) and 50 received placebo treatment of their index lesions. A total of 16% of the patients receiving HyBryte™ achieved at least a 50% reduction in their lesions (graded using a standard measurement of dermatologic lesions, the CAILS score) compared to only 4% of patients in the placebo group at 8 weeks (p=0.04) during the first treatment cycle (primary endpoint). HyBryte™ treatment in this cycle was safe and well tolerated.

In the second open-label treatment cycle (Cycle 2), all patients received HyBryte™ treatment of their index lesions. Evaluation

of 155 patients in this cycle (110 receiving 12 weeks of HyBryte™ treatment and 45 receiving 6 weeks of placebo treatment followed by 6 weeks of HyBryte™ treatment), demonstrated that the response rate among the 12-week treatment group was 40% ($p<0.0001$ vs the placebo treatment rate in Cycle 1). Comparison of the 12-week and 6-week treatment responses also revealed a statistically significant improvement ($p<0.0001$) between the two timepoints, indicating that continued treatment results in better outcomes. HyBryte™ continued to be safe and well tolerated. Additional analyses also indicated that HyBryte™ is equally effective in treating both plaque (response 42%, $p<0.0001$ relative to placebo treatment in Cycle 1) and patch (response 37%, $p=0.0009$ relative to placebo treatment in Cycle 1) lesions of CTCL, a particularly relevant finding given the historical difficulty in treating plaque lesions in particular.

The third (optional) treatment cycle (Cycle 3) was focused on safety and all patients could elect to receive HyBryte™ treatment of all their lesions. Of note, 66% of patients elected to continue with this optional compassionate use / safety cycle of the study. Of the subset of patients that received HyBryte™ throughout all 3 cycles of treatment, 49% of them demonstrated a positive treatment response ($p<0.0001$ vs patients receiving placebo in Cycle 1). Moreover, in a subset of patients evaluated in this cycle, it was demonstrated that HyBryte™ is not systemically available, consistent with the general safety of this topical product observed to date. At the end of Cycle 3, HyBryte™ continued to be well tolerated despite extended and increased use of the product to treat multiple lesions.

Overall safety of HyBryte™ is a critical attribute of this treatment and was monitored throughout the three treatment cycles (Cycles 1, 2 and 3) and the 6-month follow-up period. HyBryte's™ mechanism of action is not associated with DNA damage, making it a safer alternative than currently available therapies, all of which are associated with significant, and sometimes fatal, side effects. Predominantly these include the risk of melanoma and other malignancies, as well as the risk of significant skin damage and premature skin aging. Currently available treatments are only approved in the context of previous treatment failure with other modalities and there is no approved front-line therapy available. Within this landscape, treatment of CTCL is strongly motivated by the safety risk of each product. HyBryte™ potentially represents the safest available efficacious treatment for CTCL. With very limited systemic absorption, a compound that is not mutagenic and a light source that is not carcinogenic, there is no evidence to date of any potential safety issues.
Following the first Phase 3 study of HyBryte™ for the treatment of CTCL, the FDA and the EMA indicated that they would require a second successful Phase 3 trial to support marketing approval. With agreement from the EMA on the key design components, the second, confirmatory study, called FLASH2, is expected to be initiated before the end of 2024. This study is a randomized, double-blind, placebo-controlled, multicenter study that will enroll approximately 80 subjects with early-stage CTCL. The FLASH2 study replicates the double-blind, placebo-controlled design used in the first successful Phase 3 FLASH study that consisted of three 6-week treatment cycles (18 weeks total), with the primary efficacy assessment occurring at the end of the initial 6-week double-blind, placebo-controlled treatment cycle (Cycle 1). However, this second study extends the double-blind, placebo-controlled assessment to 18 weeks of *continuous* treatment (no "between-Cycle" treatment breaks) with the primary endpoint assessment occurring at the end of the 18-week timepoint. In the first Phase 3 study, a treatment response of 49% ($p<0.0001$ vs patients receiving placebo in Cycle 1) was observed in patients completing 18 weeks (3 cycles) of therapy. In this second study, all important clinical study design components remain the same as in the first FLASH study, including the primary endpoint and key inclusion-exclusion criteria. The extended treatment for a continuous 18 weeks in a single cycle is expected to statistically demonstrate HyBryte's™ increased effect over a more prolonged, "real world" treatment course. Given the extensive engagement with the CTCL community, the esteemed Medical Advisory Board and the previous trial experience with this disease, accelerated enrollment in support of this study is anticipated, including the potential to enroll previously identified and treated HyBryte™ patients from the FLASH study. Discussions with the FDA on an appropriate study design remain ongoing. While collaborative, the agency has expressed a preference for a longer duration comparative study over a placebo-controlled trial. Given the shorter time to potential commercial revenue and the similar trial design to the first FLASH study afforded by the EMA accepted protocol, this study is being initiated. At the same time, discussions with the FDA will continue on potential modifications to the development path to adequately address their feedback.

In addition, the FDA awarded an Orphan Products Development grant to support the evaluation of HyBryte™ for expanded treatment in patients with early-stage CTCL, including in the home use setting. The grant, totaling $2.6 million over 4 years, was awarded to the University of Pennsylvania that was a leading enroller in the Phase 3 FLASH study.

About Cutaneous T-Cell Lymphoma (CTCL)

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 malignant cells migrate to the skin where they form various lesions, typically beginning as patches and may progress to raised plaques and tumors. Mortality is related to the stage of CTCL, 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 cure for CTCL. Typically, CTCL lesions are treated and regress but usually return either in the same part of the body or in new areas.

CTCL constitutes a rare group of NHLs, occurring in about 4% of the more than 1.7 million individuals living with the disease in the U.S. and Europe (European Union and United Kingdom). It is estimated, based upon review of historic published studies and reports and an interpolation of data on the incidence of CTCL that it affects approximately 31,000 individuals in the U.S. (based on SEER data, with approximately 3,200 new cases seen annually) and approximately 38,000 individuals in Europe

(based on ECIS prevalence estimates, with approximately 3,800 new cases annually).

About SGX302

Visible light-activated synthetic hypericin is a novel, first-in-class, photodynamic therapy (PDT) that is expected to avoid many of the long-term risks associated with other PDT treatments. Synthetic hypericin is a potent photosensitizer that is topically applied to skin lesions and absorbed by cutaneous T-cells. With subsequent activation by safe, visible light, T-cell apoptosis is induced, addressing the root cause of psoriasis lesions. Other PDTs have shown efficacy in psoriasis with a similar apoptotic mechanism, albeit using ultraviolet (UV) light associated with more severe potential long-term safety concerns. The use of visible light in the red-yellow spectrum has the advantage of deeper penetration into the skin (much more than UV light) potentially treating deeper skin disease and thicker plaques and lesions, similar to what was observed in the positive Phase 3 FLASH (Fluorescent Light Activated Synthetic Hypericin) study in CTCL.

In an ongoing Phase 2a study in mild-to-moderate psoriasis, patients enrolled in the initial portion of the trial (Part A) have completed treatment. In Cohort 1, the initial five patients enrolled received twice weekly treatment for 18 weeks with 0.25% hypericin ointment, followed by light activation approximately 24 hours later. Light doses were increased by up to 1 J/cm2 on subsequent visits until mild erythema was observed in the treated lesions. Light doses for all patients were still being intermittently increased when the scheduled treatments ended, and light doses were generally safe and well tolerated. Evaluation of the initial cohort of five patients demonstrated a clear biological signal, with the majority of patients recording an improvement in the PASI score, providing evidence of biological improvement, but no patient met the definition of treatment success (IGA score of 0 or 1) at the 18-week treatment timepoint. The second cohort of five patients were enrolled once the Cohort 1 patients had completed all treatment visits. Given how well-tolerated light treatments were in the first Cohort, it was determined that the second cohort of patients could safely receive an accelerated light treatment with increases in the light dose by up to 2 J/cm2 at each visit and allowing the maximum light dose (25 J/cm2) to be reached earlier by approximately week 14, allowing more treatments at the maximum light dose to be completed in the 18-week treatment schedule. Two of the four evaluable patients from Cohort 2 achieved a clinical success score at some point during the 18-week treatment period and all evaluable patients improved, yielding an average reduction of approximately 50% in the PASI score. One patient in Cohort 2 dropped out of the study for personal reasons unrelated to the study.

This treatment approach avoids the risk of secondary malignancies (including melanoma) inherent with both the frequently used DNA-damaging drugs and other phototherapies that are dependent on UV A or B exposure. The use of synthetic hypericin coupled with safe, visible light also avoids the risk of serious infections and cancer associated with the systemic immunosuppressive treatments used in psoriasis.

About Psoriasis

Psoriasis is a chronic, non-communicable, itchy and often painful inflammatory skin condition for which there is no cure. Psoriasis has a significantly detrimental impact on patients' quality of life, and is associated with cardiovascular, arthritic, and metabolic diseases, as well as psychological conditions such as anxiety, depression and suicide. Many factors contribute to development of psoriasis including both genetic and environmental factors (e.g., skin trauma, infections, and medications). The lesions develop because of rapidly proliferating skin cells, driven by autoimmune T-cell mediated inflammation. Of the various types of psoriasis, plaque psoriasis is the most common and is characterized by dry, red raised plaques that are covered by silvery-white scales occurring most commonly on the elbows, knees, scalp, and lower back. Approximately 80% of patients have mild-to-moderate disease. Mild psoriasis is generally characterized by the involvement of less than 3% of the body surface area (BSA), while moderate psoriasis will typically involve 3-10% BSA and severe psoriasis greater than 10% BSA. Between 20% and 30% of individuals with psoriasis will go on to develop chronic, inflammatory arthritis (psoriatic arthritis) that can lead to joint deformations and disability. Studies have also associated psoriasis, and particularly severe psoriasis, with an increased relative risk of lymphoma, particularly CTCL. Although psoriasis can occur at any age, most patients present with the condition before age 35.

Treatment of psoriasis is based on its severity at the time of presentation with the goal of controlling symptoms. It varies from topical options including PDT to reduce pain and itching, and potentially reduce the inflammation driving plaque formation, to systemic treatments for more severe disease. Most common systemic treatments and even current topical photo/photodynamic therapy such as UV A and B light, carry a risk of increased skin cancer.

Psoriasis is the most common immune-mediated inflammatory skin disease. According to the World Health Organization (WHO) Global Report on Psoriasis 2016, the prevalence of psoriasis is between 1.5% and 5% in most developed countries, with some suggestions of incidence increasing with time. It is estimated, based upon review of historic published studies and reports and an interpolation of data, that psoriasis affects 3% of the U.S. population or more than 7.5 million people. Current estimates have as many as 60-125 million people worldwide living with the condition. The global psoriasis treatment market was valued at approximately $15 billion in 2020 and is projected to reach as much as$40 billion by 2027.

About Soligenix

Soligenix is a late-stage biopharmaceutical company focused on developing and commercializing products to treat rare diseases where there is an unmet medical need. Our Specialized BioTherapeutics business segment is developing and moving

toward potential commercialization of HyBryte™ (SGX301 or synthetic hypericin sodium) as a novel photodynamic therapy utilizing safe visible light for the treatment of cutaneous T-cell lymphoma (CTCL). With successful completion of the second Phase 3 study, regulatory approvals will be sought to support potential commercialization worldwide. Development programs in this business segment also include expansion of synthetic hypericin (SGX302) into psoriasis, our first-in-class innate defense regulator (IDR) technology, dusquetide (SGX942) for the treatment of inflammatory diseases, including oral mucositis in head and neck cancer, and (SGX945) in Behçet's Disease.

Our Public Health Solutions business segment includes development programs for RiVax®, our ricin toxin vaccine candidate, as well as our vaccine programs targeting filoviruses (such as Marburg and Ebola) and CiVax™, our vaccine candidate for the prevention of COVID-19 (caused by SARS-CoV-2). The development of our vaccine programs incorporates the use of our proprietary heat stabilization platform technology, known as ThermoVax®. To date, this business segment has been supported with government grant and contract funding from the National Institute of Allergy and Infectious Diseases (NIAID), the Defense Threat Reduction Agency (DTRA) and the Biomedical Advanced Research and Development Authority (BARDA).

For further information regarding Soligenix, Inc., please visit the Company's website at https://www.soligenix.com and follow us on LinkedIn and Twitter at @Soligenix_Inc.

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