

Soligenix Receives Japanese Patent for Improved Production of Synthetic Hypericin Composition Active Ingredient in HyBryte™ for the Treatment of Cutaneous T-Cell Lymphoma

PRINCETON, N.J., May 20, 2021 /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 Japan Patent Office has allowed the patent application titled "Systems and Methods for Producing Synthetic Hypericin". The allowed claims are directed to unique, proprietary methods to produce a novel, highly purified form of synthetic hypericin, and are similar to those previously allowed in the United States (U.S.). Synthetic hypericin is the active pharmaceutical ingredient in HyBryte™ (SGX301), the Company's photodynamic therapy, for which positive primary endpoint results in a pivotal Phase 3 study for the [treatment of cutaneous T-cell lymphoma](#) (CTCL) were recently announced. This new patent is the first allowed in Japan covering the proprietary methods developed by the Company and further expands the comprehensive HyBryte™ patent estate, which includes protection on the composition of the purified synthetic hypericin, methods of synthesis and therapeutic methods of use in both CTCL and psoriasis, and is being pursued worldwide.

HyBryte™ (synthetic hypericin) is a novel first-in-class photodynamic therapy for first-line treatment of early stage CTCL. In the recently completed pivotal Phase 3 FLASH (Fluorescent Light Activated Synthetic Hypericin) trial, HyBryte™ achieved a statistically significant treatment response rate (p=0.04) in the primary endpoint after just 6 weeks (Cycle 1) of therapy when compared to placebo. This positive treatment response continued to significantly improve with extended [HyBryte™ treatment](#) in the open-label treatment cycles after 12 weeks (Cycle 2) and 18 weeks (Cycle 3) total treatment, reinforcing the positive HyBryte™ primary endpoint treatment response demonstrated in Cycle 1. In addition, HyBryte™ has demonstrated a statistically significant response in both patch and plaque lesions through 12 weeks of treatment (Cycle 2), highlighting the unique benefit of using visible light with its deeper skin penetration. HyBryte™ was well tolerated throughout the study and no mutagenic risks have been identified, unlike other second-line or off-label treatments, including other phototherapies, which utilize ultraviolet light. The Company believes HyBryte™ has compelling competitive advantages over existing therapies for early stage CTCL and represents a significant commercial opportunity.

"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 the support of key patient advocacy organizations, such as the Cutaneous Lymphoma Foundation, and key opinion leaders, we are moving towards marketing approval and commercialization of HyBryte™, with the initial focus on the U.S. market, with partnership opportunities being explored to leverage ex-U.S. markets."

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 approximate 700,000 individuals living with the disease. 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 over 25,000 individuals in the U.S., with approximately 3,000 new cases seen annually.

About HyBryte™

HyBryte™ (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 visible light 16 to 24 hours later which triggers apoptosis of the cell. 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) and Promising Innovative Medicine (PIM) and "Innovation Passport" under the Innovative Licensing and Access Pathway (ILAP) from the Medicines and Healthcare Products Regulatory Agency (MHRA) of the United Kingdom.

The Phase 3 FLASH (Fluorescent Light Activated Synthetic Hypericin) 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, 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 the first 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 groups also revealed a statistically significant improvement ($p<0.0001$) between the two groups, 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 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. Follow-up visits were completed in Q4 2020, and the clinical study report to support the NDA is in the process of being finalized.

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. Its 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 no 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.

The Phase 3 CTCL clinical study was partially funded by the National Cancer Institute via a Phase II SBIR grant (#1R44CA210848-01A1) awarded to Soligenix, Inc.

About Soligenix, Inc.

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™ (HyBryte™ or synthetic hypericin) as a novel photodynamic therapy utilizing safe visible light for the treatment of cutaneous T-cell lymphoma (CTCL). With a successful Phase 3 study completed, regulatory approval is being sought and commercialization activities for this product candidate are being advanced initially in the U.S. Development programs in this business segment also include 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 proprietary formulations of oral beclomethasone 17,21-dipropionate (BDP) for the prevention/treatment of gastrointestinal (GI) disorders characterized by severe inflammation including pediatric Crohn's disease (SGX203) and acute

radiation enteritis (SGX201).

Our Public Health Solutions business segment includes active development programs for RiVax[®], our ricin toxin vaccine candidate, and SGX943, our therapeutic candidate for antibiotic resistant and emerging infectious disease, and 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>.

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