

Expanded HyBryte™ Treatment Demonstrating Positive Outcomes in Early-Stage Cutaneous T-Cell Lymphoma

Study Supported by \$2.6 Million FDA Orphan Products Development Grant

PRINCETON, N.J., July 9, 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 an interim update on the open-label, investigator-initiated study (IIS) evaluating extended HyBryte™ treatment for up to 12 months in patients with early-stage cutaneous T-cell lymphoma (CTCL). The trial is sponsored by Ellen Kim, MD, Director, Penn Cutaneous Lymphoma Program, Vice Chair of Clinical Operations, Dermatology Department, and Professor of Dermatology at the Hospital of the University of Pennsylvania who was a leading enroller in the [Phase 3 FLASH \(Fluorescent Light Activated Synthetic Hypericin\) study](#) for the treatment of early-stage CTCL. To date six patients have been enrolled and treated with HyBryte™ over a time period ranging up to 44 weeks. Patients have responded positively to HyBryte™ therapy with 75% (3 of the 4 subjects who have completed at least 12 weeks of therapy) already achieving "Treatment Success", as predefined in the study's protocol as $\geq 50\%$ improvement in their cumulative mCAILS (modified Composite Assessment of Index Lesion Severity) score compared to Baseline. Of the three Treatment Successes, two were achieved within the first 12 weeks of treatment and the third within 18 weeks. Of the remaining three patients, two have only recently started HyBryte™ therapy and have not yet reached their first efficacy evaluation visit (i.e., at Week 6) and the other had a substantial improvement documented at the Week 18 visit, but has not yet achieved the success threshold. In addition, HyBryte™ appears to be safe and well tolerated in all patients, with no treatment-related adverse events reported to date.

"In the Phase 3 FLASH study, HyBryte™ was shown to be efficacious with a promising safety profile. With limited treatment options, especially in the early stages of their disease, CTCL patients are often searching for alternative treatments. In our U.S. Food and Drug Administration (FDA)-funded study, initial results evaluating the expanded use of HyBryte™ in a 'real world' treatment setting are promising, further supporting and extending results from the previous positive Phase 2 and 3 clinical trials," noted Dr. Kim, Principal Investigator of the IIS. "We look forward to continuing to work with the FDA to complete this study and to participating in the upcoming confirmatory Phase 3 placebo-controlled study."

"We are pleased with the initial study results and with the FDA's support of the IIS that provides CTCL patients an opportunity to access HyBryte™ in an open-label setting," stated Christopher J. Schaber, President and CEO of Soligenix, Inc. "CTCL is an incredibly difficult to treat orphan disease and remains an area of unmet medical need with a very limited number of safe and effective treatment options. Following the initial Phase 3 FLASH study which demonstrated the safety and efficacy of shorter courses of HyBryte™ therapy, we are pleased to see that continuing treatment for longer time periods is resulting in the anticipated improved outcomes for patients. As the body of compelling data continues to grow in support of this novel therapy, we look forward to working with Dr. Kim on this important study as well as embarking on our confirmatory Phase 3 replication study later this year. We will continue to provide additional updates on the IIS as data becomes available."

The clinical study [RW-HPN-MF-01](#), "Assessment of Treatment with Visible Light Activated Synthetic Hypericin Ointment in Mycosis Fungoides Patients" is designed as an open-label, multicenter clinical trial enrolling up to 50 patients at select U.S. clinical centers. Patients have the potential to be treated for up to 12 months with twice a week dosing (visible light activation following ointment application by 24 ± 6 hours). The study also allows for potential transition to a "real-world" setting with home-use. The primary endpoint for the study is evaluating the number of treatment successes defined as $\geq 50\%$ reduction in the cumulative mCAILS score from Baseline to end of the treatment.

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 United States 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 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.](#)

This press release may contain forward-looking statements that reflect Soligenix's current expectations about its future results, performance, prospects and opportunities, including but not limited to, potential market sizes, patient populations, clinical trial enrollment, the expected timing for closing the offering described herein and the intended use of proceeds therefrom. Statements that are not historical facts, such as "anticipates," "estimates," "believes," "hopes," "intends," "plans," "expects," "goal," "may," "suggest," "will," "potential," or similar expressions, are forward-looking statements. These statements are subject to a number of risks, uncertainties and other factors that could cause actual events or results in future periods to differ materially from what is expressed in, or implied by, these statements, and include the expected amount and use of proceeds from the offering and the expected closing date of the offering. Soligenix cannot assure you that it will be able to successfully develop, achieve regulatory approval for or commercialize products based on its technologies, particularly in light of the significant uncertainty inherent in developing therapeutics and vaccines against bioterror threats, conducting preclinical and clinical trials of therapeutics and vaccines, obtaining regulatory approvals and manufacturing therapeutics and vaccines, that product development and commercialization efforts will not be reduced or discontinued due to difficulties or delays in clinical trials or due to lack of progress or positive results from research and development efforts, that it will be able to successfully obtain any further funding to support product development and commercialization efforts, including grants and awards, maintain its existing grants which are subject to performance requirements, enter into any biodefense procurement contracts with the U.S. Government or other countries, that it will be able to compete with larger and better financed competitors in the biotechnology industry, that changes in health care practice, third party reimbursement limitations and Federal and/or state health care reform initiatives will not negatively affect its business, or that the U.S. Congress may not pass any legislation that would provide additional funding for the Project BioShield program. In addition, there can be no assurance as to the timing or success of any of its clinical/preclinical trials. Despite the statistically significant result achieved in the first HyBryte™ (SGX301) Phase 3 clinical trial for the treatment of cutaneous T-cell lymphoma, there can be no assurance that the second HyBryte™ (SGX301) Phase 3 clinical trial will be successful or that a marketing authorization from the FDA or EMA will be granted. Additionally, although the EMA has agreed to the key design components of the second HyBryte™ (SGX301) Phase 3 clinical trial, no assurance can be given that the Company will be able to modify the development path to adequately address the FDA's concerns or that the FDA will not require a longer duration comparative study. Notwithstanding the result in the first HyBryte™ (SGX301) Phase 3 clinical trial for the treatment of cutaneous T-cell lymphoma and the Phase 2a clinical trial of SGX302 for the treatment of psoriasis, there can be no assurance as to the timing or success of the clinical trials of SGX302 for the treatment of psoriasis. Further, there can be no assurance that RiVax® will qualify for a biodefense Priority Review Voucher (PRV) or that the prior sales of PRVs will be indicative of any potential sales price for a PRV for RiVax®. Also, no assurance can be provided that the Company will receive or continue to receive non-dilutive government funding from grants and contracts that have been or may be awarded or for which the Company will apply in the future. These and other risk factors are described from time to time in filings with the Securities and Exchange Commission (the "SEC"), including, but not limited to, Soligenix's reports on Forms 10-Q and 10-K. Unless required by law, Soligenix assumes no obligation to update or revise any forward-looking statements as a result of new information or future events.

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