

HyBryte™ Phase 3 FLASH Study for the Treatment of Cutaneous T-Cell Lymphoma Published in JAMA Dermatology

- Published findings demonstrate that HyBryte™ treatment statistically significantly reduced CTCL lesion size
- HyBryte™ has potential to address a critical gap in treatment of early-stage CTCL

PRINCETON, N.J., July 20, 2022 /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 results of its successful Phase 3 FLASH (Fluorescent Light Activated Synthetic Hypericin) study evaluating HyBryte™ (synthetic hypericin) for the treatment of cutaneous T-cell lymphoma (CTCL) has been published in the [*Journal of the American Medical Association \(JAMA\) Dermatology*](#).

"The peer reviewed publication of these data in *JAMA Dermatology* is a testament and further validation to the importance of the findings for the scientific and CTCL disease communities," stated Ellen Kim, MD, Professor of Dermatology and Medical Director, Dermatology Clinic, Perelman Center for Advanced Medicine at the Hospital of the University of Pennsylvania, and the Lead Principal Investigator for the Phase 3 FLASH study. "With its chronic course and major impact on patient quality of life, CTCL is an orphan disease in urgent need of additional treatment options that are well-tolerated and safe over the long haul. The results from this Phase 3 study, which is the largest double-blind, randomized, placebo-controlled trial in CTCL to date, represents an important leap forward in the development of potential therapies to meet this unmet medical need."

The published findings demonstrate that HyBryte™ treatment statistically significantly reduced lesion size, with the treatment response further improving over successive 6-week treatment cycles. The primary endpoint evaluated the CAILS (Composite Assessment of Index Lesion Severity) score of three treated index lesions and success was defined as $\geq 50\%$ reduction in CAILS score relative to baseline. Lesion response continuously improved with treatment duration. After the first 6-week treatment window, 16% of patients had a response ($p=0.04$ versus patients with 6 weeks of placebo treatment; primary endpoint). This response rate continued to significantly increase to 49% through 18 weeks of treatment ($p<0.0001$ versus patients with 6-week hypericin or placebo treatment). Throughout the study, HyBryte™ was safe and well-tolerated. Importantly, HyBryte™ was observed to perform similarly against both patch and thicker plaque lesions characteristic of CTCL.

"In treating CTCL, which is a chronic cancer with no cure, long-term safety is of paramount concern. Most current treatment options for CTCL are associated with significant safety concerns, including black-box warnings. HyBryte™ treatment has demonstrated strong and rapid efficacy with a very benign safety profile," stated Dr. Richard Straube, MD, Senior Vice President and Chief Medical Officer of Soligenix. "This is of significant benefit to patients living with this difficult disease. The substantial increase in efficacy with longer treatment and the similar performance against both patch and plaque lesions are particularly encouraging. As one of the largest studies in CTCL, this study and this publication establishes a new benchmark in CTCL treatment."

About JAMA Dermatology

[*JAMA Dermatology*](#) is an international peer-reviewed journal published online weekly and in print/ online issue 12 times a year. It is one of the highest ranked journals in dermatology, with an acceptance rate of 9%. The journal, which has been in continuous publication since 1882, publishes studies in the areas of medical, surgical, pediatric, geriatric dermatology, oncologic and aesthetic dermatology. It prioritizes clinical and laboratory studies that reveal new information pertinent to the interests and needs of the medical dermatologist, dermatologic surgeon, and all those concerned with state-of-the-art care of cutaneous disease. The journal believes that knowledge derived from well-designed clinical trials and studies of cost-effectiveness are especially important for improving the practice of dermatology. *JAMA Dermatology* is a member of the JAMA Network family of journals, which includes *JAMA*, 11 JAMA Network specialty journals, and *JAMA Network Open*.

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 visible light 16 to 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 FDA, as well as orphan designation from the European Medicines Agency (EMA).

The [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, 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 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 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 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 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™ (SGX301 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> and follow us on [LinkedIn](#) and Twitter at [@Soligenix_Inc](#).

This press release may contain forward-looking statements that reflect Soligenix, Inc.'s current expectations about its future results, performance, prospects and opportunities, including but not limited to, potential market sizes, patient populations and clinical trial enrollment. 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, such as experienced with the COVID-19 outbreak. 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 HyBryte™ (SGX301) Phase 3 clinical trial for the treatment of cutaneous T-cell lymphoma, there can be no assurance that a marketing authorization from the FDA or EMA will be successful. 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, 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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