Soligenix Investor Relations

# FDA Grants Soligenix Orphan Drug Designation for the Treatment of T-cell Lymphoma

## Extension of hypericin orphan designation beyond cutaneous T-cell lymphoma

PRINCETON, N.J., Sept. 9, 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 Office of Orphan Products Development of the United States (U.S.) Food and Drug Administration (FDA) has granted orphan drug designation to the active ingredient hypericin for the treatment of T-cell lymphoma, extending the target population beyond cutaneous T-cell lymphoma (CTCL) as previously granted.

The U.S. 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 upon final FDA approval, orphan drug designation also positions Soligenix to be able to leverage a wide range of financial and regulatory benefits, including government grants for conducting clinical trials, waiver of expensive FDA user fees for the potential submission of a New Drug Application (NDA), and certain tax credits.

"The FDA's decision to grant and expand our hypericin orphan drug designation beyond CTCL signifies an important step for Soligenix as we continue to advance the program toward NDA filing in the first half of 2022," stated Christopher J. Schaber, PhD, President & Chief Executive Officer of Soligenix. "HyBryte™'s biologic activity was clearly demonstrated in the positive Phase 3, pivotal FLASH (Fluorescent Light Activated Synthetic Hypericin) study in patients suffering with early stage CTCL. The marketing exclusivity that this broadened orphan drug designation imparts adds significantly to the existing patent estate surrounding hypericin."

**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 previously received orphan drug and fast track designations from the U.S. 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 for CTCL.

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 CTCL 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.

**About T-Cell Lymphoma**

T-cell lymphomas can develop in lymphoid tissues such as the lymph nodes and spleen, or outside of lymphoid tissues (i.e., gastrointestinal tract, liver, nasal cavity, skin, and others). A similar lymphocyte called a natural killer (NK) cell shares many features with T cells. When NK cells become cancerous, the cancer is called NK or NK/T-cell lymphoma and is generally grouped with other T-cell lymphomas. T-cell lymphomas account for about seven percent of all NHLs in the U.S. according to the Surveillance, Epidemiology, and End Results (SEER) program. Each particular subtype of T-cell lymphoma is very uncommon. They can be aggressive (fast-growing) or indolent (slow-growing).

Lymphomas are often, but not always, named from a description of the normal cell that leads to cancer. There are three main categories of T-cell lymphomas: Peripheral T-cell lymphoma (PTCL), CTCL and those arising from immature T-cells or lymphoblatic lymphoma. Treatment of T-cell lymphomas is driven by the specific cancer subtype and the organs affected, and can range from skin directed therapies to systemic therapies to stem cell transplantation.

PTCL represents about 60% of all mature T-cell lymphomas and is characterized by a number of sub-types. The three most common subtypes include PTCL, Not Otherwise Specified (PTCLNOS, ~20% of all T-cell lymphomas), Anaplastic Large Cell Lymphoma (ALCL, ~11%) and Angioimmunoblastic T-Cell Lymphoma (AITL, ~7%). In general, PTCLs will include some degree of skin involvement, and some subtypes may be specifically related to latent viral infections (e.g., AITL). Involvement of peripheral organs only, such as skin or lymph nodes, is generally associated with a better prognosis.

CTCL accounts for about 3-4 percent of all NHL cases and usually affects adults. The term CTCL describes a group of typically indolent lymphomas that appear on, and are most often confined to, the skin. Mycosis fungoides, which appears as skin patches, plaques, or tumors, is the most common type of CTCL. Patches are usually flat, possibly scaly, and look like a rash; plaques are thicker, raised, usually itchy lesions that are often mistaken for eczema, psoriasis, or dermatitis; and tumors are raised bumps, which may or may not ulcerate. More than one type of lesion may be present at any time. Sézary syndrome is a less common form of CTCL that affects both the skin and blood. The most common symptoms are swollen lymph nodes and a red, very itchy rash that covers large portions of the body. 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. Typically, CTCL lesions are treated and regress but usually return either in the same part of the body or in new areas. More information on CTCL can be accessed through the Cutaneous Lymphoma Foundation.

There are other rarer types of T-cell lymphoma, including those arising in patients after transplantation and immunosuppression, viral infection such as human T-lymphotropic virus type 1 (HTLV-1) and lymphoblastic lymphoma. For a more detailed description, please refer to the fact sheet provided by the Lymphoma Research Foundation.

**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 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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