Soligenix Investor Relations

# HyBryte™ Clinical Results Demonstrate Continued Improvement Post-Treatment

***Significant Efficacy against Plaque Lesions Also Demonstrated with HyBryte™***

PRINCETON, N.J., Dec. 2, 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 analysis of the post-treatment data from the open-label study (protocol HPN-CTCL-04) comparing HyBryte™ (synthetic hypericin) to Valchlor® (mechlorethamine) has demonstrated continued improvement in HyBryte™ treated patients and their individual lesions even after stopping treatment. The study, which enrolled 10 patients randomized 1:1 with 12 weeks of treatment and 4 weeks of follow-up post-treatment, was previously reported to demonstrate a positive difference in the overall per patient treatment response rate (60% in the HyBryte™ group vs. 20% in the Valchlor® group) at the end of treatment. After the 4-week follow-up period (Week 16), the majority (3 of 5) of HyBryte™ patients continued to demonstrate improvement with at least a further 10% improvement (absolute difference) at Week 16 relative to the primary outcome measure at Week 12, including one of the HyBryte™ patients achieving a "complete response". In contrast, of the four patients that completed the Valchlor® arm of the study, none achieved this level of improvement by Week 16. For patients, a treatment response was defined as a ≥50% improvement in their cumulative mCAILS (modified Composite Assessment of Index Lesion Severity) score over 3 to 5 lesions. Treatment response was also assessed on individual lesions. There was a similar continued improvement in the lesion responses over time, with the plaque lesions of particular interest given their increasing association with risk of overall disease progression and long-term mortality. At the 12-week (end of treatment) timepoint, the HyBryte™ treated plaque lesions were statistically significantly improved compared to the Valchlor® treated plaques (63%, [10/16] treatment success with HyBryte™ vs. 17%, [2/12] with Valchlor®, p=0.02). By Week 16, the response rates in lesions treated with HyBryte™ were statistically significant responses for all lesions (72% HyBryte™ vs 28% Valchlor®, p=0.02) and specifically for plaque lesions (75% responding plaque lesions with HyBryte™ treatment vs. 17% with Valchlor®, p=0.006) relative to the Valchlor® group. No safety concerns with HyBryte™ were raised during the follow-up period.

"Following the positive results from the previous Phase 2 and 3 studies where we previously participated in evaluating HyBryte™, we were excited to support Soligenix's effort to conduct a prospective comparative assessment of HyBryte™ versus Valchlor®," stated Dr. Brian Poligone, Director of the Rochester Skin Lymphoma Medical Group, and Principal Investigator for the comparability study. "Despite the small study sample size and a randomization that resulted in the HyBryte™ group having patients with more extensive disease, HyBryte™ continues to demonstrate its rapid onset of action and benign safety profile, compared to one of the most widely prescribed approved drugs for early-stage CTCL. The potentially enhanced effect on plaque lesions mirrors the promising activity against very difficult to treat lesions, such as refractory folliculotropic lesions, which we also observed in the first Phase 3 study. We look forward to continuing our support of Soligenix in the development of HyBryte™ by participating in the upcoming confirmatory Phase 3 placebo-controlled study."

"These results support the positive HyBryte™ data from the previously completed Phase 3 FLASH study and demonstrates that a relatively short treatment period with the drug can result in clinically meaningful outcomes," stated Christopher J. Schaber, PhD, President and Chief Executive Officer of Soligenix. "This relatively rapid response to HyBryte™ therapy fits nicely into the treatment arsenal for CTCL and reinforces the relative safety of HyBryte™ in these patients compared to other therapies currently in use. We look forward to continuing to work with Dr. Poligone and all of our committed clinical investigators to initiate the 80-patient confirmatory Phase 3 replication study (FLASH2) next month."

The purpose of the HPN-CTCL-04 study was to obtain preliminary comparative assessment of the safety and efficacy of Valchlor® versus HyBryte™ following 12 weeks of treatment as measured in 3 to 5 prospectively identified index lesions for each patient. HyBryte™ was administered twice weekly with light exposure approximately 24 hours after drug application, while Valchlor® was applied as often as daily as per the package insert. At the end of the 12-week treatment period, 60% of the HyBryte™ patients met the prospectively defined level of "Treatment Success" (≥50% improvement in their cumulative mCAILS score compared to Baseline) compared to only 20% of the Valchlor® patients; although due to the small sample size the results do not achieve statistical significance. Of the remaining two HyBryte™ patients that did not achieve treatment success, both saw a substantial (≥30%) reduction in their mCAILS score. In contrast, in the Valchlor® group, of the remaining 4 patients that did not achieve treatment success, one worsened and dropped from the study, one improved less than 30% and two improved ≥30%. The average cumulative improvement in mCAILS at 12 weeks was 52.5% in the HyBryte™ patients versus 34.7% in the Valchlor® patients. HyBryte™ was well tolerated in all patients whereas 1 of the 5 patients receiving Valchlor® had to be withdrawn from the trial because of a clinically significant allergic contact dermatitis from Valchlor®.

During the 4-week follow-up period (Week 16) the majority (3 of 5) of HyBryte™ patients continued to demonstrate lesion improvement with at least a further 10% reduction (absolute difference) at Week 16 relative to the primary outcome measure at Week 12, including one of these patients achieving a "complete response". The remaining two HyBryte™ subjects showed either a modest (<5%) decrease or increase relative to their primary endpoint response at Week 12. In contrast, of the four patients that completed the Valchlor® arm of the study, one worsened (>15% change), one had a modest decrease, one

remained static, and one had a modest improvement by Week 16. Analysis of the individual lesion responses showed similar response profiles, with treatment response observed in 61% of HyBryte™ treated lesions vs. 33% response in Valchlor® treated lesions (p=0.18) at Week 12. The lesions responses increased over the 4 weeks following treatment to 72% responding lesions with HyBryte™ treatment and decreased over the 4 weeks following treatment to 28% with Valchlor, p=0.02. Focusing specifically on the plaque lesions, 63% of HyBryte™ treated plaque lesions (10/16) responded to treatment vs. 17% of Valchlor® treated plaque lesions (2/12; p=0.02). Again, the responses of the HyBryte™ treated lesions increased over the 4 weeks following treatment to 75% responding plaque lesions with HyBryte™ treatment and the Valchlor® treated lesions response rate was unchanged at 17%, p=0.006. Plaque lesions have been acknowledged as both more difficult to treat and, more recently, as potentially linked to disease progression. The link with disease progression was most recently reported at the European Organisation for Research and Treatment of Cancer (EORTC) Cutaneous Lymphoma Tumour Group Annual Meeting in Lausanne, Switzerland on October 9-11, 2024.

When comparing the tolerance of the topical therapies (i.e., reactions where the drug was applied to the skin) in this trial, it is notable that all patients tolerated HyBryte™ well and had no adverse events "Related" to the therapy. In contrast, 60% of the Valchlor® treated patients had at least one adverse event "Related" to the therapy. These adverse events in the Valchlor® group included rashes, application site sensitivity, allergic contact dermatitis, and dermatitis, with one patient requiring steroid treatment, one requiring temporary interruption of Valchlor® treatments, and one requiring permanent discontinuation of Valchlor®. No such instances were reported in the HyBryte™ group.

**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 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 athttps://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. Additionally, despite the biologic activity observed in aphthous ulcers induced by chemotherapy and radiation, there can be no assurance as to the timing or success of the clinical trials of SGX945 for the treatment of Behçet's Disease. 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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For further information: COMPANY CONTACT: Jonathan Guarino, CPA, CGMA, Senior Vice President and Chief Financial Officer, (609) 538-8200; www.soligenix.com; Soligenix, Inc., 29 Emmons Drive, Suite B-10, Princeton, NJ 08540

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