Complete 72-Week Results from Phase 3 HOPE Study of Oxbryta® (voxelotor) Tablets Published in The Lancet Haematology Show Significantly Improved Hemoglobin, Hemolysis and Overall Health Status in Sickle Cell Disease Patients

April 8, 2021

SOUTH SAN FRANCISCO, Calif., April 08, 2021 (GLOBE NEWSWIRE) -- Global Blood Therapeutics, Inc. (GBT) (NASDAQ: GBT) today announced *The Lancet Haematology* has published the complete analysis of 72-week data from the Phase 3 HOPE Study of Oxbryta® (voxelotor) tablets in patients with sickle cell disease (SCD). The results showed significant and sustained improvement in hemoglobin levels, reduction in hemolysis and improved overall health status in patients treated with Oxbryta. These findings support the long-term use of Oxbryta to reduce hemolytic anemia and hemolysis in SCD, potentially mitigating life-threatening complications of the condition.

Oxbryta, a first-in-class oral, once-daily therapy, directly inhibits hemoglobin polymerization, the root cause of the sickling and destruction of red blood cells in SCD. Oxbryta is approved in the United States for the treatment of SCD in patients ages 12 years and older.

“Sickle cell disease is a devastating disease that can lead to organ damage and a shortened life expectancy and is complicated by significant disparities in access to quality care,” said lead author Professor Jo Howard of Guy’s and St. Thomas’ NHS Foundation Trust and King’s College London. “Fortunately, we have entered a new era of treatment. The HOPE Study is the longest registrational trial to date among recently approved therapies for sickle cell disease, and these results further demonstrate that by sustainably improving both the hemolysis and anemia manifestations of the disease, Oxbryta has the potential to be a safe and effective disease-modifying treatment in patients with sickle cell disease.”

The HOPE Study, a randomized, double-blind, placebo-controlled, international, multicenter trial in 274 patients ages 12 to 65 years with SCD, showed treatment with the U.S. FDA-approved dose of Oxbryta 1500 mg resulted in rapid and durable improvements in hemoglobin levels throughout 72 weeks of treatment. Approximately 90 percent of patients treated with Oxbryta achieved a hemoglobin improvement of >1 g/dL from baseline at one or more time points during the study compared to placebo (25 percent). In addition, approximately 59 percent of patients treated with Oxbryta 1500 mg were able to achieve a hemoglobin increase of >2 g/dL and 20 percent achieved >3 g/dL at one or more time points, compared to approximately 3 percent and no patients in the placebo group, respectively. The analysis also showed that study participants treated with Oxbryta had numerically fewer vaso-occlusive crises (VOCs), consistent with the trends at 24 weeks, and were three times less likely to experience an acute anemic episode (decrease in hemoglobin >2 g/dL from baseline).

Additionally, approximately 74 percent of patients (39 of 53) taking Oxbryta had their overall clinical status rated as “moderately improved” or “very much improved” by their clinician compared with approximately 47 percent (24 of 51) of the placebo group, a statistically significant difference. Treatment with Oxbryta remained generally well tolerated, and rates of adverse events were similar between treatment groups over 72 weeks.

“The sickle cell disease community, which for decades has been dramatically underserved, deserves treatments that address the sickling and destruction of red blood cells due to hemoglobin polymerization – the root cause of this disease,” said Ted W. Love, M.D., president and chief executive officer of GBT. “The HOPE Study represents a significant milestone in advancing the treatment of SCD, and we are building on this groundbreaking trial with our commitment to increase access to Oxbryta and develop novel therapeutics that can transform SCD into a well-managed disease.”

Findings from a post hoc analysis of the HOPE Study published recently in the *American Journal of Hematology* evaluated the incidence and outcomes of leg ulcers in SCD patients and further support the foundational role of hemoglobin S polymerization inhibition in SCD treatment.[1] Results of the analysis showed leg ulcers improved or resolved by week 72 in all patients (5 of 5) receiving Oxbryta 1500 mg compared with 63 percent of patients (5 of 8) in the placebo group. Resolution of leg ulcers was associated with increases in hemoglobin levels and decreases in hemolysis. Patients who experienced a hemoglobin increase of >1.0 g/dL while treated with Oxbryta were most likely to experience resolution of their leg ulcers within 24 weeks. These results highlight the potential of Oxbryta to meaningfully impact major patient outcomes.

About Sickle Cell Disease

Sickle cell disease (SCD) affects an estimated 100,000 people in the United States,[2] an estimated 52,000 people in Europe,[3] and millions of people throughout the world, particularly among those whose ancestors are from sub-Saharan Africa.[2] It also affects people of Hispanic, South Asian, Southern European and Middle Eastern ancestry.[2] SCD is a lifelong inherited rare blood disorder that impacts hemoglobin, a protein carried by red blood cells that delivers oxygen to tissues and organs throughout the body.[4] Due to a genetic mutation, individuals with SCD form abnormal hemoglobin known as sickle hemoglobin. Through a process called hemoglobin polymerization, red blood cells become sickled – deoxygenated, crescent-shaped and rigid.[4-6] The sickling process causes hemolytic anemia (low hemoglobin due to red blood cell destruction) and blockages in capillaries and small blood vessels, which impede the flow of blood and oxygen throughout the body. The diminished oxygen delivery to tissues and organs can lead to life-threatening complications, including stroke and irreversible organ damage.[5-8]

About Oxbryta® (voxelotor) Tablets

Oxbryta (voxelotor) is an oral, once-daily therapy for patients with sickle cell disease (SCD). Oxbryta works by increasing hemoglobin’s affinity for oxygen. Since oxygenated sickle hemoglobin does not polymerize, GBT believes Oxbryta blocks polymerization and the resultant sickling and destruction of red blood cells, which are primary pathologies faced by every single person living with SCD. Through addressing hemolytic anemia and improving oxygen delivery throughout the body, GBT believes that Oxbryta has the potential to modify the course of SCD. On Nov. 25, 2019, Oxbryta

received U.S. Food and Drug Administration (FDA) accelerated approval for the treatment of SCD in adults and children 12 years of age and older.[9]

As a condition of accelerated approval, GBT will continue to study Oxbryta in the HOPE-KIDS 2 Study, a post-approval confirmatory study using transcranial Doppler (TCD) flow velocity to assess the ability of the therapy to decrease stroke risk in children 2 to 15 years of age.

In recognition of the critical need for new SCD treatments, the FDA granted Oxbryta Breakthrough Therapy, Fast Track, Orphan Drug and Rare Pediatric Disease designations for the treatment of patients with SCD. Additionally, Oxbryta has been granted Priority Medicines (PRIME) designation from the European Medicines Agency (EMA), and the European Commission (EC) has designated Oxbryta as an orphan medicinal product for the treatment of patients with SCD.

The EMA has accepted for review GBT's Marketing Authorization Application (MAA) seeking full marketing authorization of Oxbryta in Europe to treat hemolytic anemia in SCD patients ages 12 years and older. GBT also plans to seek regulatory approval to expand the potential use of Oxbryta in the United States for the treatment of SCD in children as young as 4 years old.

Important Safety Information
Oxbryta should not be taken if the patient has had an allergic reaction to voxelotor or any of the ingredients in Oxbryta. See the end of the patient leaflet for a list of the ingredients in Oxbryta. Oxbryta can cause serious side effects, including serious allergic reactions. Patients should tell their health care provider or get emergency medical help right away if they get rash, hives, shortness of breath or swelling of the face.

Patients receiving exchange transfusions should talk to their health care provider about possible difficulties with the interpretation of certain blood tests when taking Oxbryta.

The most common side effects of Oxbryta include headache, diarrhea, stomach (abdominal) pain, nausea, tiredness, rash and fever. These are not all the possible side effects of Oxbryta.

Before taking Oxbryta, patients should tell their health care provider about all medical conditions, including if they have liver problems; if they are pregnant or plan to become pregnant as it is not known if Oxbryta can harm an unborn baby; or if they are breastfeeding or plan to breastfeed as it is not known if Oxbryta can pass into breastmilk or if it can harm a baby. Patients should not breastfeed during treatment with Oxbryta and for at least two weeks after the last dose.

Patients should tell their health care provider about all the medicines they take, including prescription and over-the-counter medicines, vitamins and herbal supplements. Some medicines may affect how Oxbryta works. Oxbryta may also affect how other medicines work.

Patients are advised to call their doctor for medical advice about side effects. Side effects can be reported to the FDA at 1-800-FDA-1088. Side effects can also be reported to Global Blood Therapeutics at 1-833-428-4968 (1-833-GBT-4YOU).

Full Prescribing Information for Oxbryta is available at Oxbryta.com.

About Global Blood Therapeutics
Global Blood Therapeutics (GBT) is a biopharmaceutical company dedicated to the discovery, development and delivery of life-changing treatments that provide hope to underserved patient communities. Founded in 2011, GBT is delivering on its goal to transform the treatment and care of sickle cell disease (SCD), a lifelong, devastating inherited blood disorder. The company has introduced Oxbryta® (voxelotor), the first FDA-approved treatment that directly inhibits sickle hemoglobin polymerization, the root cause of red blood cell sickling in SCD. GBT is also advancing its pipeline program in SCD with inclacumab, a P-selectin inhibitor in development to address pain crises associated with the disease, and GBT021601 (GBT601), the company's next- generation hemoglobin S polymerization inhibitor. In addition, GBT's drug discovery teams are working on new targets to develop the next wave of treatments for SCD. To learn more, please visit www.gbt.com and follow the company on Twitter @GBT_news.

Forward-Looking Statements
Certain statements in this press release are forward-looking within the meaning of the Private Securities Litigation Reform Act of 1995, including statements containing the words "will," "anticipates," "plans," "believes," "forecast," "estimates," "expects" and "intends," or similar expressions. These forward-looking statements are based on GBT's current expectations and actual results could differ materially. Statements in this press release may include statements that are not historical facts and are considered forward-looking within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. GBT intends these forward-looking statements, including statements regarding GBT's priorities, dedication, commitment, focus, goals, mission and vision; safety, efficacy and mechanism of action of Oxbryta and other product characteristics; significance of reducing hemolysis and raising hemoglobin; commercialization, delivery, availability, use and commercial and medical potential of Oxbryta; significance of the HOPE Study results, including support for the long-term use of Oxbryta; ongoing and planned studies and related protocols, activities and expectations; regulatory submissions, review and approval to potentially expand the approved use of Oxbryta for more patients in the U.S. and to treat patients in Europe; altering the treatment, course and care of SCD and mitigating related complications; potential and advancement of GBT's pipeline, including inclacumab and other product candidates; and working on new targets and discovering, developing and delivering treatments, to be covered by the safe harbor provisions for forward-looking statements contained in Section 27A of the Securities Act and Section 21E of the Securities Exchange Act, and GBT makes this statement for purposes of complying with those safe harbor provisions. These forward-looking statements reflect GBT's current views about its plans, intentions, expectations, strategies and prospects, which are based on the information currently available to the company and on assumptions the company has made. GBT can give no assurance that the plans, intentions, expectations or strategies will be attained or achieved, and, furthermore, actual results may differ materially from those described in the forward-looking statements and will be affected by a variety of risks and factors that are beyond GBT's control, including, without limitation, risks and uncertainties relating to the COVID-19 pandemic, including the extent and duration of the impact on GBT's business, including commercialization activities, regulatory efforts, research and development, corporate development activities and operating results, which will depend on future developments that are highly uncertain and cannot be accurately predicted, such as the ultimate duration of the pandemic, travel restrictions, quarantines, social distancing and business closure requirements in the U.S. and in other countries, and the effectiveness of actions taken globally to contain and treat the disease; the risks that GBT is continuing to establish its commercialization capabilities and may not be able to successfully commercialize Oxbryta; risks associated with GBT's dependence on third parties for development, manufacture, distribution and commercialization activities related to Oxbryta; government and third-party payor actions, including those relating to reimbursement and pricing; risks and uncertainties relating to competitive products and other changes that may limit demand for Oxbryta; the risks regulatory authorities may require additional studies or data to support continued commercialization of Oxbryta; the risks that drug-related adverse events may be observed during commercialization or

clinical development; data and results may not meet regulatory requirements or otherwise be sufficient for further development, regulatory review or approval; compliance with obligations under the Pharmakon loan; and the timing and progress of GBT's and Syros' research and development activities under their collaboration; along with those risks set forth in GBT's Annual Report on Form 10-K for the fiscal year ended December 31, 2020, filed with the U.S. Securities and Exchange Commission, as well as discussions of potential risks, uncertainties and other important factors in GBT's subsequent filings with the U.S. Securities and Exchange Commission. Except as required by law, GBT assumes no obligation to update publicly any forward-looking statements, whether as a result of new information, future events or otherwise.

References

1. Minniti CP, et al. The impact of voxelotor treatment on leg ulcers in patients with sickle cell disease. *Am J Hematol*. 2021. https://doi.org/10.1002/ajh.26101. Accessed March 2, 2021.
2. Centers for Disease Control and Prevention website. Sickle Cell Disease (SCD). https://www.cdc.gov/ncbddd/sicklecell/data.html. Accessed June 3, 2019.
3. European Medicines Agency. https://www.ema.europa.eu/en/medicines/human/orphan-designations/eu3182125. Accessed June 12, 2020.
4. National Heart, Lung, and Blood Institute website. Sickle Cell Disease. https://www.nhlbi.nih.gov/health-topics/sickle-cell-disease. Accessed August 5, 2019.
5. Rees DC, et al. *Lancet*. 2010;376(9757):2018-2031.
6. Kato GJ, et al. *Nat Rev Dis Primers*. 2018;4:18010.
7. Kato GJ, et al. *J Clin Invest*. 2017;127(3):750-760.
8. Caboot JB, et al. *Paediatr Respir Rev*. 2014;15(1):17-23.
9. Oxbryta (voxelotor) tablets prescribing information. South San Francisco, Calif. Global Blood Therapeutics, Inc.; November 2019.

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Source: Global Blood Therapeutics, Inc.