



GBT Presents Positive New Real-World Evidence Data at EHA2022 Congress Further Supporting Clinical Use of Oxbritya® (voxelotor) in Sickle Cell Disease

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Positive results from Phase 1 study of GBT601, including incremental new data, support advancing into planned Phase 2/3 trial by mid-year

GBT to hold investor conference call and webcast today at 3:00 p.m. CEST (9:00 a.m. EDT) to highlight EHA data and provide business updates

SOUTH SAN FRANCISCO, Calif., June 10, 2022 (GLOBE NEWSWIRE) -- Global Blood Therapeutics, Inc. (GBT) (NASDAQ: GBT) today announced new data from a large multicenter real-world evidence study supporting the clinical use of Oxbritya® (voxelotor) for the treatment of sickle cell disease (SCD) in patients 12 years of age and older. In addition, Phase 1 data of GBT021601 (GBT601), the company's next-generation sickle hemoglobin (HbS) polymerization inhibitor, support its progression into the Phase 2 portion of a Phase 2/3 trial that is anticipated to commence by mid-year. These data, as well as new research from the United Kingdom demonstrating that an improvement of anemia as measured by hemoglobin (Hb) reduces the risk of end-organ damage in SCD patients, will be presented at the [European Hematology Association \(EHA\) 2022 Hybrid Congress](#) from June 9-12, 2022 in Vienna, Austria and online.

"At EHA2022 this week, we presented data from the first multicenter retrospective study of SCD patients treated with Oxbritya in a real-world setting, which demonstrated the positive clinical impact of Oxbritya – results that were consistent with the pivotal Phase 3 HOPE Study. In addition, our study in the U.K. of the impact of the improvement of anemia adds to the growing body of data that supports the need to maximize hemoglobin levels in sickle cell patients in order to help protect against end-organ damage," said Ted W. Love, M.D., president and chief executive officer of GBT. "As more clinicians gain experience with Oxbritya and we build on our recent regulatory approvals by the European Commission and in the Middle East, we're very pleased with our progress on making this transformative, first-in-class therapy available to more patients around the world."

Retrospective Analysis of Real-World Oxbritya Treatment

Data from the Retrospective Study to Evaluate Outcomes in Patients with Sickle Cell Disease Treated with Oxbritya (RETRO) (Poster # P1485), the first multicenter, retrospective study to examine the real-world effectiveness of Oxbritya, demonstrated an improvement in anemia and hemolysis as measured by an increase in Hb levels and decrease in markers of hemolysis – results consistent with the Phase 3 HOPE Study. A first-in-class, once-daily oral therapy, Oxbritya directly inhibits sickle hemoglobin polymerization, the root cause of the sickling and destruction of red blood cells in SCD. RETRO analyzed laboratory and clinical data from medical records of 216 patients treated at nine sites in the U.S., covering one year before and one year or more after initiation of Oxbritya treatment. In the study, Hb levels increased and were maintained over the 12-month treatment period and peak Hb levels increased from baseline by a mean of 1.4 g/dL. Markers of hemolysis improved, with mean indirect bilirubin and mean reticulocyte percentage decreasing over the 12-month treatment period. Oxbritya was well tolerated, with the majority of treatment-emergent adverse events (TEAEs) being mild to moderate. Overall safety data was consistent with the Phase 3 HOPE Study of SCD patients ages 12 years and older.

In a separate retrospective analysis (Poster #P1488), researchers examined 12 years of data from the Clinical Practice Research Datalink and the Hospital Episode Statistics databases in the U.K., which provided sufficient data to observe end-organ damage events in patients with SCD. The analysis found that an increase in Hb of 1 g/dL was associated with a statistically significant ($p < 0.001$) reduction in the risk for leg ulcers, pulmonary hypertension, chronic kidney disease, end-stage renal disease, acute chest syndrome and stroke.

SCD Pipeline: GBT601 and Inclacumab Presentations

In the Phase 1 trial, six adult patients with SCD (HbSS genotype) were studied in a single-arm, intra-patient single-dose and multiple ascending dose (MAD) trial to evaluate the safety and tolerability of GBT601, a next-generation HbS polymerization inhibitor. The EHA2022 oral presentation (#S268) will be held on June 12 at 11:30 a.m. CEST (5:30 a.m. EDT).

During the MAD portion of the trial, patients received a loading dose of 300 mg on day one and a 200 mg loading dose on day two, followed by a daily maintenance dose of 50 mg for five weeks (MAD-1). This was immediately followed by the second MAD phase, with patients receiving a loading dose of 500 mg on the first day and a 400 mg loading dose the next day, followed by a daily maintenance dose of 100 mg for three weeks (MAD-2).

In the MAD cohort at the end of treatment, a mean Hb occupancy of 32.6% was achieved, Hb increased by a mean of 2.3 g/dL, and there was an improvement in markers of hemolysis (reticulocytes, absolute reticulocytes, bilirubin and lactate dehydrogenase). In addition, improved red blood cell (RBC) health was reflected by ektacytometry results and peripheral blood smears. At the end of treatment, there was a mean decrease of 76.1% in the number of sickled RBCs (relative to pre-GBT601 dose measurements), and, following the 15-week washout period, the number returned near the pre-dose level. A similar trend was observed with Hb levels returning to near pre-dose levels following the washout period. There were no significant changes in the erythropoietin levels or other evidence of impaired oxygen delivery.

GBT601 demonstrated a favorable tolerability profile in both the SCD and the healthy volunteer portions of the trial. Overall, the majority of TEAEs were grade 1 or 2 and not related to GBT601. No TEAEs led to study discontinuation.

"We are encouraged by these Phase 1 data, which demonstrate that GBT601 has the potential to achieve greater hemoglobin occupancy levels and increases in hemoglobin while improving red blood cell health at lower doses than Oxbritya in patients with sickle cell disease," said Kim Smith-Whitley, M.D., executive vice president and head of research and development of GBT. "These results support the continued development of this potential best-in-class therapy for people living with this devastating, lifelong condition. Based on patient interest, we have restarted the Phase 1 trial to explore a 150 mg maintenance dose and will be starting the Phase 2 portion of our planned Phase 2/3 trial."

GBT's pivotal Phase 3 studies of inclacumab, the company's P-selectin inhibitor, will also be highlighted at EHA2022 (Poster #P1486). Currently enrolling patients, the two pivotal Phase 3 THRIVE studies are evaluating the safety and efficacy of inclacumab in reducing vaso-occlusive crises (VOCs) and readmissions due to VOCs. An additional THRIVE open-label expansion (OLE) study will examine the long-term safety of inclacumab in individuals with SCD.

Conference Call and Webcast Today at 3:00 p.m. CEST (9:00 a.m. EDT)

GBT will host a conference call for the investment community today, Friday, June 10, 2022 at 3:00 p.m. CEST (9:00 a.m. EDT) to discuss new data on its sickle cell programs presented at EHA2022, along with other business and R&D updates. This includes a presentation of preclinical and clinical data demonstrating Oxbryta's potential to limit the progression of early chronic kidney disease, which will be made by Santosh Saraf, M.D., assistant professor of medicine in the Division of Hematology/Oncology at the University of Illinois Hospital and Health Sciences System.

To participate in the conference call, please dial (877) 407-3982 (U.S.) or +1 (201) 493-6780 (international). A live webcast including presentation slides can be accessed on GBT's website at www.gbt.com in the Investors section. The archived webcast will be available for three months following the event.

About Sickle Cell Disease

Sickle cell disease (SCD) affects more than 100,000 people in the United States,¹ an estimated 52,000 people in Europe² and millions of people throughout the world, particularly among those whose ancestors are from sub-Saharan Africa.³ It also affects people of Hispanic, South Asian, Southern European and Middle Eastern ancestry.⁴ 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. When sickle hemoglobin becomes deoxygenated, it polymerizes to form rods, which deforms the red blood cells into sickled – crescent-shaped, rigid – cells.^{4,5,6} The recurrent sickling process causes destruction of the red blood cells and hemolytic anemia (low hemoglobin due to red blood cell destruction) and blockages in capillaries and small blood vessels (vaso-occlusion), which impede the flow of blood and oxygen delivery throughout the body, commonly referred to as vaso-occlusive crises (VOCs). The diminished oxygen delivery to tissues and organs can lead to life-threatening complications, including stroke and irreversible organ damage.^{5,6,7,8} Complications of SCD begin in early childhood and can include neurocognitive impairment, acute chest syndrome, and silent and overt stroke, among other serious issues.⁹

About Oxbryta® (voxelotor)

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, Oxbryta inhibits sickle hemoglobin polymerization and the resultant sickling and destruction of red blood cells leading to hemolysis and hemolytic anemia, 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.

In November 2019, the U.S. Food and Drug Administration (FDA) granted accelerated approval for Oxbryta tablets for the treatment of SCD in adults and children 12 years of age and older, and in December 2021, the FDA expanded the approved use of Oxbryta for the treatment of SCD in patients 4 years of age and older in the United States.¹⁰ As a condition of accelerated approval for patients ages 4 and older in the United States, 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 14 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 received the prestigious 2021 Prix Galien USA award for "Best Biotechnology Product" from The Galien Foundation.

Oxbryta has been granted Priority Medicines (PRIME) designation from the European Medicines Agency (EMA), Oxbryta was designated by the European Commission (EC) as an orphan medicinal product for the treatment of patients with SCD, and Oxbryta was granted Promising Innovative Medicine (PIM) designation in the United Kingdom from the Medicines and Healthcare products Regulatory Agency (MHRA). In February 2022, the European Commission (EC) granted Marketing Authorization for Oxbryta for the treatment of hemolytic anemia due to SCD in adult and pediatric patients 12 years of age and older as monotherapy or in combination with hydroxycarbamide (hydroxyurea). In addition, Oxbryta has been approved in the United Arab Emirates (UAE) and Oman for the treatment of SCD in adults and children 12 years of age and older.

Please click here for [Important Safety Information](#) and full [Prescribing Information](#), including [Patient Information](#) for Oxbryta in the U.S.

About GBT601

Discovered and designed by GBT's research and development team, GBT021601 (GBT601) has the same mechanism of action as Oxbryta® (voxelotor), but with the potential for greater efficacy by achieving higher hemoglobin levels and occupancy at lower doses. GBT601 is being studied in a Phase 1 study assessing the safety, tolerability, pharmacokinetics and pharmacodynamics of GBT601 in patients with SCD ages 18 to 60 years. The Phase 2 portion of a Phase 2/3 study of GBT601 is expected to initiate in mid-2022. The U.S. Food and Drug Administration has granted both orphan drug and rare pediatric disease designations for GBT601 for the treatment of SCD.

About Inclacumab

Inclacumab is a novel, fully human monoclonal antibody that selectively targets P-selectin, a protein that mediates cell adhesion and is clinically validated to reduce pain due to VOCs in people with SCD. Preclinical results suggest that inclacumab has the potential to be a best-in-class option for reducing VOCs in people with SCD, with the potential for quarterly, rather than monthly dosing. GBT has exclusive worldwide rights to inclacumab as part of the company's licensing agreement with Roche. The safety, tolerability and pharmacokinetics of inclacumab have been evaluated by Roche in more than 700 non-SCD patients. The U.S. Food and Drug Administration has granted both orphan drug and rare pediatric disease designations for inclacumab for the treatment of SCD.

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, starting with sickle cell disease (SCD). Founded in 2011, GBT is delivering on its goal to transform the treatment and care of SCD, a lifelong, devastating inherited blood disorder. The company has introduced Oxbryta® (voxelotor), the first

FDA-approved medicine that directly inhibits sickle hemoglobin (HbS) 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 Phase 3 development to address pain crises associated with the disease, and GBT021601 (GBT601), the company's next generation HbS polymerization inhibitor. In addition, GBT's drug discovery teams are working on new targets to develop the next generation of treatments for SCD. To learn more, please visit www.gbt.com and follow the company on Twitter [@GBT_news](https://twitter.com/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, commitment, dedication, focus, goals, mission, vision, and positioning; the safety, efficacy, and mechanism of action of Oxbryta, and other product characteristics; the commercialization, awareness, delivery, availability, use, and commercial and medical potential of Oxbryta; making Oxbryta available to more patients and related progress; presentation of data at EHA and their significance; the significance and use of real-world evidence; ongoing and planned studies, clinical trials and registries, and related protocols, activities, timing, and other expectations; impacting the treatment, care, and course of SCD and mitigating related complications; significance of study results of GBT601, including supporting its advancement; safety, efficacy, mechanism of action, advancement and potential of inclacumab, GBT601 and GBT's other drug candidates and its pipeline; 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 research, development, manufacture, distribution, and commercialization activities; government and third-party payer actions, including those relating to reimbursement and pricing; risks and uncertainties relating to competitive treatments 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 activities under GBT's collaboration, license and distribution agreements; along with those risks set forth in GBT's Annual Report on Form 10-K for the fiscal year ended December 31, 2021, and in GBT's most recent Quarterly Report on Form 10-Q 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. Centers for Disease Control and Prevention website. Sickle Cell Disease Research. <https://www.cdc.gov/ncbddd/hemoglobinopathies/scdc-understanding-sickle-cell-disease.html>. Accessed February 23, 2022.
2. European Medicines Agency. <https://www.ema.europa.eu/en/medicines/human/orphan-designations/eu3182125>. Accessed February 23, 2022.
3. Centers for Disease Control and Prevention website. Sickle Cell Disease (SCD). <https://www.cdc.gov/ncbddd/sicklecell/data.html>. Accessed February 23, 2022.
4. National Heart, Lung, and Blood Institute website. Sickle Cell Disease. <https://www.nhlbi.nih.gov/health-topics/sickle-cell-disease>. Accessed February 23, 2022.
5. Kato GJ, et al. *Nat Rev Dis Primers*. 2018;4:18010.
6. Rees DC, et al. *Lancet*. 2010;376(9757):2018-2031.
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. Kanter J, et al. *Blood Rev*. 2013 Nov;27(6):279-87.
10. Oxbryta (voxelotor) tablets and tablets for oral suspension prescribing information. South San Francisco, Calif. Global Blood Therapeutics, Inc.; December 2021.

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