



## U.S. FDA Approves Supplemental New Drug Application for Expanded Indication of Oxbryta® (voxelotor) for Children as Young as 4 Years of Age with Sickle Cell Disease

December 17, 2021

*New dispersible tablet dosage form also approved*

*Oxbryta is the first medicine that addresses the root cause of red blood cell sickling*

**SOUTH SAN FRANCISCO, Calif., Dec. 17, 2021 (GLOBE NEWSWIRE)** -- Global Blood Therapeutics, Inc. (GBT) (NASDAQ: GBT) today announced the U.S. Food and Drug Administration (FDA) has granted accelerated approval of a supplemental New Drug Application (sNDA) for Oxbryta® (voxelotor) tablets for the treatment of sickle cell disease (SCD) in children ages 4 to less than 12 years. This approval expands the previously approved use of Oxbryta to treat SCD in patients ages 12 years and older in the United States. The FDA also approved GBT's separate New Drug Application (NDA) for Oxbryta (voxelotor) tablets for oral suspension, a new dispersible, once-daily tablet dosage form suitable for patients ages 4 to less than 12 years as well as for older patients who have difficulty swallowing whole tablets. Oxbryta is the first and only approved medicine that directly targets sickle hemoglobin polymerization, the root cause of the sickling and destruction of red blood cells in SCD.

"For decades, the sickle cell disease community has been profoundly underserved, and there have been limited treatment options for younger patients with their whole lives ahead of them. Complications of SCD that can cause irreversible organ damage are known to begin in the first few years of life, which is why earlier intervention is critical," said Ted W. Love, M.D., president and chief executive officer of GBT. "Today's FDA approval of Oxbryta for children as young as 4 years old – and with a pediatric-friendly dosage form – is an important advance in the treatment of this devastating, lifelong condition. GBT is proud to lead the development of new medicines to address the inadequacies of care for SCD patients."

Of the more than 100,000 people in the United States living with SCD,<sup>1</sup> an inherited blood disorder that causes lifelong health challenges, approximately 16,000 are children between the ages of 4 to 11 years.<sup>2</sup> Complications of SCD begin in early childhood and include neurocognitive impairment, acute chest syndrome, and silent and overt stroke, among other serious issues.<sup>3</sup> In addition, SCD limits children's educational attainment and social lives due to disease complications that often lead to repeated hospitalizations.<sup>4-6</sup> Early intervention and treatment of SCD are critical and have shown potential to modify the course of this disease, reduce symptoms and events, prevent long-term organ damage and extend life expectancy.<sup>7</sup>

Oxbryta will now be available in two dosage forms for patients 4 years and older based on the patient's age, weight, and ability to swallow tablets: 500 mg tablets and 300 mg dispersible tablets. The dispersible tablet form includes grape flavoring and is intended to be dispersed in room-temperature clear drinks for ease of swallowing (such as drinking water or clear soda), making Oxbryta easier to take for patients who have difficulty swallowing whole tablets, particularly younger children.

The FDA's approval of the sNDA is based on data from the open-label Phase 2a HOPE-KIDS 1 Study (GBT440-007), which showed that weight-based treatment with the dispersible tablet formulation of Oxbryta resulted in rapid and sustained improvements in hemoglobin. Concurrent reduction of hemolysis (or red blood cell destruction) was also demonstrated.<sup>8</sup>

"As clinicians, we have had very few approved treatment options for sickle cell disease and many patients are untreated, which is very troubling for younger children who may benefit from early intervention," said Clark Brown, M.D., Ph.D., director of sickle cell clinical research at the Aflac Cancer and Blood Disorders Center of Children's Healthcare of Atlanta and a primary investigator of the Phase 2a HOPE-KIDS 1 Study. "This approval is a significant milestone in the treatment of younger children with SCD – providing a therapy that addresses the root cause of the disease. I believe the new dispersible tablets can help patients and their caregivers achieve daily beneficial treatment and that Oxbryta will make a meaningful difference in improving the lives of children living with sickle cell disease."

"The Sickle Cell Disease Association of America congratulates GBT for the approval of Oxbryta in children as young as 4 years old. Having the new formulation and approval down to 4 years of age is meaningful for families living with sickle cell disease and the community more broadly," said Lewis Hsu, M.D., Ph.D., chief medical officer of the Sickle Cell Disease Association of America. "Due to the many medical complications associated with sickle cell disease, kids face challenges every day in their ability to go to school and have a typical childhood. Adding another new FDA-approved treatment option for children will enhance care and provide more choices for children living with sickle cell disease. SCDAA will advocate for patient-centered decision aids to guide choices. We will work closely with GBT, our partners, and the sickle cell community to promote awareness and education about this new therapy to allow patients to make informed decisions, while advocating for equitable access to care."

The FDA instituted its accelerated approval pathway to allow for earlier approval of drugs that treat serious conditions and that fill an unmet medical need based on a surrogate endpoint.<sup>9</sup> 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 flow velocity to assess the ability of the therapy to decrease stroke risk in children 2 to 14 years of age. In addition, GBT is continuing to conduct the HOPE-KIDS 1 Study to demonstrate the benefit of Oxbryta and support its potential use in children with SCD as young as 9 months of age, and an ongoing open-label extension study for all patients less than 18 years of age who have participated in Oxbryta clinical trials.

GBT is committed to ensuring that patients who are prescribed Oxbryta can access their medicine. GBT Source Solutions® was established by GBT as a comprehensive program for patients who are prescribed Oxbryta that provides a wide range of practical, educational and financial support

customized to each patient's needs. GBT Source Solutions provides support by reviewing insurance coverage options and explaining benefits; explaining specialty pharmacy benefits and working with the specialty pharmacies that coordinate shipments of Oxbryta; helping eligible, commercially insured patients with co-pay assistance; and helping appropriate patients stay on treatment with a nurse support team. More information is available at [Oxbryta.com](http://Oxbryta.com) or 1-833-428-4968 (1-833-GBT-4YOU).

### **About Sickle Cell Disease**

Sickle cell disease (SCD) affects more than 100,000 people in the United States,<sup>1</sup> an estimated 52,000 people in Europe,<sup>10</sup> and millions of people throughout the world, particularly among those whose ancestors are from sub-Saharan Africa.<sup>11</sup> It also affects people of Hispanic, South Asian, Southern European and Middle Eastern ancestry.<sup>11</sup> 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.<sup>12</sup> 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.<sup>7, 12-13</sup> 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.<sup>7, 13-15</sup> Complications of SCD begin in early childhood and can include neurocognitive impairment, acute chest syndrome, and silent and overt stroke, among other serious issues.<sup>3</sup>

### **About Oxbryta® (voxelotor) Tablets and Tablets for Oral Suspension**

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 U.S. FDA expanded the approved use of Oxbryta for the treatment of SCD in patients 4 years of age and older.<sup>16</sup>

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 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 December 2021, the Committee for Medicinal Products for Human Use (CHMP) of the EMA adopted a positive opinion recommending marketing authorization for Oxbryta in Europe for the treatment of hemolytic anemia due to SCD in adults and pediatric patients 12 years of age and older as monotherapy or in combination with hydroxycarbamide (hydroxyurea). The Ministry of Health and Prevention (MOHAP) in the United Arab Emirates (UAE) has granted marketing authorization for Oxbryta for the treatment of SCD in adults and children 12 years of age and older.

### **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 healthcare provider or get emergency medical help right away if they get rash, hives, shortness of breath (difficult breathing) or swelling of the face.

The most common side effects of Oxbryta include headache, diarrhea, stomach-area (abdominal) pain, nausea, rash or hives, and fever. The most common side effects of Oxbryta in children ages 4 to less than 12 years of age include fever, vomiting, rash, stomach-area (abdominal) pain, diarrhea, and headache. These are not all the possible side effects of Oxbryta. Before taking Oxbryta, patients should tell their healthcare 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 2 weeks after the last dose.

Patients should tell their healthcare 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 and may affect the results of certain blood tests.

Patients are advised to call their doctor for medical advice about side effects. Side effects can be reported to 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](http://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) tablets and tablets for oral suspension, 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 wave of potential treatments for SCD. To learn more, please visit [www.gbt.com](http://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, dedication, commitment, focus, goals, mission and vision; safety, efficacy and mechanism of action of Oxbritya and other product characteristics; significance of reducing sickling and hemolysis and raising hemoglobin; commercialization, delivery, availability, use and commercial and medical potential of Oxbritya; ongoing and planned studies, clinical trials and registries, and related protocols, activities, timing and other expectations; significance of the FDA’s approval of GBT’s regulatory submissions to expand the approved use of Oxbritya for more patients and in a pediatric formulation in the U.S., including in advancing the treatment of SCD, the suitability, use and potential of such pediatric formulation and the impact on patients, their caregivers and others; impact of having a new treatment option on the care for children living with SCD, and benefit of earlier intervention in SCD; GBT’s commitment to ensuring access to Oxbritya, including the availability, use and impact of GBT Source; expanding the approved use of Oxbritya to treat patients in Europe and other territories, including potential regulatory review, timing and approval; altering the treatment, course and care of SCD and mitigating related complications; safety, efficacy, mechanism of action, advancement and potential of GBT’s drug candidates and 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 Oxbritya; 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 Oxbritya; the risks regulatory authorities may require additional studies or data to support continued commercialization of Oxbritya; 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, 2020, 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.

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