

Calliditas Therapeutics Submits Supplemental New Drug Application to U.S. Food and Drug Administration for Full Approval of TARPEYO®

Calliditas Therapeutics AB (Nasdaq: CALT, Nasdaq Stockholm: CALTX) (“Calliditas”) today announced the submission of a supplemental New Drug Application (“sNDA”) to the U.S. Food and Drug Administration (“FDA”) seeking full approval of TARPEYO® (budesonide) delayed release capsules for the entire study population from the Phase 3 NeflgArd study.

TARPEYO is currently approved under accelerated approval to reduce proteinuria in adults with primary IgA nephropathy (“IgAN”) at risk of rapid disease progression, generally a urine protein-to-creatinine ratio (UPCR) ≥ 1.5 g/g.

The sNDA submission is based on the full data set from the Phase 3 NeflgArd clinical trial, a randomized, double-blind, multicenter study which assessed the efficacy and safety of TARPEYO (developed under the project name Nefecon®) dosed at 16 mg once daily versus placebo on a background of optimized RASi therapy in adult patients with primary IgAN. The trial met its primary endpoint, with TARPEYO demonstrating a highly statistically significant benefit over placebo (p value < 0.0001) in estimated glomerular filtration rate (eGFR) over the two-year period of 9-months of treatment with TARPEYO or placebo and 15-months of follow-up off drug.

“The eGFR treatment benefit observed across the entire study population, irrespective of UPCR levels, provides further evidence that targeting IgAN at its source can offer patients a treatment that holds the promise of being disease modifying. We are pleased to be able to provide the FDA with the full results of our Phase 3 study, and we look forward to interactions with the FDA regarding full approval of TARPEYO,” stated Renée Aguiar-Lucander, Chief Executive Officer of Calliditas Therapeutics.

In addition to the U.S. FDA submission, Calliditas is collaborating with its European commercial partner, STADA Arzneimittel AG, to seek full approval of Nefecon (branded as Kinpeygo®) by the European Commission in the full study population.

Indication

TARPEYO® (budesonide) delayed release capsules is a corticosteroid indicated to reduce proteinuria in adults with primary immunoglobulin A nephropathy (IgAN) at risk of rapid disease progression, generally a urine protein-to-creatinine ratio (UPCR) ≥ 1.5 g/g.

This indication is approved under accelerated approval based on a reduction in proteinuria. It has not been established whether TARPEYO slows kidney function decline in patients with IgAN. Continued approval for this indication may be contingent upon verification and description of clinical benefits in a confirmatory clinical trial.

Important Safety Information

Contraindications: TARPEYO is contraindicated in patients with hypersensitivity to budesonide or any of the ingredients of TARPEYO. Serious hypersensitivity reactions, including anaphylaxis, have occurred with other budesonide formulations.

Warnings and Precautions

Hypercorticism and adrenal axis suppression: When corticosteroids are used chronically, systemic effects such as hypercorticism and adrenal suppression may occur. Corticosteroids can reduce the response of the hypothalamus-pituitary-adrenal (HPA) axis to stress. In situations where patients are subject to surgery or other stress situations, supplementation with a systemic corticosteroid is recommended. When discontinuing therapy [*see Dosing and Administration*] or switching between corticosteroids, monitor for signs of adrenal axis suppression.

Patients with moderate to severe hepatic impairment (Child-Pugh Class B and C, respectively) could be at an increased risk of hypercorticism and adrenal axis suppression due to an increased systemic exposure to oral budesonide. Avoid use in patients with severe hepatic impairment (Child-Pugh Class C). Monitor for increased signs and/or symptoms of hypercorticism in patients with moderate hepatic impairment (Child-Pugh Class B).

Risks of immunosuppression: Patients who are on drugs that suppress the immune system are more susceptible to infection than healthy individuals. Chicken pox and measles, for example, can have a more serious or even fatal course in susceptible patients or patients on immunosuppressive doses of corticosteroids. Avoid corticosteroid therapy in patients with active or quiescent tuberculosis infection; untreated fungal, bacterial, systemic viral, or parasitic infections; or ocular herpes simplex. Avoid exposure to active, easily transmitted infections (eg., chicken pox, measles). Corticosteroid therapy may decrease the immune response to some vaccines.

Other corticosteroid effects: TARPEYO is a systemically available corticosteroid and is expected to cause related adverse reactions. Monitor patients with hypertension, prediabetes, diabetes mellitus, osteoporosis, peptic ulcer, glaucoma, cataracts, a family history of diabetes or glaucoma, or with any other condition in which corticosteroids may have unwanted effects.

Adverse reactions: In clinical studies, the most common adverse reactions with TARPEYO (occurring in $\geq 5\%$ of TARPEYO patients and $\geq 2\%$ higher than placebo) were hypertension (16%), peripheral edema (14%), muscle spasms (13%), acne (11%), dermatitis (7%), weight increase (7%), dyspnea (6%), face edema (6%), dyspepsia (5%), fatigue (5%), and hirsutism (5%).

Drug interactions: Budesonide is a substrate for CYP3A4. Avoid use with potent CYP3A4 inhibitors, such as ketoconazole, itraconazole, ritonavir, indinavir, saquinavir, erythromycin, and cyclosporine. Avoid ingestion of grapefruit juice with TARPEYO. Intake of grapefruit juice, which inhibits CYP3A4 activity, can increase the systemic exposure to budesonide.

Use in specific populations

Pregnancy: The available data from published case series, epidemiological studies, and reviews with oral budesonide use in pregnant women have not identified a drug-associated risk of major birth defects,

miscarriage, or other adverse maternal or fetal outcomes. There are risks to the mother and fetus associated with IgAN. Infants exposed to in utero corticosteroids, including budesonide, are at risk for hypoadrenalism.

Please see [Full Prescribing Information](#).

About TARPEYO¹

Calliditas has introduced TARPEYO, the first FDA-approved therapy for the treatment of the autoimmune renal disease primary IgA Nephropathy, or IgAN, to reduce proteinuria in adults with primary IgAN who are at risk of rapid disease progression, generally a UPCR \geq 1.5g/g. This indication is approved under accelerated approval based on a reduction in proteinuria. It has not been established whether TARPEYO slows kidney function decline in patients with IgAN. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory clinical trial.

TARPEYO is an oral, delayed release formulation of budesonide, a corticosteroid with potent glucocorticoid activity and weak mineralocorticoid activity that undergoes substantial first pass metabolism. TARPEYO is as a 4 mg delayed release capsule and is enteric coated and designed to remain intact until it reaches the ileum. Each capsule contains coated beads of budesonide that target mucosal B-cells present in the ileum, including the Peyer's patches, which are responsible for the production of galactose-deficient IgA1 antibodies (Gd-Ag1) causing IgA nephropathy. It is unclear to what extent TARPEYO's efficacy is mediated via local effects in the ileum vs systemic effects.

About the NeflgArd Study

The global clinical trial NeflgArd is a Phase 3, randomized, double-blind, placebo-controlled, multicenter study to evaluate the efficacy and safety of TARPEYO 16 mg once daily vs placebo in adult patients with primary IgAN (N=364), as an addition to optimized RAS inhibitor therapy. Part A of the study included a 9-month blinded treatment period and a 3-month follow-up period. The primary endpoint was UPCR, and eGFR was a secondary endpoint. Part B included a 12-month observational period off drug and assessed eGFR over the entire 2-year period for patients who were treated with the TARPEYO or placebo regimen in Part A. The full NeflgArd trial met its primary endpoint. Topline data from the full NeflgArd study were reported on March 12, 2023.

About Primary Immunoglobulin A Nephropathy

Primary immunoglobulin A nephropathy (IgA nephropathy or IgAN or Berger's Disease) is a rare, progressive, chronic autoimmune disease that attacks the kidneys and occurs when galactose-deficient IgA1 is recognized by autoantibodies, creating IgA1 immune complexes that become deposited in the glomerular mesangium of the kidney.^{2,3} This deposition in the kidney can lead to progressive kidney damage and potentially a clinical course resulting in end-stage renal disease. IgAN most often develops between late teens and late 30s.^{3,4}

About Calliditas

Calliditas Therapeutics is a biopharma company headquartered in Stockholm, Sweden, focused on identifying, developing, and commercializing novel treatments in orphan indications, with an initial focus on renal and hepatic diseases with significant unmet medical needs.

Calliditas is listed on Nasdaq Stockholm (ticker: CALTX) and the Nasdaq Global Select Market (ticker: CALT).

Visit [Calliditas.com](https://www.calliditas.com) for further information.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, statements regarding Calliditas' strategy, business plans, regulatory submissions, and focus. The words "may," "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," "estimate," "predict," "project," "potential," "continue," "target," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Any forward-looking statements in this press release are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties, and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this press release, including, without limitation, any related to Calliditas' business, operations, continued FDA approval for TARPEYO, the potential to expand TARPEYO's FDA approval to the entire Phase 3 study population, the potential to achieve full approval of Kinpeygo from the EC and MHRA, market acceptance of TARPEYO, clinical trials, supply chain, strategy, goals and anticipated timelines, competition from other biopharmaceutical companies, and other risks identified in the section entitled "Risk Factors" in Calliditas' reports filed with the Securities and Exchange Commission. Calliditas cautions you not to place undue reliance on any forward-looking statements, which speak only as of the date they are made. Calliditas disclaims any obligation to publicly update or revise any such statements to reflect any change in expectations or in events, conditions, or circumstances on which any such statements may be based, or that may affect the likelihood that actual results will differ from those set forth in the forward-looking statements. Any forward-looking statements contained in this press release represent Calliditas' views only as of the date hereof and should not be relied upon as representing its views as of any subsequent date.

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The information was sent for publication, through the agency of the contact persons set out above, on June 21, 2023 at 9.00 a.m. CET.

¹ TARPEYO® (budesonide) [prescribing information]. Stockholm, SE: Calliditas Therapeutics AB; 2021

² Barratt, J., & Feehally, J. (2005). IgA nephropathy. *J Am Soc Nephrol*, 16(7), 2088-2097.
<https://doi.org/10.1681/ASN.2005020134>

³ Barratt, J., Rovin, B. H., Cattran, D., et al. (2020). Why Target the Gut to Treat IgA Nephropathy? *Kidney Int Rep*, 5(10), 1620-1624. <https://doi.org/10.1016/j.ekir.2020.08.009>

⁴ Jarrick, S., Lundberg, S., Welander, A., et al. (2019). Mortality in IgA Nephropathy: A Nationwide Population-Based Cohort Study. *J Am Soc Nephrol*, 30(5), 866-876.
<https://doi.org/10.1681/ASN.2018101017>