

Calliditas Presents Additional Data Analyses from the NeflgArd Phase 3 trial at the American Society of Nephrology (ASN) Kidney Week 2023

Calliditas Therapeutics AB (Nasdaq: CALT, Nasdaq Stockholm: CALTX) (“Calliditas”), today announced data presentations highlighting additional analyses from the Phase 3 NeflgArd study with Nefecon in adults with primary IgA nephropathy (IgAN), as well as pre-clinical data on the treatment of Alport syndrome with setanaxib, a novel NOX inhibitor, presented at the American Society of Nephrology (ASN) Kidney Week 2023 in Philadelphia, PA on November 1-5, 2023.

“The additional analyses of data from the NeflgArd Phase 3 trial that we and our scientific collaborators presented at ASN Kidney Week showcased our commitment to advancing the science in understanding IgA nephropathy and to shaping a better future for patients with rare diseases,” said Richard Philipson, Chief Medical Officer at Calliditas.

Oral Presentation Analyses

NeflgArd Phase 3 Trial full analysis

The Phase 3 double-blind, randomized NeflgArd study evaluated the impact of Nefecon, a novel targeted-release formulation of budesonide, vs placebo on eGFR in adults with IgAN. The 2-year study period consisted of nine months of treatment with Nefecon (16 mg/day) or placebo, followed by a 15-month follow-up period off the study drug. The full analysis of the 364 patients randomized 1:1 to Nefecon or placebo showed:

- A statistically significantly smaller proportion of Nefecon-treated patients saw a 30% eGFR reduction compared to placebo-treated patients
- A delayed progression to a confirmed 30% eGFR reduction was observed in the Nefecon arm compared to the placebo arm
- Use of rescue medication did not alter the response to Nefecon vs placebo according to a pre-defined analysis

Late-Breaking Poster Presentation Analyses

NeflgArd Phase 3 trial population sub-analysis

The 2-year NeflgArd trial included 62 patients with IgAN from mainland China (n=32 in Nefecon arm, n=30 in the placebo arm), with similar baseline characteristics as the global study population. In these patients, Nefecon treatment for 9 months resulted in:

- Lower time-weighted average change in eGFR from baseline in the Nefecon arm
- 66% less deterioration in renal function over the 2-year study period in the Nefecon arm, as well as reduced 2-year eGFR total slope
- 31% greater mean reduction in urine: protein creatinine ratio at 9 months in patients treated with Nefecon vs placebo, which was sustained at 2 years
- A higher proportion of Nefecon-treated patients did not display microhematuria during the observational follow-up period compared to patients who received placebo

Poster Presentations Analyses

Additional analyses were conducted from Part A of the Phase 3 NeflgArd trial(n=160)

- Serum samples collected from patients enrolled in Part A of the NeflgArd study were analyzed for functional protein interaction and showed that Nefecon modulates serum biomarkers associated with proteins known to play a role in the intestinal immune network for IgA production and control of B cell activation. These data further support a disease-modifying effect of Nefecon at the site of IgA synthesis and reinforce the link between the ileal gut-associated lymphoid tissue (GALT) and the kidneys.
- Levels of circulating anti-gliadin IgA and anti-casein IgA were reduced in IgAN patients treated with Nefecon vs placebo in Part A of the NeflgArd study at the 3-, 6- and 9-month mark after randomization. Levels of secretory IgA and fatty acid-binding protein, a gut permeability marker, were unchanged at these same time points. Reduction in IgA antibodies directed at dietary antigens supports a local disease-modifying effect for Nefecon via targeted action in the ileal GALT rather than modulation of gut permeability and antigen exclusion.
- Levels of three soluble biomarkers known for modulating B cell maturation, CD23, CD27, and CD30, were reduced in response to Nefecon 16 mg/day at the 3-, 6-, and 9-month post-randomization mark when compared to placebo responses. The degree of reduction in soluble CD23, CD27, and CD30 correlated with the magnitude of B-cell activating factor (BAFF) reduction at the same three study timepoints. Reduction in CD30 levels also correlated with the magnitude of IgA/IgG immune complex reduction at the 6- and 9-month timepoints. Together, these biomarker data add to the body of evidence supporting a disease-modification effect for Nefecon, including modulation of immune complex formation.

Additional analysis from the full Phase 3 NeflgArd trial

- Modeling analyses leveraging the two-year eGFR total slope from 352 patients enrolled in the Phase 3 trial were applied to the records of 192 real-world IgAN patients to evaluate the long-term clinical potential of Nefecon. Using published linear regression analysis, Nefecon was predicted to substantially delay progression to renal failure, with a modeled 62 % risk reduction vs placebo and a median delay to progression of 12.8 years.

Setanaxib

The potential of setanaxib, a novel dual NOX inhibitor to modulate renal function and fibrosis was evaluated in a mouse model of Alport syndrome, a rare genetic disease characterized by fibrosis and progressive kidney damage. Setanaxib was evaluated alone or in combination with standard of care ramipril, an ACE inhibitor.

- Combined daily oral administration of setanaxib 60mg/kg and ramipril 10mg/kg resulted in a statistically significant reduction of urine albumin and albumin/creatinine ratio compared to vehicle alone after a 2-week and 4-week treatment duration.
- Histological analysis showed that this combination treatment decreased fibrosis and glomerular sclerosis.
- *In silico* and proteomics analyses demonstrated a reduction in both glomerular basement membrane proteins and collagen proteins in mice treated with both setanaxib and ramipril

All presentations are available on the [Presentations and Publications page](#) on the Calliditas' corporate website.

For further information, please contact:

Åsa Hillsten, Head of Investor Relations & Sustainability, Calliditas

Tel.: +46 76 403 35 43, email: asa.hillsten@calliditas.com

The information was sent for publication, through the agency of the contact persons set out above, on November 6, 2023 at 20:30 p.m. CET.

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 commercial stage biopharma company based 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' lead product, developed under the name Nefecon[®], has been granted accelerated approval by the US FDA under the trade name TARPEYO[®] and conditional marketing authorization by the European Commission under the trade name Kinpeygo[®]. Kinpeygo is being commercialized in the European Union Member States by Calliditas' partner, STADA Arzneimittel AG. Additionally, Calliditas is conducting a Phase 2b clinical trial in primary biliary cholangitis and a Phase 2 proof-of-concept trial in head and neck cancer with its NOX inhibitor product candidate, setanaxib. Calliditas' common shares

are listed on Nasdaq Stockholm (ticker: CALTX) and its American Depositary Shares are listed on the Nasdaq Global Select Market (ticker: CALT).

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, commercialization efforts, business plans, regulatory submissions, clinical development plans 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 approval for Nefecon, market acceptance of Nefecon, 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.

References:

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>