Chinook Therapeutics Presents Data During the ISN World Congress of Nephrology 2021

April 15, 2021

- ***Poster presentation on BION-1301 including Gd-IgA1 biomarker data in healthy volunteers from Parts 1 and 2 of the ongoing phase 1b study of BION-1301 and data from the phase 1 IV to SC bioavailability study in healthy volunteers***
- ***Poster presentation on atrasentan's effect to rapidly reduce albuminuria and downregulate intra-renal transcriptional proliferative, inflammatory and fibrotic signaling in the gddY mouse IgAN model***
- ***Poster presentation on atrasentan's effect to attenuate human renal mesangial cell activation induced by endothelin-1 or IgAN patient immune-derived immune complexes in a translational model system***
- ***Two informational poster presentations on the phase 3 ALIGN trial design for atrasentan in IgA nephropathy (IgAN) and the phase 2 AFFINITY trial design for atrasentan in proteinuric glomerular diseases***
- ***Encore poster presentation on CHK-336, a first-in-class oral small molecule lactate dehydrogenase A (LDHA) inhibitor with the potential to treat all subtypes of primary hyperoxaluria (PH) and other disorders arising from excess oxalate***

SEATTLE, April 15, 2021 (GLOBE NEWSWIRE) -- Chinook Therapeutics, Inc. (NASDAQ: KDNY), a biopharmaceutical company focused on the discovery, development and commercialization of precision medicines for kidney diseases, today announced six poster presentations at the ISN World Congress of Nephrology 2021 (WCN '21).

"The depth and breadth of our presence at this year's WCN '21 is a testament to Chinook's role as a leading kidney disease company," said Eric Dobmeier, president and chief executive officer of Chinook. "Our data demonstrating BION-1301's ability to significantly reduce Gd-IgA1 levels in healthy volunteers, as well as the favorable pharmacodynamics of subcutaneous administration of BION-1301, position the program well to move forward in demonstrating its disease-modifying potential for IgA nephropathy patients. In addition, our preclinical poster presentations on atrasentan provide broader insights into its anti-fibrotic and anti-inflammatory properties that are additive and complementary to its proteinuria-lowering mechanism of action."

WCN21-0706: A Phase 1, Open Label, Randomized, Single Dose, Parallel Group Safety and Bioavailability Study of BION-1301 Administered by Intravenous (IV) and Subcutaneous (SC) Routes

BION-1301 is a novel anti-APRIL monoclonal antibody currently in phase 1 clinical development for IgAN. Blocking APRIL is a potential disease-modifying approach to treating IgAN by reducing circulating levels of Gd-IgA1 to prevent the formation of immune complexes that deposit in the glomeruli of the kidney, causing damage.

The ongoing phase 1 multi-center trial (see www.clinicaltrials.gov, identifier NCT03945318) evaluated the safety and tolerability of BION-1301 in 63 healthy volunteers in double-blinded, placebo-controlled single-ascending dose (SAD) and multiple-ascending dose (MAD) settings. Healthy volunteers in the SAD portion of the study received placebo or a single intravenous (IV) dose of BION-1301 ranging from 10 mg to 1350 mg on day 1. Healthy volunteers in the MAD portion of the study received placebo or IV doses of BION-1301 ranging from 50 mg to 450 mg on days 1, 15 and 29 (three doses total).

As previously presented, BION-1301 was well-tolerated with no serious adverse events (SAEs), a pharmacokinetic (PK) half-life of approximately 33 days and demonstrated dose-dependent pharmacodynamic (PD) effects characterized by durable reductions in serum levels of IgA and IgM, with a lesser reduction in IgG. Recently analyzed data from this study in healthy volunteers also demonstrated that BION-1301 produced dose-dependent reductions in serum Gd-IgA1 levels that were greater in magnitude than previously reported for total IgA concentrations. In the MAD cohort, BION-1301 reduced Gd-IgA1 levels by 39%, 51% and 55% on Day 29 following the first two doses but prior to the third dose of BION-1301 at 50 mg, 150 mg and 450 mg, respectively, compared to a mean 6% increase in Gd-IgA1 in the placebo group. Upon further follow-up on Day 85, which was 56 days after the third and final dose of BION-1301, Gd-IgA1 reductions were sustained, with mean reductions of 24%, 48% and 70%, at 50 mg, 150 mg and 450 mg, respectively, compared to a mean 4% increase in Gd-IgA1 in the placebo group. Data figures from Day 85 were not included in the poster presentation, but can be found in Chinook's corporate presentation located on the Events and Presentations section of Chinook's website.

Part 3 of the phase 1 study is ongoing to evaluate BION-1301 in adult IgAN patients in an open-label setting. Preliminary data from Part 3 will be presented at nephrology conferences in 2021.

With the aim to reduce patient burden with a more convenient alternative administration route, BION-1301 was further studied in a single-dose phase 1 study to determine safety and bioavailability of BION-1301 administered via IV infusion or SC injection in healthy volunteers. This was a phase 1, open-label, randomized, parallel group, safety and bioavailability study of 300 mg BION-1301 administered intravenously or subcutaneously to adult healthy volunteers in the United States.

Key highlights from the bioavailability study include the following:

- BION-1301 was well tolerated when administered by both IV and SC routes in healthy volunteers, and no injection site or infusion-related reactions were reported.

- The PK profile of BION-1301 was consistent with previous clinical studies and minimal differences in drug concentration were observed between administration routes after one week, following the absorption phase.

- After SC administration, BION-1301 absorption rate was typical of a monoclonal antibody with bioavailability of approximately 50%.

- Magnitude of pharmacodynamic responses were largely retained with SC dosing compared to IV dosing:
    - SC administration generated approximately 81% of the maximum free APRIL reduction;
    - SC administration generated approximately 75% of the maximum IgA reduction.

- No anti-drug antibodies (ADAs) were observed in the SC cohort

Data generated in this study will be used to enable SC administration of BION-1301 in ongoing and future clinical studies.

WCN21-0358: Selective ETA Antagonist Atrasentan, Rapidly Reduces Albuminuria and Downregulates Intra-renal Pro-Inflammatory and Pro-Fibrotic Transcriptional Networks in the g-ddY Mouse Model of Spontaneous IgA Nephropathy

The effect of short-term treatment of selective ETA antagonist atrasentan was investigated in gddY mice, a spontaneous and accelerated model of IgAN.

Four days of treatment with atrasentan reduced urinary albumin to creatinine ratio (UACR) from baseline by 28%, 62% and 63% at 10 mg/kg/day, 20 mg/kg/day and 30 mg/kg/day, respectively. This effect was statistically significant at the two higher doses.

Five days of treatment with atrasentan demonstrated dose-dependent effects on intra-renal gene expression profiles, assessed by RNA sequencing analysis of the kidney cortex. Gene set enrichment analysis (GSEA) to define hallmark pathways was performed and cross-validated to the transcriptome of kidney biopsy samples from publicly available IgAN patient datasets. In the biopsies of patients with IgAN, the gene pathways found to be dysregulated in the glomeruli included a down-regulation of oxidative metabolism and up-regulation of gene pathways associated with proliferation, inflammation and fibrosis. GSEA showed that treatment with 30 mg/kg of atrasentan in gddY mice consistently reversed the gene pathways found to be dysregulated in IgAN patients.

The dynamic transcriptional changes in the kidney, following only five days of treatment and prior to sustained long-term reductions in albuminuria and blood pressure that could mediate this benefit, are consistent with direct anti-inflammatory and antifibrotic effects of ETA blockade in IgAN. These results support the therapeutic potential of atrasentan in IgAN to reduce proteinuria and kidney inflammation and fibrosis, key drivers of IgAN progression.

WCN21-0398: Human Renal Mesangial Cell Activation Induced by Endothelin-1 or IgA Nephropathy Patient-Derived Immune Complexes is Blocked by Selective ETA Antagonist Atrasentan

Human renal mesangial cell (HRMC) activation is considered the initiating intra-renal event in the pathogenesis of IgAN and occurs in response to the deposition of pathogenic galactose-deficient IgA (Gd-IgA)-containing immune complexes. This activation results in increased cellular proliferation and inflammatory cytokine secretion. The role of ETA receptor activation in HRMC activation in response to endothelin-1 (ET-1) and IgAN patient-derived immune complexes was investigated.

ET-1 resulted in increased HRMC proliferation and IL-6 secretion, which was blocked by atrasentan in a concentration-dependent manner. RNA sequencing and gene set enrichment analysis of HRMCs following treatment with ET-1 identified upregulation of cell proliferation, pro-fibrotic and pro-inflammatory pathways, which were reversed with atrasentan treatment.

HRMCs cultured with purified IgA-containing immune complexes isolated from IgAN patient serum, had five-fold higher proliferation compared to treatment with IgA-complexes from matched healthy controls. Atrasentan significantly attenuated the proliferation induced by IgAN patient-derived IgA-containing immune complexes.

Exogenous ET-1 directly stimulates mesangial cell activation, inducing proliferative, pro-inflammatory and pro-fibrotic pathways, which can be blocked by atrasentan. Atrasentan prevented HRMC hyperproliferation in response to IgAN patient-derived immune complexes. This suggests that the autocrine action of endogenously produced ET-1 on ETA receptors contributes to mesangial cell activation resulting from pathogenic IgA-containing immune complexes. These results support the therapeutic potential of atrasentan in patients with IgAN, not only via its well characterized effect of reducing proteinuria, but also by potentially reducing mesangial cell activation, a hallmark of IgA nephropathy.

WCN21-0848: A Phase 3, Randomized, Double-Blind, Placebo-Controlled Study of Atrasentan in Patients with IgA Nephropathy (The ALIGN Study)

The ALIGN Study (see www.clinicaltrials.gov, identifier NCT04573478) is a global, randomized, multicenter, double-blind, placebo-controlled phase 3 clinical trial comparing the efficacy and safety of atrasentan versus placebo in patients with IgAN at risk of progressive loss of kidney function. Approximately 320 patients with biopsy-proven IgAN will be randomized to receive 0.75 mg atrasentan or placebo as a once-daily oral pill for approximately 2.5 years. Patients will continue receiving an optimized and stable dose of a RASi as standard of care. The study will also include patients that are unable to tolerate RASi therapy.

The primary efficacy endpoint of the ALIGN Study is to evaluate the effect of atrasentan versus placebo on proteinuria as measured by urine protein to creatinine ratio (UPCR) from baseline to 24 weeks. Secondary and exploratory objectives include evaluating the change in kidney function over time as measured by eGFR, safety and tolerability, as well as quality of life. Chinook expects to report top-line data from the 24-week primary endpoint

efficacy analysis in 2023.

WCN21-0717: Atrasentan in Patients with Proteinuric Glomerular Diseases (The AFFINITY Study)

The AFFINITY Study (see www.clinicaltrials.gov, identifier NCT04573920) is a phase 2, open-label, basket study to evaluate the efficacy and safety of atrasentan in patients with proteinuric glomerular disease who are at risk of progressive loss of renal function. Four initial cohorts will consist of patients with: IgAN with UPCR of 0.5 to less than 1.0 g/g, focal segmental glomerulosclerosis (FSGS), Alport syndrome and diabetic kidney disease (DKD) in combination with an SGLT2 inhibitor. Additional cohorts may be added to the study over time. Approximately 20 patients will be enrolled in each cohort to receive 0.75 mg atrasentan for 52 weeks. Patients in all cohorts will continue receiving an optimized and stable dose of a RAS inhibitor as standard of care. The AFFINITY Study will enroll patients in the United States, Australia, South Korea, the United Kingdom, Italy and Spain.

The primary efficacy endpoint of the AFFINITY Study is the effect on proteinuria as measured by UPCR in patients with IgAN, FSGS and Alport syndrome and the change in albuminuria as measured by urine albumin to creatinine (UACR) in patients with DKD, from baseline to 12 weeks. Chinook expects to report data from initial cohorts of patients in the AFFINITY Study during 2022.

WCN21-0612: Discovery of CHK-336: A First-in-Class, Liver-Targeted, Small Molecule Inhibitor of Lactate Dehydrogenase for the Treatment of Hyperoxaluria

CHK-336, is a first-in-class, liver-targeted oral small molecule LDHA inhibitor for the treatment of PH. LDHA catalyzes the final step in the production of oxalate in the liver, and therefore LDHA inhibition has the potential to treat all forms of PH – PH1, PH2 and PH3 – as well as other disorders arising from excess oxalate. As previously presented, CHK-336 demonstrates sub-nM enzyme potency and a cellular IC_{50} in hepatocytes across multiple species ranging from 50 to approximately 300 nM. CHK-336 demonstrates tight LDHA binding and a very slow enzyme off-rate, to extend the duration of action and enable the potential of once-daily dosing in humans. CHK-336 was engineered with a liver-targeted distribution profile to effectively block hepatic oxalate synthesis while minimizing systemic exposures.

CHK-336, dosed orally, once-daily, produced significant reductions in urinary oxalate in a mouse model of PH1, with the majority of CHK-336-treated mice reaching the normal range seen in wild-type mice. The non-clinical safety assessment of CHK-336 supports continued development and CHK-336 is currently progressing through IND-enabling GLP studies with IND submission planned for late 2021/early 2022.

About Chinook Therapeutics, Inc.
Chinook Therapeutics, Inc. is a clinical-stage biotechnology company developing precision medicines for kidney diseases. Chinook's product candidates are being investigated in rare, severe chronic kidney disorders with opportunities for well-defined clinical pathways. Chinook's lead program is atrasentan, a phase 3 endothelin receptor antagonist for the treatment of IgA nephropathy and other proteinuric glomerular diseases. BION-1301, an anti-APRIL monoclonal antibody is being evaluated in a phase 1b trial for IgA nephropathy. In addition, Chinook is advancing CHK-336, an oral small molecule LDHA inhibitor for the treatment of primary hyperoxaluria, as well as research programs for other rare, severe chronic kidney diseases. Chinook is building its pipeline by leveraging insights in kidney single cell RNA sequencing, human-derived organoids and new translational models, to discover and develop therapeutics with differentiating mechanisms of action against key kidney disease pathways. To learn more, visit www.chinooktx.com.

Cautionary Note on Forward-Looking Statements
Certain of the statements made in this press release are forward looking, including those relating to Chinook's business, future operations, advancement of its product candidates and product pipeline, clinical development of its product candidates, including expectations regarding timing of initiation and results of clinical trials. In some cases, you can identify these statements by forward-looking words such as "may," "will," "continue," "anticipate," "intend," "could," "project," "expect" or the negative or plural of these words or similar expressions. Forward-looking statements are not guarantees of future performance and are subject to risks and uncertainties that could cause actual results and events to differ materially from those anticipated, including, but not limited to, our ability to develop and commercialize our product candidates, including initiation of clinical trials, whether results of early clinical trials or preclinical studies, such as those described in this press release, will be indicative of the results of future trials, our ability to obtain and maintain regulatory approval of our product candidates, our ability to operate in a competitive industry and compete successfully against competitors that may be more advanced or have greater resources than we do, our ability to obtain and adequately protect intellectual property rights for our product candidates and the effects of COVID-19 on our clinical programs and business operations. Many of these risks are described in greater detail in our filings with the SEC. Any forward-looking statements in this press release speak only as of the date of this press release. Chinook assumes no obligation to update forward-looking statements whether as a result of new information, future events or otherwise, after the date of this press release.

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Source: Chinook Therapeutics, Inc.