Chinook Therapeutics Presents Data Across Kidney Disease Pipeline During the American Society of Nephrology (ASN) Kidney Week 2020 Reimagined

October 22, 2020

- ***Informational poster presentation on phase 3 ALIGN trial design for atrasentan in IgA nephropathy***
- ***Encore poster presentation on phase 1 healthy volunteer data for BION-1301 in IgA nephropathy***
- ***Preclinical 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***
- ***Chinook to host investor conference call and webcast today at 4:30 pm EDT with Richard Lafayette, M.D., F.A.C.P., Associate Professor of Nephrology and Director of the Stanford Glomerular Disease Center***

VANCOUVER, British Columbia and SEATTLE, Oct. 22, 2020 (GLOBE NEWSWIRE) -- Chinook Therapeutics, Inc. (NASDAQ: KDNY), a clinical-stage biopharmaceutical company focused on the discovery, development and commercialization of precision medicines for kidney diseases, today announced three poster presentations and one oral presentation at ASN's Kidney Week 2020 Reimagined.

"Our strong presence at this year's ASN showcases the breadth of Chinook's clinical and research programs for kidney diseases with significant unmet medical needs, including presentations illustrating developmental progress on our atrasentan and BION-1301 programs, as well as extensive preclinical data on our CHK-336 and ADPKD programs," said Andrew King, D.V.M., Ph.D., head of renal discovery and translational medicine of Chinook. "In particular, we are excited to unveil our first home-grown program, CHK-336, which is a potential first-in-class therapy for the treatment of primary hyperoxaluria. CHK-336's differentiated profile as an oral potent small molecule may enable greater target inhibition relative to injectable siRNAs currently in development, potentially resulting in superior urinary oxalate reduction and a more favorable impact on clinical manifestations, including kidney stones, as well as overall disease progression."

King continued, "Our rapid trajectory is a testament to our strong research team and academic collaborations, positioning Chinook as a leader in developing precision medicines for kidney disease."

INFO29: **Phase 3, Randomized, Double-Blind, Placebo-Controlled Study of Atrasentan in Patients with IgA Nephropathy (The ALIGN Study)**

Atrasentan is a potent, selective endothelin A receptor (ET_A) antagonist that has been evaluated in over 5,300 diabetic kidney disease patients in studies that demonstrated clinically significant and sustained reductions in proteinuria, as well as reduced risk of kidney function decline, when administered on top of a maximally tolerated dose of a RAS inhibitor (RASi). Blocking ET_A can reduce mesangial cell activation, protect podocytes and reduce proteinuria as well as tubulointerstitial inflammation and fibrosis, all hallmark characteristics of progressive IgA nephropathy.

Chinook's Phase 3 ALIGN trial (see www.clinicaltrials.gov, identifier NCT04573478), which is planned to begin enrollment in early 2021, will assess the efficacy, safety and tolerability of atrasentan in IgA nephropathy patients at risk of progressive kidney function loss. Approximately 320 patients across North America, South America, Europe and Asia-Pacific with biopsy-proven IgA nephropathy who are already on a maximally tolerated and stable dose of RASi will be randomized to receive 0.75 mg atrasentan or placebo daily for 132 weeks. The study will also include a cohort of patients who are unable to tolerate RASi. Patients will have assessments of safety and efficacy over 2.5 years. An open-label extension will allow participants who complete the study to receive active atrasentan.

- The primary endpoint for the ALIGN study is change in proteinuria, based on paired 24-hour urine collections from baseline to week 24.
- The key secondary endpoint for the study is change in estimated glomerular filtration rate (eGFR) from baseline to week 136, which is four weeks after discontinuation of treatment.
- Key patient enrollment criteria for the ALIGN study include ≥18 years of age, a history of biopsy-proven IgA nephropathy, a urinary protein to creatinine ratio (UPCR) of at least 1g/g based on a first morning void sample, eGFR of at least 30ml/min, no recent use of systemic immunosuppressants and no other cause of other chronic kidney disease.

PO1843: Results of a Phase 1 Trial to Investigate the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of BION-1301 in Healthy Volunteers

BION-1301 is a novel anti-APRIL monoclonal antibody currently in phase 1 clinical development for IgA nephropathy. Blocking APRIL is a potential disease-modifying approach to treating IgA nephropathy by reducing circulating levels of galactose-deficient IgA 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, key highlights from the poster presentation include the following:

- BION-1301 was well-tolerated, with no SAEs, treatment discontinuations or events meeting stopping criteria, across a wide range of doses.
  - Non-neutralizing ADAs occurred in less than 10% of subjects with no correlation to dose.
- The PK profile of BION-1301 was well-behaved, generally dose proportional, and had a half-life of approximately 33 days, suggesting the potential for monthly dosing.
- BION-1301 demonstrated a dose-dependent increase in target engagement as measured by free APRIL levels in serum; over 90% reduction in free APRIL concentrations was achieved with a single 450 mg dose.
- BION-1301 dose-dependently and durably reduced IgA and IgM levels, and to a lesser extent, IgG levels. At all doses tested, IgG levels remained in the normal lab range, thereby providing a pharmacodynamic window to potentially exploit reductions in IgA, while tempering reductions in IgG.
- Work is underway to develop Gd-IgA1 and other biomarker assays to fully characterize the pharmacodynamic response to BION-1301.

Part 3 of the phase 1 study is currently enrolling adult patients with IgA nephropathy in an open-label setting. In this study, BION-1301 is administered by IV infusion every two to four weeks for 12 weeks after which patients may be eligible for a long-term extension trial for an additional 2 years. A phase 1 IV-subcutaneous (SC) bioavailability study in healthy volunteers is ongoing with potential transition to SC administration in the long-term extension and phase 2 studies.

PO1620: Discovery of CHK-336: A First-in-Class, Liver-Targeted, Small Molecule Inhibitor of Lactate Dehydrogenase for the Treatment of Primary Hyperoxaluria

Chinook's first internally-developed therapeutic candidate, CHK-336, is a first-in-class, liver-targeted oral small molecule LDHA inhibitor for the treatment of primary hyperoxaluria (PH). Hyperoxalurias, including PH, are diseases caused by excess oxalate, a potentially toxic metabolite typically filtered by the kidneys and excreted as a waste product in urine. Symptoms of PH include recurrent kidney stones, severe pain, blood in the urine and urinary tract infections, which when left untreated, can result in kidney failure requiring dialysis or dual kidney/liver transplantation. In patients with hyperoxalurias, excess oxalate combines with calcium to form calcium oxalate crystals that deposit in the kidney, resulting in the formation of painful kidney stones and driving progressive kidney damage over time. PH, 1-3 are ultra-rare diseases caused by genetic mutations that result in excess oxalate, and in its most severe forms, can lead to end-stage kidney disease at a young age.

LDHA catalyzes the terminal step in the production of oxalate from glyoxalate in the liver, therefore LDHA inhibition has the potential to treat all forms of PH as well as other disorders arising from excess oxalate. An oral, liver-targeted LDHA small molecule inhibitor has the potential for robust efficacy by rapidly distributing to the site of oxalate production, while minimizing systemic exposures and potential for off-target activity, to facilitate a favorable tolerability profile required in this chronic disease.

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. In order to reduce the potential for any systemic toxicities, the Chinook team engineered a liver-targeted tissue distribution profile using a strategy that involves incorporating structural elements that result in liver-selective OATP transporter uptake and by reducing non-specific passive permeability.

As expected, CHK-336 exhibits a liver-targeted tissue distribution profile in mice, rats and non-human primates with high liver concentrations associated with low plasma and extra-hepatic tissue exposures. Driven by target-mediated drug disposition and the slow off-rate from LDHA, a long liver half-life was observed across species. Human PK predictions are supportive of a low, once-daily oral dose in humans.

To evaluate the efficacy of CHK-336, a mouse model of PH 1 was generated by CRISPR-Cas9 deletion of the Agxt gene and CHK-336 was dosed orally, once-daily for seven days. CHK-336 demonstrated significant reductions in urinary oxalate, 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 advancement into IND-enabling studies, with an excellent in vitro safety profile, low drug-drug interaction potential and a promising non-GLP in vivo safety profile. CHK-336 is currently progressing through IND-enabling studies with phase 1 initiation planned for the second half of 2021.

SA-OR21: Single Cell Transcriptomic Analysis to Define Cellular Heterogeneity in Human ADPKD

Human autosomal dominant polycystic kidney disease (ADPKD) is the most common inherited kidney disease, with approximately 50 percent of patients progressing to end-stage kidney disease (ESKD) by age 60. The kidney has nearly 30 distinct cell types and in ADPKD, cysts arise from less than one percent of nephrons and only from discrete cell populations. Single cell transcriptional resolution is therefore required to define the central molecular drivers of cystogenesis in ADPKD. Through Chinook's academic collaboration with the laboratory of Benjamin Humphreys, M.D., Ph.D., Joseph Friedman Professor of Renal Diseases in Medicine and Chief of Nephrology at Washington University School of Medicine in St. Louis, a single cell transcriptomic atlas of human ADPKD was generated, which has the potential to provide unprecedented mechanistic insight into the disease.

The abstract will be presented in an oral presentation by Yoshiharu Muto, M.D., Ph.D. during the *Kidneyomics: From Cysts to Populations* session on

Saturday, October 24, 2020 from 5:00 – 7:00 pm EDT.

Conference Call and Webcast Details
To access today's conference call, please dial (844) 309-0604 (domestic) or (574) 990-9932 (international) and provide the Conference ID 5981714 to the operator. To access the live webcast and subsequent archived recording of this and other company presentations, please visit the Events & Presentations page in the Investors section of Chinook's website. The archived webcast will remain available for replay on Chinook's website for 90 days.

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, an investigational Phase 3-ready endothelin receptor antagonist for the treatment of IgA nephropathy and other primary glomerular diseases. BION-1301, an investigational anti-APRIL monoclonal antibody is being evaluated in a Phase 1b trial for IgA nephropathy. In addition, Chinook is advancing CHK-336, a small-molecule preclinical development candidate for the treatment of primary hyperoxaluria, as well as research programs for other rare, severe chronic kidney diseases, including polycystic kidney disease. 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, whether results of early clinical trials or preclinical studies 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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