Chinook Therapeutics Presents Data from CHK-336 Phase 1 Trial in Healthy Volunteers and New Insights into the Role of Failed Repair in Chronic Kidney Disease at the 60th European Renal Association (ERA) Congress

June 17, 2023

- ***CHK-336 was generally well tolerated in healthy volunteers (HV) who received single doses up to 500 mg and multiple doses up to 60 mg for 14 days***
- ***Pharmacokinetics (PK) was well characterized with dose-proportional exposures and a half-life that supports once-daily dosing***
- ***Successful implementation of a novel $^{13}C_2$-glycolate tracer established proof-of-mechanism of CHK-336 to block hepatic oxalate production in HVs***
- ***One serious adverse event (SAE) of anaphylaxis occurred in a multiple ascending dose HV who received one 125 mg dose CHK-336, resulting in voluntary study pause***
- ***Additional research presented on the impact of maladaptive tubular epithelial cells on progression of chronic kidney disease***

SEATTLE, June 17, 2023 (GLOBE NEWSWIRE) -- Chinook Therapeutics, Inc. (Nasdaq: KDNY), a biopharmaceutical company focused on the discovery, development and commercialization of precision medicines for kidney diseases, announced a free communication presentation on CHK-336 presented today at the 60th ERA Congress being held virtually and live in Milan, Italy.

“The data presented from the phase 1 study of CHK-336 at this year’s ERA Congress successfully demonstrates hepatic LDH target engagement in healthy volunteers and establishes proof-of-mechanism for CHK-336 to decrease hepatic oxalate production,” said Andrew King, chief scientific officer of Chinook Therapeutics. “As we continue to investigate the SAE observed in the 125 mg MAD cohort and consider next steps, the CHK-336 program will remain paused.”

CHK-336, A First-in-Class Orally Administered LDH Inhibitor: Safety, PK and Target Engagement in a First-in-Human Phase 1 Healthy Volunteer Study

CHK-336 is an oral small molecule LDHA inhibitor with liver-targeted tissue distribution in development for the treatment of patients with primary hyperoxaluria (PH) and other kidney stone disorders driven by endogenous overproduction of oxalate.

The phase 1 single-center trial (see www.clinicaltrials.gov, identifier NCT05367661) was designed to evaluate the safety, tolerability, pharmacokinetic profile of CHK-336 in 104 healthy volunteers in randomized, placebo-controlled, double-blinded, single-ascending dose (SAD) and multiple-ascending dose (MAD) settings. Healthy volunteers in the SAD portion of the study received placebo or a single dose of CHK-336 ranging from 15 mg to 500 mg on day 1. Healthy volunteers in the MAD portion of the study were to receive placebo or multiple doses of CHK-336 ranging from 30 mg to 500 mg given daily for 14 days.

Key highlights from the presentation include the following:

- CHK-336 was generally well tolerated in HVs who received single doses up to 500 mg and multiple doses (14 days) up to 60 mg.
  - There were no dose-related trends in adverse events, vital signs or EKG findings.
  - The most common treatment emergent adverse event was headache in six subjects receiving CHK-336 (8.8%) and no placebo subjects, with no dose-related trend.
- There was one serious adverse event (SAE) of anaphylaxis that occurred in a single HV following the first dose in the 125 mg MAD group. The SAE had a rapid onset within one hour following the first dose and rapidly resolved after treatment with an antihistamine, without requiring epinephrine administration. The HV had clinically significant elevations in serum tryptase levels during the event, confirming anaphylaxis. This SAE resulted in voluntary pausing of the trial to enable further investigation.
- PK was well characterized with dose proportional exposures, a plasma half-life consistent with once daily oral dosing and no exposure accumulation following repeat dosing.
- The successful utilization of a novel $^{13}C_2$-glycolate tracer in the trial establishes proof-of-mechanism for CHK-336 as an orally administered small molecule inhibitor of hepatic LDH. CHK-336 effectively blocked conversion of the $^{13}C_2$-glycolate tracer to $^{13}C_2$-oxalate with maximal inhibition observed following a single dose of CHK-336 at 60-125 mg.

Accumulation of Maladaptive Tubular Epithelial Cells (TECs) is Ubiquitous in Chronic Kidney Diseases and Represents a Common Initiating Mechanism of Disease Progression

Disease-associated maladaptive TECs have been described in rodent models and are characterized by a failed repair phenotype that contributes to tubulointerstitial inflammation and fibrosis. This study explores the significance of maladaptive TECs in the NURTuRE chronic kidney disease (CKD)

cohort by integrating clinical, histological, transcriptomic and proteomic data from blood and urine to gain insights into mechanisms of CKD progression. The NURTuRE consortium biobank comprises patient samples from a broad range of CKD diagnoses and kidney functional states with rich clinical data from over 3,500 subjects.

Human gene signatures for two maladaptive tubule subtypes were identified in human CKD scRNA-Seq datasets. Based on unbiased analysis, maladaptive tubule signatures were found to be among the most highly associated with CKD progression in the NURTuRE cohort and a high maladaptive tubule gene signature score at time of biopsy was significantly associated with shorter renal event-free survival in the NURTuRE cohort (304 patients across 12 disease etiologies). The emergence of maladaptive tubules is associated with disease progression across multiple CKDs and targeting these cells may potentially be an effective strategy to preserve kidney function broadly in CKD.

About Chinook Therapeutics, Inc.
Chinook Therapeutics, Inc. is a clinical-stage biopharmaceutical 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 proteinuric glomerular diseases. Zigakibart (BION-1301), an anti-APRIL monoclonal antibody, is being evaluated in a phase 1/2 trial for IgA nephropathy. CHK-336, an oral small molecule LDHA inhibitor for the treatment of hyperoxalurias, is in phase 1 development. In addition, Chinook's research and discovery efforts are focused on building a pipeline of precision medicines for rare, severe chronic kidney diseases with defined genetic and molecular drivers. Chinook is leveraging insights from kidney single cell RNA sequencing and large CKD patient cohorts that have been comprehensively panomically phenotyped, with retained biosamples and prospective clinical follow-up, to discover and develop therapeutic candidates with mechanisms of action targeted against key kidney disease pathways. To learn more, visit www.chinooktx.com.

Forward-Looking Statements
In addition to historical information, this communication contains forward-looking statements within the meaning of applicable securities law, including statements regarding the advancement of its product candidates and product pipeline, and the clinical development of its product candidates, including expectations regarding the results of clinical trials. In addition, when used in this communication, the words "will," "expects," "could," "would," "may," "anticipates," "intends," "plans," "believes," "seeks," "targets," "estimates," "looks for," "looks to," "continues" and similar expressions, as well as statements regarding our focus for the future, are generally intended to identify forward-looking statements. Each of the forward-looking statements we make in this communication involves risks and uncertainties that could cause actual results to differ materially from these forward-looking statements. Factors that might cause or contribute to such differences include, but are not limited to: expected revenues, cost savings, synergies and other benefits from the proposed merger might not be realized within the expected time frames or at all and costs or difficulties relating to integration matters, including but not limited to employee retention, might be greater than expected; the requisite regulatory approvals and clearances for the proposed transaction may be delayed or may not be obtained (or may result in the imposition of conditions that could adversely affect the combined company or the expected benefits of the proposed merger); the requisite approval of Company stockholders may be delayed or may not be obtained, the other closing conditions to the proposed merger may be delayed or may not be obtained, or the merger agreement may be terminated; business disruption may occur following or in connection with the proposed merger; Novartis or Chinook's businesses may experience disruptions due to transaction-related uncertainty or other factors making it more difficult to maintain relationships with employees, other business partners or governmental entities; the milestones for the proposed CVRs may not be achieved; the possibility that the proposed merger is more expensive to complete than anticipated, including as a result of unexpected factors or events; and diversion of management's attention from ongoing business operations and opportunities as a result of the proposed merger or otherwise. Additional factors that may affect the future results of Novartis and Chinook are set forth in their respective filings with the U.S. Securities and Exchange Commission (the "SEC"), including in the most recently filed annual report of Novartis on Form 20-F, subsequently filed Current Reports on Form 6-K and other filings with the SEC, which are available on the SEC's website at www.sec.gov, and Chinook's most recently filed Annual Report on Form 10-K, subsequent Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and other filings with the SEC, which are available on the SEC's website at www.sec.gov. The risks described in this communication and in Novartis and Chinook's filings with the SEC should be carefully reviewed. Undue reliance should not be placed on these forward-looking statements, which speak only as of the date they are made. Novartis and Chinook undertake no obligation to publicly release any revisions to the forward-looking statements or reflect events or circumstances after the date of this communication, except as required by law.

Additional Information and Where to Find It
In connection with the proposed merger between Novartis and Chinook, Novartis and Chinook intend to file relevant materials with the SEC, including a preliminary and definitive proxy statement to be filed by Chinook. The definitive proxy statement and proxy card will be delivered to the stockholders of Chinook in advance of the special meeting relating to the proposed merger. CHINOOK'S STOCKHOLDERS ARE URGED TO READ THE DEFINITIVE PROXY STATEMENT IN ITS ENTIRETY WHEN IT BECOMES AVAILABLE AND ANY OTHER DOCUMENTS FILED BY EACH OF NOVARTIS AND CHINOOK WITH THE SEC IN CONNECTION WITH THE PROPOSED MERGER OR INCORPORATED BY REFERENCE THEREIN BECAUSE THEY WILL CONTAIN IMPORTANT INFORMATION ABOUT THE PROPOSED TRANSACTION AND THE PARTIES TO THE PROPOSED TRANSACTION. Investors and security holders will be able to obtain a free copy of the proxy statement and such other documents containing important information about Novartis and Chinook, once such documents are filed with the SEC, through the website maintained by the SEC at www.sec.gov. Novartis and Chinook make available free of charge at the Novartis website and Chinook's website, respectively (in the "Investors" section), copies of materials they file with, or furnish to, the SEC. The contents of the websites referenced above are not deemed to be incorporated by reference into the proxy statement.

Participants in the Solicitation
This document does not constitute a solicitation of proxy, an offer to purchase or a solicitation of an offer to sell any securities. Novartis, Chinook and their respective directors, executive officers and certain employees may be deemed to be participants in the solicitation of proxies from the stockholders of Chinook in connection with the proposed merger. Information regarding the special interests of these directors and executive officers in the proposed merger will be included in the definitive proxy statement referred to above. Security holders may also obtain information regarding the names, affiliations and interests of the Novartis directors and executive officers in the Novartis Annual Report on Form 20-F and Form 20-F/A for the fiscal year ended December 31, 2022, which were filed with the SEC on February 1, 2023, and May 15, 2023, respectively. Security holders may obtain information regarding the names, affiliations and interests of Chinook's directors and executive officers in Chinook's Annual Report on Form 10-K for the fiscal year ended December 31, 2022, which was filed with the SEC on February 27, 2023, and its definitive proxy statement for the 2023 annual meeting of stockholders, which was filed with the SEC on April 28, 2023. To the extent the holdings of Chinook's securities by Chinook's directors and executive officers have changed since the amounts set forth in Chinook's definitive proxy statement for its 2023 annual meeting of stockholders, such changes have been or will be reflected on Statements of Change in Ownership on Form 4 filed with the SEC. Additional information regarding the interests of such individuals in the proposed merger will be included in the definitive proxy statement relating to the proposed merger

when it is filed with the SEC. These documents (when available) may be obtained free of charge from the SEC's website at www.sec.gov, the Novartis website at https://www.novartis.com and Chinook's website at https://www.chinooktx.com. The contents of the websites referenced above are not deemed to be incorporated by reference into the proxy statement.

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