First Report of Positive Dose Escalation Data Supports Best-in-Class Profile for Investigational Exarafenib as a Single Agent and in Combination with Binimetinib in BRAF-altered Cancers and NRAS Mutant Melanoma

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- *Exarafenib was well-tolerated at substantial monotherapy exposures; only 3% (n=2/60) of patients discontinued therapy due to treatment-related adverse events*
- *Breadth of responses observed across tumor types and BRAF or NRAS alterations with a total of 8 partial responses in the monotherapy and combination arms*
- *Monotherapy dose expansion ongoing at 300 mg bid; data-informed strategy prioritizes enrollment in BRAF Class II-driven melanoma and lung cancer (33% ORR); initial data expected in the first half of 2024*
- *Well-tolerated monotherapy backbone enables multiple development approaches, including the ongoing exarafenib combination arm in NRAS mutant melanoma; dose selection expected in the second half of 2023*

SAN FRANCISCO and SAN DIEGO, April 17, 2023 (GLOBE NEWSWIRE) -- Kinnate Biopharma Inc. (Nasdaq: KNTE) (Kinnate), a clinical-stage precision oncology company, today announced positive monotherapy dose escalation data for its investigational, highly selective and potent pan-RAF inhibitor, exarafenib, from Part A1 of its ongoing global Phase 1 KN-8701 clinical trial. These results will be featured in an oral presentation today at 3:35 p.m. ET during the Clinical Trials Mini Symposium Session at the American Association for Cancer Research (AACR) 2023 Annual Meeting. (Abstract #CT032)

The company today also provided details around its monotherapy dose expansion strategy (Part B) and a preliminary update on the combination arm (Part A2) evaluating exarafenib with binimetinib, a MEK inhibitor, in patients with BRAF-altered solid tumors and/or who have NRAS mutant melanoma.

Kinnate will host a virtual investor webcast today at 5:30 p.m. ET to discuss these updates, along with the expansion of its early development pipeline announced separately.

“The exarafenib dose escalation data provide striking proof of concept for a monotherapy pan-RAF inhibitor,” said Alexander Spira, MD, PhD, FACP, co-director, Virginia Cancer Specialists Research Institute. “For the first time, a pan-RAF inhibitor has shown both promising tolerability as a single agent and has achieved compelling breadth of activity with durable responses in targetable mutations. Responses in patients with BRAF Class II or NRAS alterations is meaningful because no approved targeted therapy is available today, and physicians are left with limited treatment options for advanced cancers, which means patients often have poor survival outcomes. I look forward to the further study of exarafenib’s therapeutic potential to address these patients who are currently medically underserved.”

Key Exarafenib Monotherapy Data Presented at AACR 2023

The data at AACR were based on a February 28, 2023 data cutoff. Sixty patients with a median of three prior therapies had been enrolled into six monotherapy dose escalation cohorts: 25 mg bid (dose level; DL 1), 50 mg bid (DL 2), 100 mg bid (DL 3), 200 mg bid (DL 4), 300 mg bid (DL 5) and 400 mg bid (DL 6). Treated patients included those with solid tumors driven by BRAF Class I (41.7%), Class II (13.3%) and Class III (30%) alterations or melanoma with NRAS mutations (15%). BRAF and NRAS alterations were identified by local laboratories either in tumor or plasma. As of the data cutoff, all 60 patients enrolled were part of the safety analysis population, of which 49 patients were efficacy evaluable.[1]

Favorable Tolerability Profile; Only 3% (n=2/60) of Patients Discontinued Therapy Due to Treatment-Related Adverse Events

- The maximum tolerated dose (MTD) was determined to be 300 mg bid (n=29). At therapeutically relevant exposures, there was no cutaneous (skin) evidence of paradoxical activation. Dose limiting toxicities observed at the highest dose level (400 mg bid) were Grade 3 acneiform rash (n=1) and Grade 3 macular rash (n=1).
- Treatment-related adverse events (TRAEs) reported by investigators at any Grade occurred in 73.3% (n=44) of patients, with 18.3% of TRAEs reported as Grade 3 or higher (n=11). There were no Grade 5 TRAEs reported as of the data cutoff.
- The most common TRAEs of any Grade were skin related (21.7%; n=13), with 3.3% (n=2) of patients having skin events that were Grade 3 or greater.
- Grade 2 gastrointestinal (GI) TRAEs occurred in 3.3% of patients (n=2). No Grade 3 GI TRAEs were observed.
- Reversible, asymptomatic increased alanine transaminase and/or increased aspartate aminotransferase TRAEs were

reported at Grade 3 (n=4; 6.7%) and Grade 4 (n=1; 1.7%).

- In all patients (n=60) treated with exarafenib, the overall relative mean dose intensity was 97% and was 95% in patients treated at 300 mg bid (n=29). The median for both patient sets was 100%.[2]

Dose Dependent and Steady State Unbound Exposures with Exarafenib Treatment

- Pharmacokinetic analyses demonstrated dose-dependent increases in exarafenib exposure (Cmax; peak plasma concentration and area under the curve) with increasing dose.

- Exarafenib had a half-life of eight hours in patients, which is a longer duration range than the predicted half-life preclinically, supporting a bid dosing strategy.

- At 300 mg bid, exarafenib delivered high target coverage in patients. Unbound exposures exceeded the IC_{50} values across BRAF and NRAS cell lines by two-to-ten-fold, while remaining below the wild type cells IC_{50}. We believe multiple fold target coverage is ultimately necessary for meaningful outcomes in these patient subtypes.

- Treatment with exarafenib also led to significant reductions in circulating tumor DNA across BRAF and NRAS-altered tumor types.

Promising Early Efficacy, Including RECIST Responses in Priority BRAF Class II and NRAS Subtypes

- In total, 6 patients achieved a partial response (PR) with exarafenib monotherapy treatment during dose escalation, including five confirmed PRs as evaluated by Response Evaluation Criteria in Solid Tumors (RECIST). For responders, the average tumor reduction was 61% and treatment duration was 7 months. Four of the 6 responders continue exarafenib therapy.

- Treatment with exarafenib at 300 mg bid, the MTD, in patients with BRAF Class II or NRAS alterations led to a 30% (3 of 10) overall response rate (ORR).

- The ORR in patients with BRAF Class II alterations was 33% (1 of 3) at 300 mg bid, which included a patient with non-small cell lung cancer (NSCLC) harboring a BRAF Class II fusion.

- In addition, 71% (5 of 7) of patients with BRAF Class II alterations achieved an objective tumor reduction. In all treated patients with Class II alterations, the disease control rate was 86% (6 of 7).

- The ORR in patients with NRAS alterations was 29% (2 of 7) at 300 mg bid and included patients with NRAS mutant melanoma and a patient with colorectal cancer harboring an NRAS alteration co-occurring with a BRAF Class III alteration.

- The two additional subtypes with confirmed PRs included RAF inhibitor naïve patients with BRAF Class I (V600E) papillary thyroid cancer and squamous cell carcinoma. One unconfirmed PR was reported in a RAF pretreated patient with BRAF Class I melanoma.

- Twenty-two patients achieved stable disease (SD) across dose levels, including 10 patients with objective tumor shrinkage (up to 20%), showing encouraging breadth of activity and prolonged disease control in a broad range of alterations and tumor types.

[1]Efficacy evaluable set includes all participants with documented BRAF (or melanoma with NRAS) genomic alterations (as specified for each study Part) who received at least 1 dose of exarafenib and have >= 1 measurable lesion at baseline for disease response assessment and at least 1 post-baseline efficacy assessment per RECIST Version 1.1 criteria. Response assessments performed by each respective clinical trial site (local, investigator-assessed radiology). Disease control rate is defined as the percent of participants who achieved a complete response, PR or SD as their best overall response in accordance with RECIST v1.1.

[2]Overall relative dose intensity based on assigned dose will use the full course of dose received (including intrapatient dose escalation or de-escalation) divided by the total planned dose as per the originally assigned.

Exarafenib Monotherapy Dose Expansion Strategy Optimized for Probability of Success

The expansion cohorts of the KN-8701 clinical trial opened year-end 2022 and are currently enrolling patients at the 300 mg bid dose.

Kinnate refined its dose expansion strategy to include greater enrichment of more sensitive tumor and alteration types based on the emerging profile and clinical signals observed during dose escalation.

The priority cohorts will enroll patients with BRAF Class II alterations, including BRAF fusions, across solid tumors, primarily melanoma and NSCLC. These cohorts are expected to enroll approximately 55 patients.

The company expects to provide initial monotherapy dose expansion data in the first half of 2024.

Exarafenib + Binimetinib Dose Escalation Ongoing; Early Clinical Activity Observed

Key combination updates as of March 31, 2023 include:

- Enrolled 12 patients primarily with NRAS mutant melanoma into 3 combination dose cohorts: (1) exarafenib 100 mg bid and binimetinib 45 mg bid, (2) exarafenib 100 mg bid and binimetinib 15 mg bid, and (3) exarafenib 200 mg bid and binimetinib 15 mg bid.
- Enrollment continues at exarafenib 200 mg bid dose and binimetinib 15 mg bid, with safety evaluation ongoing.
- Two of the 7 efficacy evaluable patients achieved RECIST PRs, including an unconfirmed PR in a patient with NRAS mutant melanoma and a confirmed PR in a patient with BRAF Class II pancreatic cancer. One additional patient with NRAS mutant melanoma experienced a 25% reduction in their target lesions. Patients who responded continue combination therapy.
- Kinnate will prioritize development of the exarafenib combination in patients with NRAS mutant melanoma. The trial will also enroll RAF pre-treated patients with a BRAF Class I alteration.
- The company expects to provide an update in the second half of 2023 on the combination dose that will be taken into dose expansion.

"With the selection of the maximum tolerated dose for exarafenib, we initiated monotherapy dose expansion with enrollment ongoing in patients with a meaningful unmet medical need and where we believe we have the highest probability of success with a single-agent pan-RAF, including in patients with advanced lung cancer and melanoma that harbor a BRAF Class II alteration," said Richard Williams, MBBS, PhD, chief medical officer, Kinnate Biopharma Inc. "In addition, with a well-tolerated monotherapy profile, compelling PK/PD and responses as the backbone, we continue to pursue priority pan-RAF combination approaches, such as with a MEK inhibitor in NRAS mutant melanoma, where a combination may offer additive benefit to patients."

Nima Farzan, Kinnate Biopharma Inc. chief executive officer, commented, "Kinnate was formed just five years ago, and in that time, we have evolved from a start up to a global, precision oncology company with two programs in the clinic and a growing pipeline of targeted therapy candidates developed by our own scientists. Today, we are proud to share the first clinical data from the company on exarafenib, showing early efficacy both as a monotherapy and as a combination regimen in BRAF and NRAS-altered cancers. This potential best-in-class pan-RAF inhibitor anchors our growing pipeline and positions the company for future growth."

Today's AACR presentation is available on the company's website at Kinnate.com.

Virtual Investor Webcast Information

Kinnate will host a webcast today, Monday, April 17, 2023, at 5:30 p.m. ET. Investors and the general public are invited to listen to a live webcast of the session through the "Investors and Media" section on Kinnate.com or by dialing the U.S. toll free number +1-888-256-1007 and entering confirmation code: 7465233. An archived edition of the session will be available following the event.

About Exarafenib

Exarafenib is an orally administered, potent and selective investigational small molecule pan-RAF inhibitor. Unlike currently available treatments that target only Class I BRAF kinase mutations, exarafenib is designed to target BRAF Class II and Class III alterations, where it has the potential to be a first-line targeted therapy, in addition to covering BRAF Class I alterations, and as a potential treatment for NRAS mutation-positive melanoma.

KN-8701 Clinical Trial Background

KN-8701 is an ongoing, global Phase 1 clinical trial (NCT04913285) evaluating exarafenib in patients with advanced solid tumors harboring BRAF Class I, II and III alterations, and/or who have NRAS mutant melanoma. KN-8701 contains a two-part dose escalation: Part A1 is evaluating exarafenib as a monotherapy across BRAF alterations and tumor types, and Part A2 is evaluating exarafenib in combination with binimetinib, a MEK inhibitor. Part B, dose expansion, is evaluating exarafenib at the recommended dose and schedule in patients with BRAF-altered cancers including lung cancer, melanoma and other solid tumors.

About Kinnate Biopharma Inc.

Kinnate Biopharma Inc. is a clinical-stage precision oncology company focused on expanding on the promise of targeted therapies for those battling cancer. The company is developing medicines for known oncogenic drivers where there are no approved targeted drugs and to overcome the limitations of marketed cancer therapies, such as non-responsiveness or acquired and intrinsic resistance. Kinnate has two lead clinical programs being studied in solid tumors with RAF, NRAS and FGFR-driven alterations, and is rapidly progressing a pipeline of additional small molecule drug candidates as part of the Kinnate Discovery Engine. The company is driven by the urgency and knowledge that patients are waiting for new, effective cancer medicines. For more information, visit Kinnate.com and follow us on LinkedIn.

Forward-Looking Statements

This press release contains forward-looking statements that involve substantial risks and uncertainties. These forward-looking statements include, without limitation, statements regarding the therapeutic potential, efficacy and clinical benefits of exarafenib; the safety and tolerability profile of exarafenib; the future conduct of the monotherapy and combination arms of KN-8701; the size and makeup of KN-8701 priority and dose-expansion

cohorts; plans for KN-8701 patient enrollment; development priorities; the timing and presentation of clinical data from KN-8701 for exarafenib monotherapy and of dose selection for the exarafenib and binimetinib combination; the relationship between the results from the positive dose escalation data and results of future clinical trials; the company's intention to hold a webcast; and statements by the company's chief executive officer and others. Words such as "believes," "anticipates," "plans," "expects," "will," "potential" and similar expressions are also intended to identify forward-looking statements. We have based these forward-looking statements largely on our current expectations and projections about future events and trends. Such expectations and projections may never materialize or may prove to be incorrect. These forward-looking statements are subject to a number of risks, uncertainties, assumptions and other factors, including recently transitioning to operating as a clinical-stage biopharmaceutical company with a limited operating history; the timing, progress and results of ongoing and planned preclinical studies and clinical trials for our current product candidates; that continued dose escalation in our clinical trials could increase the risk of the occurrence of adverse events; the potential for future clinical trial results to differ from initial results or from our preclinical studies; our ability to timely enroll a sufficient number of patients in our clinical trials; our ability to raise additional capital to finance our operations; our ability to discover, advance through the preclinical and clinical development of, obtain regulatory approval for and commercialize our product candidates; the novel approach we are taking to discover and develop drugs; our ability to timely file and obtain approval of investigational new drug applications for our planned clinical trials; negative impacts of the COVID-19 pandemic on our business, including ongoing and planned clinical trials and preclinical studies; competition in our industry; regulatory developments in the United States and other countries; our ability to attract, hire and retain highly skilled executive officers and employees; difficulties in managing our growth; our ability to protect our intellectual property; reliance on third parties to conduct our ongoing and planned preclinical studies and clinical trials, and to manufacture our product candidates; general economic and market conditions; and other risks. These and other risks, uncertainties, assumptions and other factors are further described under the heading "Risk Factors" in our Annual Report on Form 10-K for the fiscal year ended December 31, 2022 that we have filed with the Securities and Exchange Commission ("SEC"), as well as in our subsequent filings we make with the SEC. New risk factors emerge from time to time and it is not possible for our management to predict all risk factors, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in, or implied by, any forward-looking statements. Investors should not rely upon forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance or achievements. Our forward-looking statements speak only as of the date of this release, and except as required by law, we undertake no obligation to update publicly any forward-looking statements for any reason in the future.

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