Boundless Bio Announces First Patient Dosed in First-in-Human Phase 1/2 Clinical Trial of BBI-825 in Cancer Patients with Resistance Gene Amplifications

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STARMAP (Study Treating Acquired Resistance: MAPK Amplifications) is a first-in-human, 3-part, Phase 1/2 study of BBI-825 as a single agent and in combination with select targeted cancer therapies

BBI-825 is a novel, oral, selective ribonucleotide reductase (RNR) inhibitor and Boundless Bio's second extrachromosomal DNA (ecDNA)-directed therapy (ecDTx) to enter clinical development

Preclinically, BBI-825 has demonstrated tumor growth inhibition, including regressions, in both prevention and treatment of amplification-mediated resistance in MAPK pathway-activated tumors

SAN DIEGO--(BUSINESS WIRE)--Apr. 11, 2024-- Boundless Bio (Nasdaq: BOLD), a clinical-stage oncology company interrogating extrachromosomal DNA (ecDNA) biology to deliver transformative therapies to patients with previously intractable oncogene amplified cancers, today announced that the first patient has been dosed with BBI-825 in a first-in-human, Phase 1/2 clinical trial for patients with locally advanced or metastatic cancer with resistance gene amplifications (NCT06299761). ecDNA are a key driver of high copy number amplification in cancer, and Boundless has validated multiple drug targets that are essential for ecDNA function in cancer cells. BBI-825, the Company's second ecDNA-directed therapy (ecDTx) to enter clinical trials, is a novel, selective, oral small molecule inhibitor of ribonucleotide reductase (RNR), a rate-limiting enzyme responsible for the *de novo* synthesis of deoxyribonucleotides, the building blocks of DNA. Boundless has identified an essential role for RNR in ecDNA assembly and repair and in the survival of certain oncogene amplified cancer cells.

"We are excited to announce dosing of the first patient in our first-in-human study of BBI-825, our second program to enter the clinic," said Klaus Wagner, M.D., Ph.D., Chief Medical Officer at Boundless Bio. "BBI-825 represents a new approach in the potential treatment of oncogene amplifications, particularly in resistance associated with targeted therapy treatment of MAPK pathway-activated cancers."

"Rapid resistance is a major limitation for targeted therapies, particularly in colorectal cancer, as patients with colorectal cancer often progress within about 6 months of initiating targeted treatment," said Rona Yaeger, M.D., Gastrointestinal Oncologist and Early Drug Development Specialist at Memorial Sloan Kettering Cancer Center. "We have observed firsthand that tumors in patients treated with KRAS ^{G12C} or BRAF^{V600E} targeted therapies develop resistance via MAPK pathway and receptor tyrosine kinase gene amplifications, and those with pre-existing amplifications have an overall worse outcome. There remains an incredible need for therapies that can prevent amplification-driven resistance or treat patients that have already acquired such resistance."

"Advancing our second ecDTx into clinical development is an important milestone for Boundless Bio and underscores the power of our Spyglass platform to identify synthetic lethal targets essential to ecDNA formation and function in oncogene amplified cancers," said Zachary Hornby, President and Chief Executive Officer at Boundless Bio. "We are excited to enroll patients in this first-in-human Phase 1/2 study, focused initially on patients with *KRAS^{G12C}* and *BRAF^{V600E}* mutated colorectal cancer with resistance gene amplifications. If data are supportive, we may have the opportunity to expand into broader patient populations, including pan-tumor, pan-RAS, and pan-RAF indications, potentially addressing these populations of cancer patients with very high unmet need."

About the STARMAP Trial

STARMAP ("Study Treating Acquired Resistance: MAPK Amplifications") is an open-label, non-randomized, three-part Phase 1/2 clinical trial to evaluate the safety, pharmacokinetics, pharmacodynamic biomarkers, preliminary antitumor activity, and identify the maximum tolerated dose and recommended Phase 2 dose (RP2D) of BBI 825 administered as a single agent or in combination with select targeted therapies (NCT06299761). Part 1 is a dose escalation of BBI-825 as a monotherapy in patients with solid tumors. Part 2 is a combination dose escalation of BBI-825 and targeted therapies, encorafenib and cetuximab, or adagrasib and cetuximab, in patients with advanced or metastatic colorectal cancer with *BRAF^{V600E}* or *KRAS^{G12C}* mutations, respectively, and co-occurring resistance gene amplifications. Part 3 is a combination dose expansion to evaluate preliminary anti-tumor activity at the RP2D of BBI-825 and each targeted therapy combination from Part 2.

About BBI-825

Boundless Bio's second ecDNA-directed therapy (ecDTx), BBI-825, is a novel, oral, selective small molecule inhibitor of ribonucleotide reductase (RNR) being studied in the currently enrolling, first-in-human, Phase 1/2 STARMAP trial in cancer patients with resistance gene amplifications. In preclinical studies, BBI-825 demonstrated low double digit nanomolar RNR inhibition and tumor growth inhibition, including regressions, in both the prevention and treatment of amplification-mediated resistance in mitogen-activated protein kinase (MAPK) pathway-activated tumors. RNR is a rate-limiting enzyme responsible for cellular *de novo* synthesis of deoxynucleotide triphosphates (dNTPs), the building blocks of DNA, and is essential to the assembly and repair of ecDNA. BBI-825 was shown to starve ecDNA-reliant cancer cells of dNTPs, deplete ecDNA, and was synthetic lethal in multiple oncogene amplified preclinical cancer models.

About Boundless Bio

Boundless Bio is a clinical-stage oncology company dedicated to unlocking a new paradigm in cancer therapeutics to address the significant unmet need of patients with oncogene amplified tumors by targeting extrachromosomal DNA (ecDNA), a root cause of oncogene amplification and observed in more than 14% of cancer patients. Boundless Bio is developing the first ecDNA-directed therapy (ecDTx), BBI-355, which is an oral inhibitor of checkpoint kinase 1 and is being evaluated in a Phase 1/2 clinical trial in patients with oncogene amplified cancers. Boundless Bio's second ecDTx, BBI-825, is an oral inhibitor of ribonucleotide reductase and recently entered a Phase 1/2 clinical trial in cancer patients with resistance gene amplifications. Leveraging its Spyglass platform, Boundless Bio has additional programs advancing through preclinical development and discovery. Boundless Bio is headquartered in San Diego, CA.

For more information, visit www.boundlessbio.com.

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Forward-Looking Statements

Boundless Bio cautions you that statements contained in this press release regarding matters that are not historical facts are forward-looking statements. The forward-looking statements are based on our current beliefs and expectations and include, but are not limited to: the potential therapeutic benefits of our ecDTx in treating patients with oncogene amplified cancers; the ability of our Spyglass platform to identify synthetic lethal targets essential to ecDNA formation and function in cancer; and the potential opportunity to expand into broader patient populations. Actual results may differ from those set forth in this press release due to the risks and uncertainties inherent in our business, including, without limitation: we are early in our development efforts and our approach to discover and develop ecDTx directed against ecDNA in oncogene amplified cancers is novel and unproven; potential delays in the commencement, enrollment, data readouts or completion of clinical trials or preclinical studies; our dependence on third parties in connection with clinical trials, preclinical studies, ecDNA diagnostic development, and manufacturing; unfavorable results from clinical trials or preclinical studies; unexpected adverse side effects or inadequate efficacy of our ecDTx that may limit their development, regulatory approval, and/or commercialization; regulatory developments in the United States and foreign countries; and other risks described in our filings with the Securities and Exchange Commission (SEC), including under the heading “Risk Factors” in the final prospectus dated March 27, 2024 that we filed with the SEC and any subsequent filings with the SEC. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof, and we undertake no obligation to update such statements to reflect events that occur or circumstances that exist after the date hereof. All forward-looking statements are qualified in their entirety by this cautionary statement, which is made under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995.

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James Lee, Boundless Bio
jlee@boundlessbio.com

Media
1AB
Dan Budwick
dan@1abmedia.com

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