



Boundless Bio Presents Preclinical Data on the Discovery of its Second ecDNA-Directed Therapeutic Candidate, BBI-825, at the 2023 AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics

October 13, 2023

Preclinical findings support the advancement of BBI-825, a novel, orally available, selective inhibitor of ribonucleotide reductase (RNR), as a differentiated treatment approach for ecDNA-enabled oncogene or resistance gene amplified cancers, including resistance associated with treatment of KRAS^{G12C} mutant colorectal cancer (CRC)

A second poster presentation reveals insight into the intrinsic genomic plasticity of extrachromosomal DNA (ecDNA) across dynamic states of extrachromosomal and chromosomal-based amplification in cancer cells

SAN DIEGO--([BUSINESS WIRE](#))--[Boundless Bio](#), a clinical stage, next-generation precision oncology company interrogating extrachromosomal DNA (ecDNA) biology to deliver transformative therapies to patients with previously intractable oncogene amplified cancers, today will present preclinical data on its second ecDNA-directed therapy (ecDTx), BBI-825, as well as present additional research on the intrinsic genomic plasticity of cancer cells enabled by ecDNA at the 2023 AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics.

BBI-825 is a novel, orally available, selective inhibitor of ribonucleotide reductase (RNR), which is a rate-limiting enzyme in the cellular production of deoxynucleotide triphosphates (dNTPs), essential building blocks for ecDNA assembly and repair in cancer cells. BBI-825 has demonstrated RNR inhibition in a host of tumor cell lines and tumor regressions in ecDNA-enabled preclinical cancer models and is currently being evaluated in Investigational New Drug (IND)-enabling studies. BBI-825 was discovered using Boundless Bio's proprietary Spyglass platform, a drug discovery engine to identify and preclinically validate targets that are essential for cancer cells' reliance on ecDNA for growth, treatment resistance, and survival.

"We are excited to unveil our second ecDTx program, BBI-825, which has demonstrated promising preclinical proof of concept in multiple tumor types and across different oncogene amplifications, particularly in resistance associated with targeted therapy treatment of MAPK pathway activated cancers," said Chris Hassig, Ph.D., Chief Scientific Officer of Boundless Bio. "In addition to single agent anti-tumor activity, BBI-825 also has shown synergistic activity when combined with specific targeted therapies in ecDNA-enabled *in vivo* tumor models, and in particular, cancer models that develop resistance amplifications on ecDNA in response to KRAS^{G12C} inhibitors in KRAS^{G12C} mutated CRC. We believe a selective, oral RNR inhibitor has broad potential for patients with ecDNA-enabled and oncogene amplified cancers and that the discovery and preclinical validation of BBI-825 underscores the power of our Spyglass platform."

The second poster presentation extends the field's understanding of ecDNA and its key role in enabling resistance to cancer therapy. Unique properties of ecDNA drive genomic plasticity and tumor heterogeneity, enabling rapid acquired resistance to targeted therapies and resulting in poor patient outcomes; however, the potential adaptive and resistance properties in the chromosomal state are not well characterized. The findings from this study provide a model for how cancer cells with ecDNA-derived, chromosomally reintegrated homogeneous staining regions (HSR) retain the capacity to amplify ecDNA, thus further enabling rapid adaptation to therapeutic pressure and highlighting the urgent need for ecDNA-directed therapies for patients with oncogene amplified cancers.

Details of today's presentations are as follows:

Title: A novel, potent and selective ribonucleotide reductase (RNR) inhibitor, BBI-825, blocks extrachromosomal DNA (ecDNA) amplification-mediated resistance to KRAS^{G12C} inhibitor in colorectal cancer (CRC)

Abstract Number: B082

Session: Poster Session B

Date/Time: Friday, October 13 | 12:30 – 4:00 pm ET

Title: Intrinsic genomic plasticity of extrachromosomal DNA (ecDNA) enables oncogene amplified tumor cells to develop rapid acquired resistance to targeted therapy

Abstract Number: B092

Session: Poster Session B

Date/Time: Friday, October 13 | 12:30 – 4:00 pm ET

About BBI-825

BBI-825 is a novel, orally available, selective inhibitor of ribonucleotide reductase (RNR), a rate-limiting enzyme responsible for cellular production of deoxyribonucleotide triphosphates (dNTPs), the building blocks of DNA, and essential to the assembly and repair of ecDNA. In preclinical studies, BBI-825 starved ecDNA-reliant cancer cells of dNTPs, depleted ecDNA, and was synthetic lethal in ecDNA-bearing cancer cells. BBI-825 has demonstrated preclinical *in vivo* proof of concept in multiple tumor types and across different oncogene amplifications, including both driver oncogene and resistance settings, particularly in MAPK pathway activated cancers. RNR was identified and preclinically validated as an ecDNA essential target via Boundless Bio's proprietary Spyglass platform and led to the development of BBI-825, which is currently being evaluated in IND-enabling studies.

About Boundless Bio

Boundless Bio is a clinical-stage precision oncology company dedicated to unlocking a new paradigm in cancer therapeutics to address the significant unmet need in patients with oncogene amplified tumors by targeting extrachromosomal DNA (ecDNA), a root cause of oncogene amplification observed in more than 14% of cancer patients. Boundless Bio is developing the first ecDNA-directed therapy (ecDTx), BBI-355, which is being evaluated in a Phase 1/2 clinical trial, and has multiple other pipeline programs advancing in preclinical development and discovery. To date, Boundless Bio has raised more than \$250 million from leading life sciences investors.

For more information, visit www.boundlessbio.com.

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Contacts

James Lee, Boundless Bio
jlee@boundlessbio.com

Media

1AB
Dan Budwick
dan@1abmedia.com