



Boundless Bio Announces First Patient Dosed in First-in-Human Phase 1/2 Clinical Trial of BBI-355 in Patients with Solid Tumors Harboring Oncogene Amplification

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POTENTIATE (Precision Oncology Trial Evaluating Novel Therapeutic Interrupting Amplifications Tied to ecDNA) is a first-in-human, 3-part, Phase 1/2 study of BBI-355 as a single agent and in combination with select therapies

BBI-355 is a potentially best-in-class checkpoint kinase 1 (CHK1) inhibitor and the first extrachromosomal DNA (ecDNA)-directed therapy (ecDTx) designed to treat patients with oncogene amplified cancers

Combinations of BBI-355 and select therapies have demonstrated synergistic anti-cancer activity in ecDNA oncogene amplified tumor xenograft models

SAN DIEGO--([BUSINESS WIRE](#))--[Boundless Bio](#), a clinical stage, next-generation precision oncology company developing innovative therapeutics directed against extrachromosomal DNA (ecDNA) for patients with oncogene amplified cancer, today announced that the first patient has been dosed with BBI-355 in a first-in-human, Phase 1/2 clinical trial for patients with locally advanced or metastatic solid tumors with oncogene amplifications ([NCT05827614](#)). ecDNA is a key driver of high copy number amplification in cancer, and Boundless Bio has validated several drug targets that are essential for ecDNA function in cancer cells. As the company reported at the AACR [Annual Meeting 2022](#)¹ and the [AACR Annual Meeting 2023](#)², a critical vulnerability of tumor cells that rely upon oncogene amplification on ecDNA to grow and survive is that they exhibit very high levels of DNA replication stress. Hence ecDNA bearing cancer cells are hyper-reliant for survival on checkpoint kinase 1 (CHK1), cells' master regulator of replication stress, and are hypersensitive to inactivation of CHK1. BBI-355 is an orally available, potent, and selective small molecule inhibitor of CHK1 and represents the first ecDNA-directed therapy (ecDTx) developed for cancer patients that harbor oncogene amplification on ecDNA.

"We're delighted to work with the participating investigators in the POTENTIATE study, and we are eager to determine whether BBI-355 could represent new hope for patients with oncogene amplified tumors."

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"We are excited to announce dosing of the first patient in our first-in-human clinical study of BBI-355," said Klaus Wagner, M.D., Ph.D., Chief Medical Officer at Boundless Bio. "Preclinically, single agent BBI-355 demonstrates potent anti-cancer activity in ecDNA-enabled oncogene amplified tumor models and robust, synergistic efficacy in combination with select cancer therapies. There is a large unmet medical need for cancer patients with oncogene amplification, and we look forward to working with some of the top U.S. cancer centers to bring new and promising treatment options to these patients."

"Memorial Sloan Kettering Cancer Center (MSKCC) is excited to participate in the POTENTIATE study and advance our understanding of ecDNA-driven cancer," said Alexander Drilon, M.D., Chief of Early Drug Development Service at MSKCC and Weill Cornell Medical Center. "There is a significant need to develop new therapies for patients with cancers enabled by oncogene amplification as there are very few options for these patients."

"Initiation of the first the clinical study of our first ecDTx marks a significant milestone for Boundless Bio," said Zachary Hornby, President and Chief Executive Officer at Boundless Bio. "We're delighted to work with the participating investigators in the POTENTIATE study, and we are eager to determine whether BBI-355 could represent new hope for patients with oncogene amplified tumors."

References

¹[Chowdhry et al. Replication stress and the inability to repair damaged DNA, the potential "Achilles' heel" of ecDNA+ tumor cells \[abstract\]. Cancer Res 2022;82\(12_Suppl\): Abstract nr 1520.](#)

²[Chowdhry et al. Tumors driven by oncogene amplified extrachromosomal DNA \(ecDNA\) demonstrate enhanced sensitivity to cell cycle checkpoint kinase 1 \(CHK1\) inhibition \[abstract\]. Cancer Res 2023;83\(7_Suppl\): Abstract nr 1626.](#)

POTENTIATE Study Background

BBI-355 is being evaluated in a first-in-human Phase 1/2 clinical trial ("POTENTIATE": Precision Oncology Trial Evaluating Novel Therapeutic Interrupting Amplifications Tied to ecDNA) in patients with locally advanced or metastatic solid tumors with oncogene amplifications, whose disease has progressed despite all standard therapies or for whom no further standard or clinically acceptable therapy exists. The open-label, non-randomized, 3-part study involves: (Part 1) BBI-355 single agent dose escalation and expansion in cancer patients with oncogene amplification, (Part 2) dose escalation of BBI-355 in combination with select therapies in cancer patients with specific oncogene amplifications, and (Part 3) dose expansion of BBI-355 in combination with select therapies in cancer patients with specific oncogene amplification on ecDNA. BBI-355 is administered orally every other day. In Part 3 of the study, an ecDNA diagnostic clinical trial assay (CTA) called ECHO (ecDNA Harboring Oncogenes) will be implemented to determine the presence of oncogenes amplified on ecDNA in patient tumor samples. ECHO is a proprietary bioinformatic diagnostic algorithm designed by Boundless Bio and developed in collaboration with SOPHiA GENETICS to detect oncogenes amplified on ecDNA from tumor biopsy samples using routine clinical NGS assays.

About BBI-355

BBI-355 is a potentially best-in-class checkpoint kinase 1 (CHK1) inhibitor and the first ecDNA-directed therapy (ecDTx) being investigated to treat patients with oncogene amplified cancer. CHK1 is a master regulator of DNA replication stress (RS), which frequently arises from oncogene amplification on ecDNA. Inhibition of CHK1 by BBI-355 is synthetic lethal in cancer cells with oncogene amplification on ecDNA due to their heightened RS. CHK1 was identified and validated as an ecDNA essential target via Boundless Bio's proprietary Spyglass research platform, leading Boundless Bio to develop BBI-355, an orally available, potent, and selective CHK1 inhibitor.

About Extrachromosomal DNA (ecDNA)

ecDNA are circular units of nuclear DNA that are physically distinct from chromosomes and are found only within cancer cells. ecDNA encode full length genes, including oncogenes and regulatory regions, are highly transcriptionally active, and lack centromeres. ecDNA replicate and express within cancer cells and, due to their lack of centromeres, can be asymmetrically passed to daughter cells during cell division, leading to focal gene amplification and gene copy number heterogeneity in cancer. By leveraging the plasticity afforded by ecDNA, cancer cells can rapidly increase or decrease copy number of select genes located on ecDNA to enable survival under selective pressures, including targeted therapy, chemotherapy, or radiation, thereby making ecDNA one of cancer's primary mechanisms of growth and treatment resistance. ecDNA are a key driver of the most aggressive and difficult-to-treat cancers, specifically those characterized by high copy number amplification of oncogenes.

About Boundless Bio

Boundless Bio is a clinical stage, next-generation precision oncology company dedicated to the discovery and development of new drugs targeting a novel area of cancer biology, ecDNA, to deliver transformative therapies intended to improve and extend the lives of patients with oncogene amplified cancers.

For more information, visit www.boundlessbio.com.

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