Opna Bio Presents Promising Preclinical Data in Multiple Myeloma with OPN-6602 and in Malignant Mesothelioma with OPN-9840 Showing Significant Tumor Growth Inhibition at the American Association of Cancer Research Annual Meeting

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OPN-6602 Expected to Begin Phase 1 Clinical Study in Multiple Myeloma in Summer 2024

San Diego, CA – April 10, 2024 – Opna Bio, a clinical-stage biopharmaceutical company focused on the discovery and development of novel cancer therapeutics, presented promising preclinical data in two programs, OPN-6602, a dual EP300/CBP inhibitor in multiple myeloma, and OPN-9840, an oral, non-covalent TEAD inhibitor in malignant mesothelioma and metastatic melanoma. Data were shared at the American Association of Cancer Research (AACR) Annual Meeting, taking place April 5-10, 2024 in San Diego.

OPN-6602 Significantly Reduced Tumor Growth in Multiple Myeloma Models

OPN-6602 is an orally active, small molecule dual inhibitor of the E1A binding protein p300 (EP300) and CREB-binding protein (CBP) that demonstrated potent *in vitro* and *in vivo* anti-tumor activity in preclinical models of multiple myeloma. Multiple myeloma is an aggressive blood cancer derived from malignant plasma cells in the bone marrow.

- Significantly reduced tumor growth as single agent (71% tumor growth inhibition, or TGI) in the OPM-2 multiple myeloma cell xenograft model
- Demonstrated increased anti-tumor activity (>100% TGI) and sustained duration of response in combination studies with dexamethasone, pomalidomide and mezigdomide
- Displayed synergy with dexamethasone and lenalidomide in growth inhibition of MM1.S cells
- Showed downregulation of key drivers of the multiple myeloma signaling pathway including *MYC*, *IRF4* and *MYB* in OPM-2 xenograft tumors

A first-in-human Phase 1 study of OPN-6602 is planned for mid-2024 in patients with multiple myeloma.

"We are excited to begin our Phase 1 study of OPN-6602 in patients with multiple myeloma this summer. While we will study OPN-6602 initially as monotherapy, preclinical data supports testing the compound as a single agent and in combination with standard of care and next generation myeloma therapies," said Jackie Walling, MBChB, PhD, chief medical officer. "The unique pharmacokinetic profile of the compound, with a high c-max and short half-life, in particular, is anticipated to provide a distinct advantage in the combination setting."

OPN-9840 Demonstrated Single Agent Efficacy in Malignant Mesothelioma

OPN-9840 is an oral, non-covalent, pan transcriptional enhanced associate domain (TEAD) inhibitor that demonstrated dose-dependent and on-target *in vitro* and *in vivo* efficacy in preclinical models of malignant mesothelioma. Malignant mesothelioma is a rare and aggressive cancer that primarily affects the lining of the lungs or abdomen. In 40% of malignant mesotheliomas, neurofibromatosis 2 (*NF2*) gene mutations cause dysregulation of the Hippo pathway and increased TEAD-dependent transcription. This aberrant signaling ultimately leads to increased tumor growth and resistance to therapies.

- Significantly inhibited tumor growth (88% to >100%) in an *NF2*-mutant malignant mesothelioma mouse xenograft model. Tumor regression was observed in the 15 mg/kg (2/8 mice) and 50 mg/kg (4/8 mice) dose groups.
- OPN-9652, an analog of OPN-9840, showed increased anti-tumor activity (134% TGI) and synergistic inhibition of downstream target genes in a combination study with trametinib
- Showed no *in vitro* cytotoxicity; is well tolerated *in vivo* while showing potential for blood brain barrier penetration

Additional studies presented through a collaboration with Dr. Andrew Aplin's laboratory at Thomas Jefferson University demonstrated that Opna TEAD inhibitors enhance BRAF/MEK inhibition in melanoma models by targeting drug-resistant persister cells. Dr. Aplin is a professor in cancer research and deputy director at Jefferson's NCI-designated Sidney Kimmel Cancer Center.

OPN-9840 is set to begin IND-enabling studies and Opna is currently seeking partnerships for development.

Abstract Information

Title: OPN-6602, a potent dual EP300/CBP bromodomain inhibitor, targets multiple myeloma through concomitant suppression of IRF4 and c-MYC

Abstract Number: #660
Date and time: April 7, 2024; 1:30-5:30 pm PT
Presenter: Bernice Matusow, MS

Title: OPN-9840, a non-covalent potent pan-TEAD inhibitor, exhibits single agent efficacy in preclinical malignant mesothelioma models
Abstract Number: #7264
Date and time: April 10, 2024; 9 am-12:30 pm PT
Presenter: Pan-Yu Chen, PhD

Title: Targeting TAZ-TEAD in minimal residual disease enhances the duration of targeted therapy in melanoma models
Abstract Number: #7201
Date and time: April 10, 2024; 9 am-12:30 pm PT
Presenter: Connor Ott, PhD candidate, Thomas Jefferson University

About Opna Bio
Opna Bio is a clinical-stage biopharmaceutical company focused on the discovery and development of novel oncology therapeutics. The company's broad portfolio targets multiple drivers of cancer, including a novel oncology discovery program focused on the fragile-X mental retardation protein (FMRP) and a diversified pipeline of validated oncology assets. The Opna team has a proven track record of scientific expertise and commercial value creation, having advanced multiple FDA-approved drugs to market. In addition to its discovery-stage FMRP program, Opna's lead clinical compound, OPN-6602, an E1A binding protein (EP300)/ CREB binding protein (CBP) inhibitor, is expected to begin a Phase 1 clinical trial in multiple myeloma later this year. For more information, please visit opnabio.com.

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