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Phase 1 clinical study of FB849, HPK1 inhibitor as a next-generation immuno-oncology therapy

1ST Biotherapeutics, Inc.

Disease Area	Oncology
Product Type	NCE
Indication	Advanced solid tumor
Target	HPK1 kinase inhibitor
Mechanism of Action	• Hematopoietic progenitor Kinase 1 (HPK1), also known as MAP4K1, is a negative immune regulator of T cell receptor (TCR) and B cell signaling. • Inhibition of HPK1 elicits anti-tumor immune response by promoting T cell functions through T cell activation and proliferation while reinvigorating T cell exhaustion, enhancing APC function by promoting dendritic cell maturation and activation leading to enhanced antigen presenting cell function and suppressing Prostaglandin E2-mediated tumorigenesis.
Competitiveness	• The most selective HPK1 inhibitor in the clinic, minimizing off target liabilities. • Exhibits ideal ADME properties and PK profiles, showcasing excellent bioavailability and permeability. • Elicits strong anti-cancer potency through reinvigoration of exhausted T cells, increase of tumor-specific T cells and non-T cell-driven efficacy, providing a favorable TME for combination with T cell-based therapies.
Development Stage	Phase I/II
Route of Administration	Oral Administration (PO)
Key Data	• Potency, selectivity, target engagement, and mechanism of action, confirmed in various *in vitro* studies. • Strong efficacy confirmed as a standalone and in combination with anti-PD-1 therapies in various *in vivo* models including, but not limited to, CT-26, MC-38, and EMT-6 with underlying mechanism identified as the modulation of myeloid lineage cell types to provide a favorable TME for combination therapy with T cell-driven efficacy. • Translational research confirming activation and proliferation of T cells, including reinvigoration of exhausted T cells, and cytokine production in patient-derived tumor infiltrating lymphocytes. • Ideal ADME, PK, and toxicological profiles confirmed in various *in vitro*, *in vivo*, toxicological studies. • Clear dose-dependent PK/PD correlation confirmed in phase Ia • No safety concerns reported up to the current cohort 3
IP	Proprietary compound series secured by world-wide patents filed.