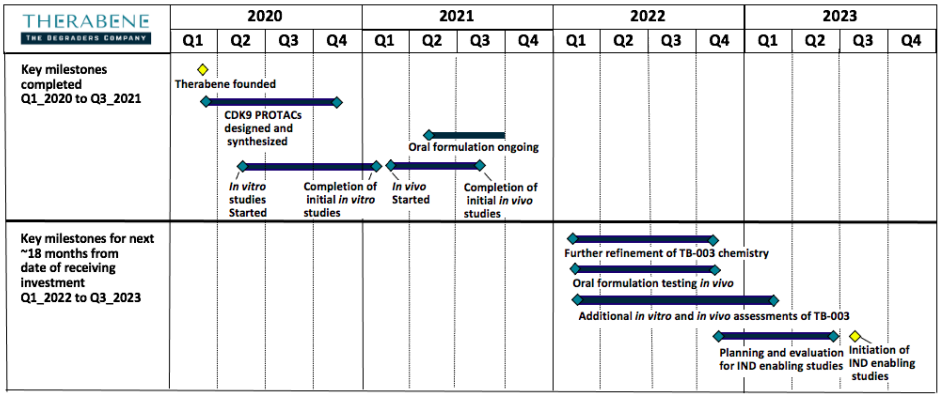
Executive Summary: Therabene (est. Mar 2020, Mansfield, MA) is a start-up company developing degraders for the treatment of cancer and other diseases. Its lead degrader product, TB-003, is a first-in-class, Cyclin-dependent Kinase 9 (CDK9) Degrader for the treatment of Triple Negative Breast Cancer (TNBC), which accounts for more than 15% of all breast cancers and represents a substantial unmet medical need. Preliminary data show that TB-003 has a unique bimodal anti-tumor mechanism of action in TNBC. The founders of Therabene have privately financed the seed capital, covering operational and research expenditures to date. Therabene is now looking to raise $5MM in capital or seek a partner to reach the IND-enabling stage within the next 18 months for its lead product (TB-003).

TNBC treatment landscape and market potential: High unmet need and new therapeutic strategies required. TNBC does not respond to hormonal therapy or therapies that target HER2 receptors such as Herceptin (trastuzumab). The current treatment regimen for TNBC combines surgery, radiotherapy, and chemotherapy; furthermore, TNBC is more likely to spread beyond the breast and has chances of reoccurrence after 3 years. The global TNBC treatment market valuation is estimated to be well over $1B by 2030.

Company performance (Mar 2020 - To date): Therabene is developing first-in-class CDK9 hetero-bifunctional small molecule degraders using proteolysis-targeting chimeras (PROTAC) technology. As shown in Figure 1 (key milestones completed), we have developed a series of CDK9 degraders including TB-003.

Figure 1. Key Milestones and Timelines



Current results demonstrate TB-003:

- is highly selective for CDK9 (>200X compared to CDK1, CDK2, CDK7)
- causes decrease in cell viability *in-vitro* and reduces tumor volume in HCC1187 TNBC xenograft mice *in-vivo* following 10mg/kg i.p. treatment Q2D x 3 weeks and subsequent 2 weeks of observation
- is well tolerated with no change in body weight

We hypothesize that TB-003 has a unique bimodal (cytostatic followed by cytotoxic) mechanism of action. We are currently in the process of filing IP patents for our series of CDK9 degraders as well as the novel oral formulation strategies.

Figure 2. Competitive Landscape

Compound		TB-003 (Therabene)	KB-130742 (Kronos Bio)	AZ4573 (AstraZeneca)	BAY1251152 (Vincerx)
Modality		CDK9 degrader	CDK9 inhibitor	CDK9 inhibitor	CDK9 inhibitor
Potency (biochemical IC_{50})	CDK9	5nM	15nM	3nM	3-4nM
Fold selectivity CDK9 vs. other selected CDK family members	CDK7	>200x	147x	18x	≥90x
	CDK2	>200x	447x	1x	730x
	CDK1	>200x	281x	2x	≥90x
Route of administration		IP/Oral	Oral	IV	IV

Competitive landscape: is shown in Figure 2. To our knowledge, there are no CDK9 degraders reported in clinical stages of development. TB-003 is expected to be a first-in-class CDK9 degrader.

Offering: Raise up to $5MM in capital or seek a partner to reach IND-enabling stage within 18 months. As shown in Figure 1 (key milestones for next 18 months), we expect to continue experimental work on TB-003 (and other related CDK9 degraders) largely focused on physicochemical properties/ADME/PK (permeability, solubility, chemical stability, improving oral bioavailability, formulation), chemistry, binary target engagement, ternary complex formation, target ubiquitination, degradation, animal work (multiple doses, different dosing strategies, combinations with SOC, targeted therapies, etc.). Therabene will seek an additional $15MM capital in 2H 2023 to complete IND filing and prepare for Phase I clinical development.

Potential exit options: include licensing (e.g., Vincerx in-licensed Bayer's BAY1251152 for upfront fee, development, and commercial sales milestone payments), IPO (e.g., Kronos Bio raised $288MM), merger, acquisition, etc.

Key contact: Mario DiPaola, PhD, MBA (Co-founder & CEO) founded and led Blue Stream Laboratories for 10 years. Blue Stream developed complex biologics and biosimilars and was acquired by Charles River Laboratories in 2016. DiPaola has extensive experience in basic research, development, quality, manufacturing, and regulatory functions for protein and small molecule development. mdipaola@therabene.com www.therabene.com