Epigenetic immunotherapy

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Opportunity

Clinical Need:

• Immune checkpoint inhibitors are NOT effective on “cold” tumors (no or few T-cells).

Our solution:

• Novel strategy: “First in class” degraders of KDM5 epigenetic enzymes to turn “cold” tumors into “hot” tumors.

Our market:

• Multiple cancer types including breast cancer, melanoma and prostate cancer.
Why us?

• KDM5 demethylase-activity inhibitors were developed by Genentech, Constellation, Gilead, and BMS, but these are inferior to KDM5 degraders.

• Our competitive advantage
  
  – “First in class” KDM5 degraders, in collaboration with Dr. Craig Crews, Founder of Arvinas and Dr. Jian Jin, co-founder of Cullgen

  – HiBiT-tagged reporter platform for HTS of cell-permeable degraders

  – Unique immuno-competent mouse cancer models

  – Biomarkers to monitor the effects of KDM5 degradation
Why degraders: KDM5B loss induces robust anti-tumor immunity in a demethylase activity-independent manner

Zhang et al. Nature 2021

YUMMER1.7 melanoma

YUMM1.7 melanoma

Zhang et al. Nature 2021
KDM5 degraders (YU-A to YU-F)

KDM5A/B degraders

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KDM5B-specific degraders

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Degraders designed by Dr. Craig Crews
Proposed aims for Blavatnik Award

1. Optimize KDM5 degraders to a drug candidate.
   – Timeline: Q1-2 2022

2. Examine the in vivo effects of KDM5i-PROTACs as a single agent, and in combination with immune checkpoint blockade using immuno-competent syngeneic breast cancer and melanoma models.
   – Timeline: Q3 2022

3. Expand the indications to additional cancer types, including prostate, pancreatic, colorectal and ovarian cancer.
   – Timeline: Q4 2022