

# STINGRAY **SINGNA** THERAPEUTICS

**Developing the Next Generation Of** Immunotherapy To **Combat Cancer** 



## ENPP1 IS THE ONLY KNOWN CHECKPOINT OF INNATE IMMUNITY



#### HIGH ENPP1 causes:

- Reduced immune infiltration
- Increased metastasis
- Tumors resistant to immunoand chemo-therapy

Cancer Discov. 2020 Dec 28:CD-20-0387. *Nature Cancer* volume 1, pages184–196(2020) Nat Commun. 2018 Oct 24;9(1):4424. Nat Chem Biol. 2014 Dec;10(12):1043-8





### ENPP1 EXPRESSION AND IMMUNE SUPPRESSION IN HUMAN CANCER



April 29, 2024

Nature Cancer volume 1, pages184–196(2020) Nat Commun. 2018 Oct 24;9(1):4424. Nat Chem Biol. 2014 Dec;10(12):1043-8









### LOSS OF ENPP1 SENSITIZES TUMORS TO IMMUNE CHECKPOINT BLOCKADE



4T1 syngeneic mouse model of triple negative breast cancer Highly resistant to checkpoint inhibitor



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### DEVELOPMENT OF SR-8541A AS A POTENT AND SELECTIVE **INHIBITOR OF ENPP1**



hENPP1	hENPP3	mENPP1
0.06217	18.80	0.9865





## LOW DOSES OF SR-8541A SHOW SINGLE AGENT EFFECT IN A COLON CANCER MODEL (CT-26)



Time (days)

0.2 mg/kg SR-8541A

С

Vehicle













### SR-8541A ENHANCES THE EFFECT OF CHECKPOINT INHIBITION



Treatment with SR-8541A in a breast cancer organoid model shows increased immune infiltration and enhances the effect of checkpoint based immuno-therapies.



### SR-8541A COMBINED WITH FC-ENHANCED CTLA-4 ANTIBODY SHOWS STRONG EFFECT IN CT-26 COLON CANCER MODEL







### COMBINATION WITH SR-8541A +/- FC-ENHANCED ANTI-CTLA-4 +/- ANTI-PD-1





### HIGH ENPP1: LOW RESPONSE TO CHECKPOINT INHIBITORS AND **IMPAIRED SURVIVAL**

#### **Clinical Response Rate to Checkpoint Inhibition in** cGAS High/ENPP1 High Expressing Tumor Types





#### Response to therapy:

- BRCA Breast Cancer
- TGCT Tenosynovial giant cell tumor
- SARC Sarcoma
- **PAAD Pancreatic adenocarcinoma**
- MESO Mesothelioma
- **READ** Renal cell adenocarcinoma
- STAD Stomach adenocarcinoma
- **COAD** Colon adenocarcinoma
- KIRC Kidney renal clear cell carcinoma
- ESCA Esophageal carcinoma
- OV Ovarian cancer
- LUAD Lung adenocarcinoma cancer







### A NEW STANDARD OF CARE FOR MSS COLORECTAL CANCER



April 29, 2024

#### In Phase 2/3 development by Agenus

- Adaptive immune therapies
- Checkpoint inhibitors (Bot + Bal)
- 23% response in patients **without** liver metastasis
- 7% response in patients **with** liver metastasis

#### Stingray's ENPP1 inhibitor + Bot/Bal

- Addition of an innate immune therapy
- ENPP1 is upregulated in metastatic disease
- Active collaboration with Agenus to supply Bot/Bal for upcoming trials
- Tremendous investigator enthusiasm at major cancer centers







## A TEAM OF OUTSTANDING BIOTECH SPECIALISTS





**Alexis Weston** Director, BD & Program Management









**Rend Williams MPH,** PMP Head, Clinical Development

PRECISION for medicine

MedImmune

inVentiv Health





Linda McBride RPh, RAC **Director, Regulatory** 



















### VALIDATION AND AWARD SUPPORT OF THE PROGRAM

### **Cancer Prevention and Research Institute of Texas** (CPRIT) \$14M 3-year award

- Term of December 1, 2023, to November 30, 2026
- Covers 2/3rds of expenses in the MSS CRC trial (sites, CRO, drug supply, etc.)
- Covers ½ of company overhead & other expenses
- •34 applicants tried; 5 awards received

### **National Cancer Institute Direct to Phase 2** \$2M 2-year grant

- Term of September 15, 2022, to September 15, 2024
- Paid/pays for accepted IND, toxicology, pharmacology, CMC and preclinical efficacy experiments throughout most of 2024
- Received first try, start accelerated 3 months



#### **CANCER PREVENTION & RESEARCH** INSTITUTE OF TEXAS

NATIONAL CANCER INSTITUTE

### SBIR DEVELOPMENT CENTER







### VALIDATION FROM IMPACT INVESTORS

### **GKCC Family Office (Miami)**

- •Two investments
- Focus to cure cancer
- Dean Krauss, Advisor & Board Member

### **Springhood Ventures (Boston)**

- Impact investing arm of the Charles H Hood Foundation
- Looks to fill gaps in medical innovation funding to springboard new therapies

### **Catalytic Impact Foundation**

- Two investments
- Accelerate Breakthroughs by Funding Extraordinary Innovations by Visionary Leaders







### TRACTION

- First company to start ENPP1 inhibitors for cancer ullet(2016)
- **Close to exit and capital efficient** ullet
  - Only 40 months of clinicals left
  - Sale to a big pharma in clinicals
- **Big potential** lacksquare
  - Could be a new standard of care in microsatellite stable colorectal cancer
  - Broad application across many tumors (~  $\frac{1}{2}$  of all tumors) with ۲ checkpoint inhibitors
- Tremendous Grants and Awards Received \$16M
- Notable Investors in the program  $\bullet$ 
  - <u>Venture</u> GPG Ventures (Dallas), Springhood Ventures (Boston), HonorHealth Ventures (Phoenix), **Early Investment Partners (NJ)**
  - Angels Keiretsu NW, Northern Cal, Mumbai; ۲ US Angels (Palo Alto), PP Capital (Dallas) Landmark Angels (NY), Backseat Drivers (Phoenix)



A major impact drug that may change lives.





Join a proven team that's repeating their model.





A leading program.

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