Respana Therapeutics Inc.

Novel Host-Directed Therapeutics for Respiratory Illness

The Problem

A *significant unmet medical need exists* to generate better outcomes from respiratory infections:

- Severe and lethal complications of influenza are often caused by a dysregulated immune response.
- New and mutating viruses are occurring at an accelerating rate - increasing the numbers put at risk from respiratory illness.
- Vaccines are problematic – limited uptake, limited efficacy, constant modification.
- Progression to pneumonia, sepsis and ARDS creates significant mortality worldwide.
- Most treatments today focus on supportive care, antibiotics, and respiratory support.

Respana's Solution

Respana addresses this need with a novel monoclonal antibody

RT-002

which targets the complications caused by the immune response to the infection, not the infectious agent itself.

Respana's Lead Therapeutic Candidate

RT-002:

- **is not pathogen-specific**; not subject to pathogen evolution and waning efficacy.
- **is host-directed and highly-specific;** binds to a novel target within the patient: a receptor found on lung macrophages.
- **increases survival**; 100% survival of humanized mice with influenza at 14 days compared to <25% in controls.
- **facilitates healing and repair -** returns host to proper immune function.
- **avoids off-target effects** - does not target an individual cytokine.
- **utilizes a well-studied antibody isotype** – reduces manufacturing and safety risk.

Respana's Potential

- RT-002 can be first-in-class with several large-market therapeutic opportunities:

  Initial indication: Patients presenting at acute care hospital with progressive respiratory disease with suspected/confirmed influenza

  Additional follow-on indications of interest:
  - Expansion to outpatient interventions with IM formulation (or inhalation)
  - Coronaviruses
  - RSV
  - Severe progression of respiratory infections (sepsis, ARDS)
  - Partnerships to explore non-respiratory indications: fibrosis, neurologic, animal use

Initial Indication

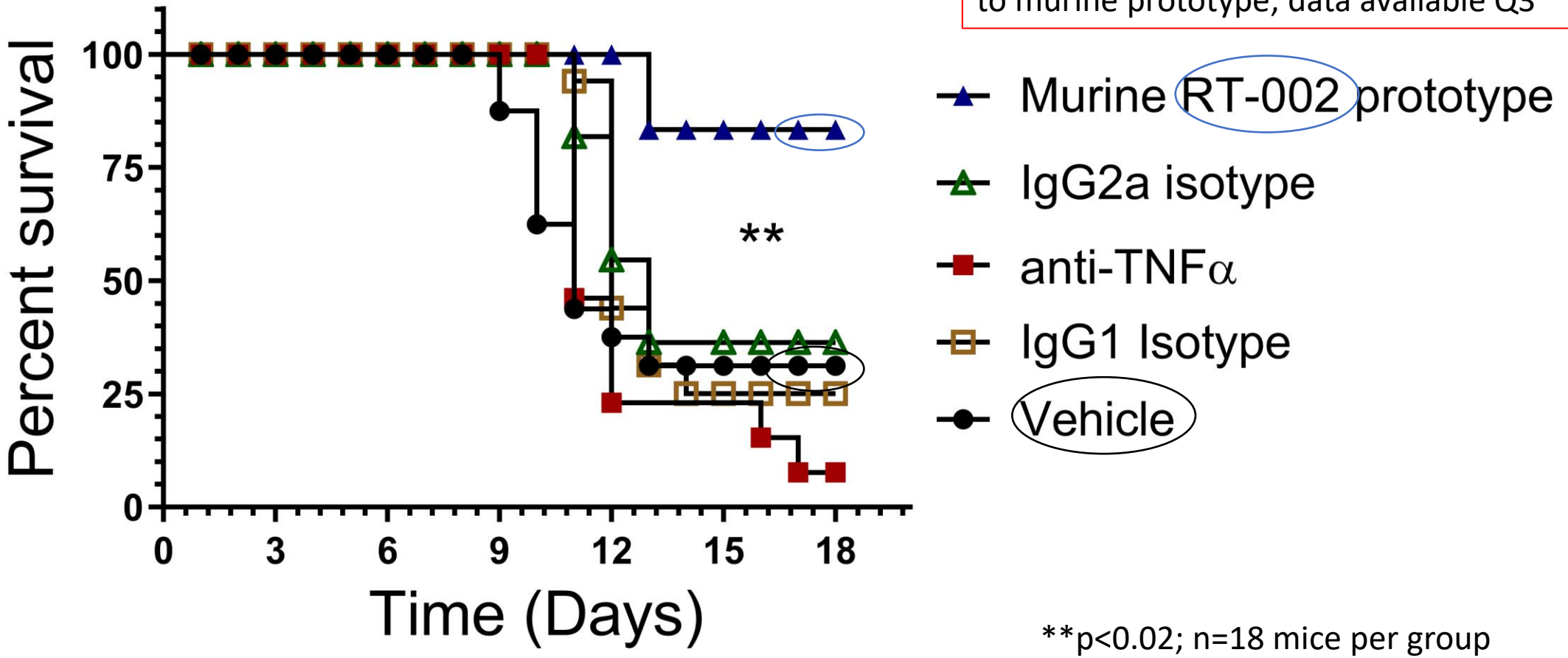
	Virus/infection	Moderate disease with pneumonia	Sepsis	ARDS
Point of Care	Physician/Urgent Care	Acute Care Hospital	Acute Care Hospital	Acute Care Hospital
Formulation	IM/inhalation	IV	IV	IV
US Market[1]	9.3-41 million - influenza only	640,000 influenza only	1.7 million cases; 350,000 deaths; 35% start as respiratory infections (600k)	200,000 cases; 80,000 deaths; 50% from respiratory infection
WW Market[2]	1 billion - influenza only	3-5 million+	49 million cases; 11 million deaths; 40% start as respiratory infections (19.6 million)	4 million cases+; 35% are fatal; 50% from respiratory infections (2 million)

Summary Results from Previous Studies

Characteristics and therapeutic modalities	Mouse RT-002 prototype clone P2H10 [n=300; Phase I STTR (1)]	Humanized clone HC2LC1 – Drug Candidate RT-002 [n= 250;Phase I (2) and Phase II STTR]
Isotype	IgG2a	IgG1
Efficacy: Recovery from severe infection	80% survival of mice compared to <25% in controls and <10% in TNFα antibody treated mice (n=5x18)	100% survival of treated humanized mice at 14 days compared to ≤25% in controls (n=8)*
Half-life in circulation (uninfected)	2.6 days, in mice	8.84 in humanized mice
Half-life in circulation (infected)	N/A	unchanged by infection
Effective dose tested so far	4 mg/kg IP, doses at 3 and 5 days after IAV infection 80% survival at 14 days	20 mg/kg IP, one dose 3 days after IAV infection 100% survival at 14 days Dose response studies in progress*
Toxicity/Safety	None found with escalating doses up to 40 mg/kg in uninfected mice	None found with escalating doses up to 40 mg/kg in uninfected mice
Biodistribution	Bronchoalveolar lavage (BAL)	Lung tissue, BAL, Urine
Pharmacodynamics	Restores gas exchange, restores pulmonary mechanics, improves histopathology, alleviates excess interferon response	Restores gas exchange, restores pulmonary mechanics*
Target engagement	N/A	Monocytic cells in human blood Alveolar macrophages in uninfected hFcRn mice*

Preclinical Efficacy and Superiority

Humanized RT-002 showing superior results to murine prototype; data available Q3



**p<0.02; n=18 mice per group

Respana's Experienced Management Team

- Kevin Harter, Chief Executive Officer
  - Serial entrepreneur, substantial operating and business development experience, successful fund-raising history.
  - Chief Innovation Officer, Penn State College of Medicine; CEO, Saladax Biomedical; Co-Founder/SVP, Life Sciences Greenhouse;
  - Co-Founder/COO, Keystone Medical Systems; Deep private and regulated board governance background.
- Scott Willett, Ph.D., Chief Technology Officer
  - 30+ years developing processes for clinical and commercial manufacture of recombinant proteins, including 5 years at Amgen
  - Extensive experience in leading internal and external development teams comprising cell culture, analytical, formulation, and purification expertise in support of tech transfer and cGMP protein manufacturing
  - Led development and manufacturing of PRM-151 (recombinant human pentraxin-2) over a 14-year span at Promedior, Inc. from early discovery through Phase III clinical testing resulting in sale of the company to Roche/Genentech
- Jeremy Middleton, Chief Business Officer
  - 35 years of biopharmaceutical executive experience holding senior leadership roles at both large and entrepreneurial companies.
  - His experience includes: Elusys Therapeutics, Valera Pharmaceuticals, Neose Technologies.
  - Global Product Director of Humira developing strategy plan that led to BASF acquisition.

Respana's Board of Directors

- Tim Pelura, PhD, Director and PI, NIH STTR grants
  - Serial life science entrepreneur with over 40 years of experience in the life science industry and has been pivotal in the development of several new therapies spanning numerous therapeutic areas.
  - Involved in several non-profit, regional and national life science initiative and served on the boards of several biotech organizations.
- Michele Washko, Director and Vice President
  - Experienced biotech operator and advisor with nearly 25 years' experience working for or advising enterprises of various types and sizes, ranging from startups to the Fortune 100.
  - Served on the boards of numerous young biotech firms and non-profit organizations and longtime member of the Corporate Faculty at Harrisburg University of Science and Technology teaching graduate courses in healthcare economics.
- Andy Agrawal, JD, Director and VP
  - Seasoned operator and advisor with more than 35 years of experience in both the public and private sector with a focus on healthcare and technology
  - Involved in various organizations and boards

Respana's Founders and Scientific Advisory Board

- Zissis C. Chroneos, PhD - Founder
  - Department of Pediatrics, Microbiology and Immunology, Pulmonary Immunology and Physiology Laboratory, Penn State College of Medicine
  - https://pennstate.pure.elsevier.com/en/persons/zissis-chroneos
- Neil Christensen, PhD - Founder
  - Professor of Pathology, and Microbiology and Immunology, Associate Chief of Experimental Pathology, Medical Director, Jake Gittlen Cancer Research Foundation, Penn State College of Medicine
  - https://pennstate.pure.elsevier.com/en/persons/neil-christense
- Lester Kobzik, M.D.
  - Pulmonary pathologist with expertise in lung host defense and infections, including evaluation of immunomodulators in pre-clinical models of influenza and other pneumonias. Professor of Pathology (Emeritus) at Harvard Medical School and currently serves as Chief Medical Officer at Cellecta, Inc in Mountain View, CA.
- Sheetal Gandhotra, M.D.
  - Dr. Sheetal Gandotra is a Pulmonary and Critical Care physician in Birmingham, AL and is affiliated with UAB Hospital. She received her medical degree from Saba University School of Medicine and has been in practice since completing fellowship in 2018. She specializes in pulmonary and critical care medicine, including procedures such as bronchoscopy and EBUS.
- Mel Billingsley, PhD
  - Former CEO, of Life Sciences Greenhouse of Central PA. Professor Emeritus of Pharmacology at Pennsylvania State University Milton S. Hershey College of Medicine, and former Professor of Biotechnology and Entrepreneurship, Penn State (Harrisburg).

Critical Milestones

Important Milestones and De-risking Activities Completed

Identification of Target	Complete
Antibody Discovery and Screening	Complete
Initial Testing of antibodies	Complete
Humanization of the antibody	Complete
Confirmational testing with humanized mAb	Complete
Select antibody and backup antibody	Complete
Manufacture research grade mab	Complete

Funded by $2+ million of STTR funds

Use of Funds:

Research Cell Bank Complete
Master Cell Bank Created/Stored
Expanded Team
Pre-IND Meeting
IND-enabling Studies
Clinical-grade material (GMP) for Trial
IND Filing
First In Human

$1.5 million of STTR funds plus combination of:

- commercialization grants ($3+MM)
- convertible debt round
- Series A/Strategic investment

Respana Therapeutics: Summary

Novel therapeutic approach

- Targets *the host, not the pathogen*
- Works *upstream* of other limited therapeutic options

Strong and expanding IP position

Seasoned scientific and management teams

Highly promising preclinical data

Priority area for Federal funding sources

Large, broad-based market opportunities

Cell Line Development nearing completion

Progress to date funded by grants and management team

Thank you.

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