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NASDAQ: LIFE

Harnessing Newly Discovered Pathways in Immunology Effected by Extracellular tRNA Synthetases

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Forward-Looking Statements

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Accelerating Value Creation from Novel Immune Pathways

Research:

Discover innovative therapeutic candidates based on extracellular functionality of tRNA synthetases

Initial focus on extracellular histidyl-tRNA synthetase (HARS)

Development:

ATYR1923 (interstitial lung diseases) in ongoing Phase 1 trial

ORCA antibody program (immuno-oncology) in IND enabling activities

Financials:

2017 year-end cash and investments at $85.1M*

Cash runway into 3Q 2019

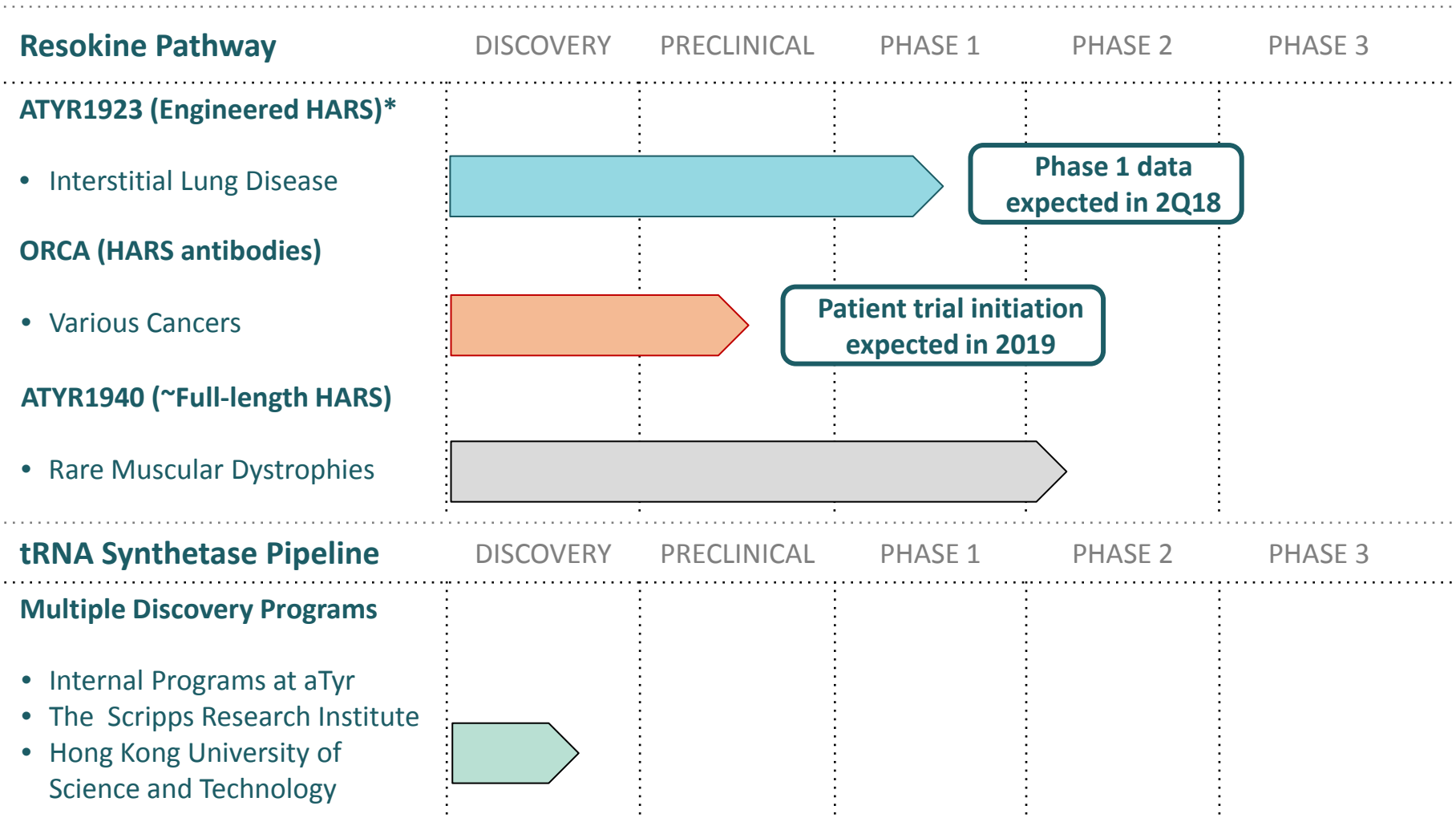
Upcoming Catalysts:

ATYR1923 Phase 1 data – 2Q 2018

First publication of ORCA data at key oncology and immunology conferences in 2018

**Estimated cash, cash equivalents, and investments provided pending completion of year-end financial close and external audit*

Therapeutic Candidate Pipeline



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***HARS:** Histidyl-tRNA synthetase

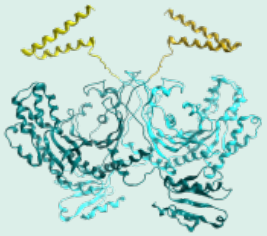
ATYR1923 (Engineered HARS): Engineered fusion protein with HARS splice variant (additional information on slide 9)

Resokine: Extracellular Proteins Derived From HARS Gene

tRNA Synthetase Genes:

AARS
CARS
DARS
EPRS
FARS
GARS
HARS
IARS
KARS
LARS
MARS
NARS
QARS
RARS
SARS
TARS
VARS
WARS
YARS

Intracellular:
(Cytoplasm)

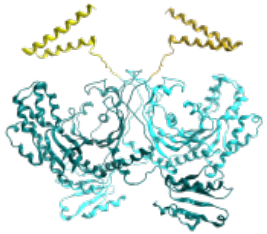


Histidyl-tRNA synthetase (HARS)

Enzymes that catalyze **protein synthesis**

Secretion

Extracellular:
(Circulation)



Full-length HARS

Splice variant of HARS
One example of multiple splice variant proteins

"Resokine Pathway"
Homeostatic pathway that controls the set point for activation of key immune cells

aTyr has built an intellectual property estate, to protect its pipeline, comprising over 300 potential protein compositions derived from all 20 human tRNA synthetase genes.

Resokine MOA Hypothesis: Regulates T Cell Activation

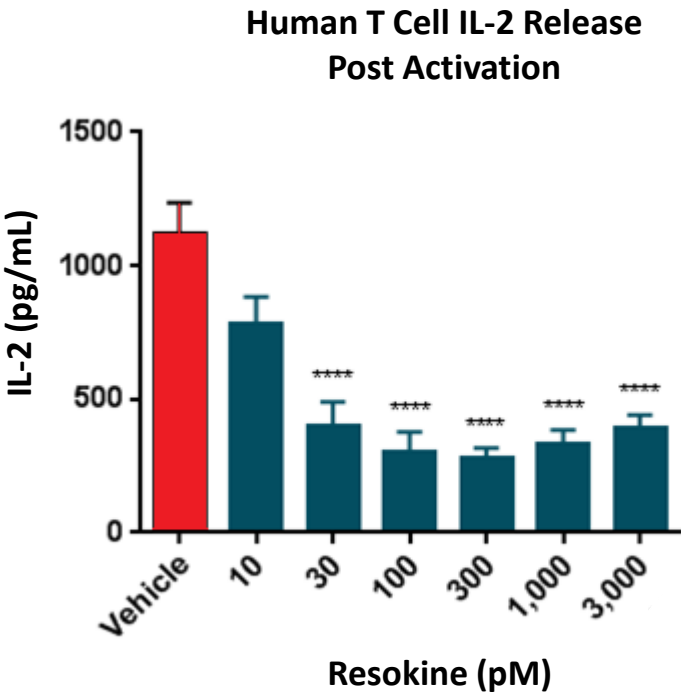
Acts on both CD4 and CD8 T cells

Effector functions at levels closer to a resting T cell

Stimulatory pathways at levels closer to a resting T cell

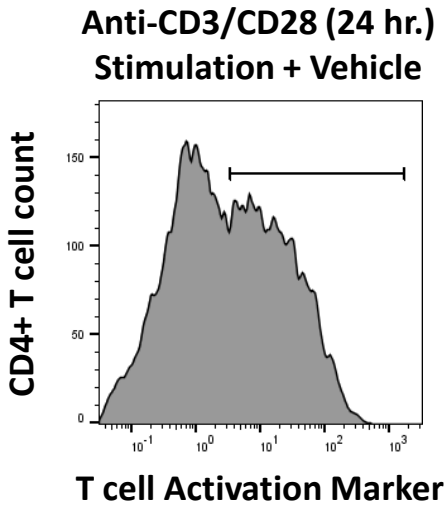
Shifts trafficking and residence closer to a resting T cell

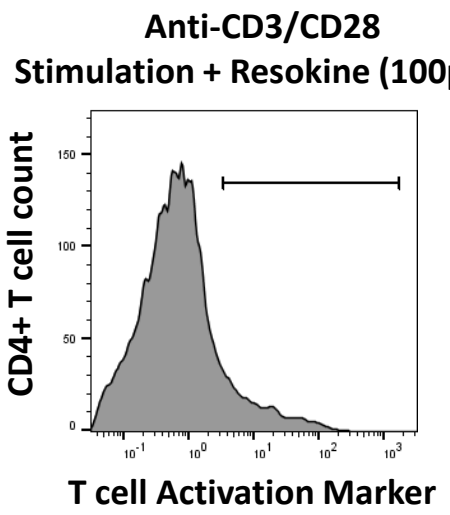
Resokine Regulates T Cell Activation



**** $p < 0.0001$

Similar for: INFγ, TNFα…
Similar to hitting PD-1 pathway





Similar for:
CD69, 4-1BB,
PD-1, ICOS…

Graphs on Right: *T cells were stimulated with anti-CD3/CD28 antibodies in the presence of vehicle or Resokine. After 24 hours, supernatants were collected and analyzed by ELISA. Statistics by T test.*

ATYR1923 for the Treatment of Interstitial Lung Diseases

Engineered HARS Splice Variant (iMod.Fc)

ATYR1923: Program Snapshot

ATYR1923 (iMod.Fc):

Engineered fusion protein with HARS splice variant

Refer to splice variant as the "iMod domain"

(iMod for **i**mmuno-**mod**ulatory function)

Patients:

Interstitial lung diseases (ILDs) characterized by an immune component

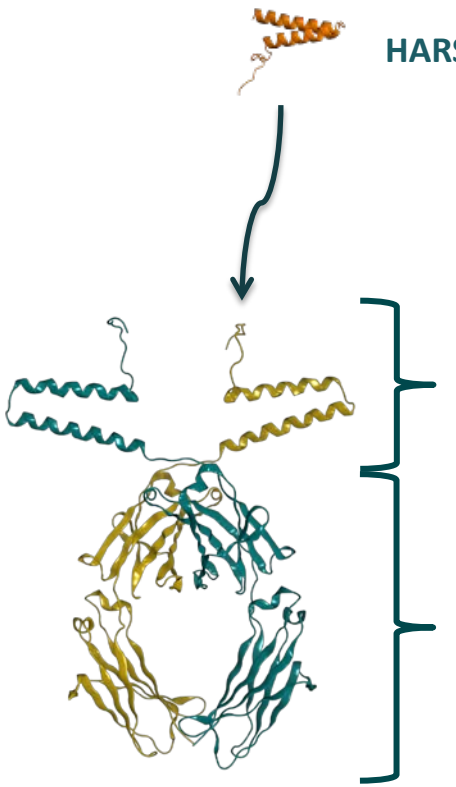
Mechanism:

Regulation of T cell activation via the Resokine pathway

Rationale:

Functional knockout of Resokine pathway in humans and rodents results in T cell mobilization and lung damage

Immune dysfunction is key to pathophysiology of ILDs



Target Dosing:

Improved pharmacokinetic profile that supports once/twice monthly IV infusion

Interstitial Lung Diseases Share Persistent Immune Engagement

Idiopathic Pulmonary Fibrosis (IPF)

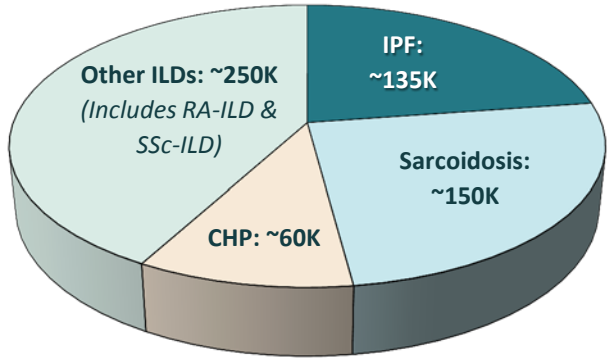
Rheumatoid Arthritis – ILD (RA-ILD)

Chronic Hypersensitivity Pneumonitis (CHP)

Systemic Sclerosis – ILD (SSc-ILD)

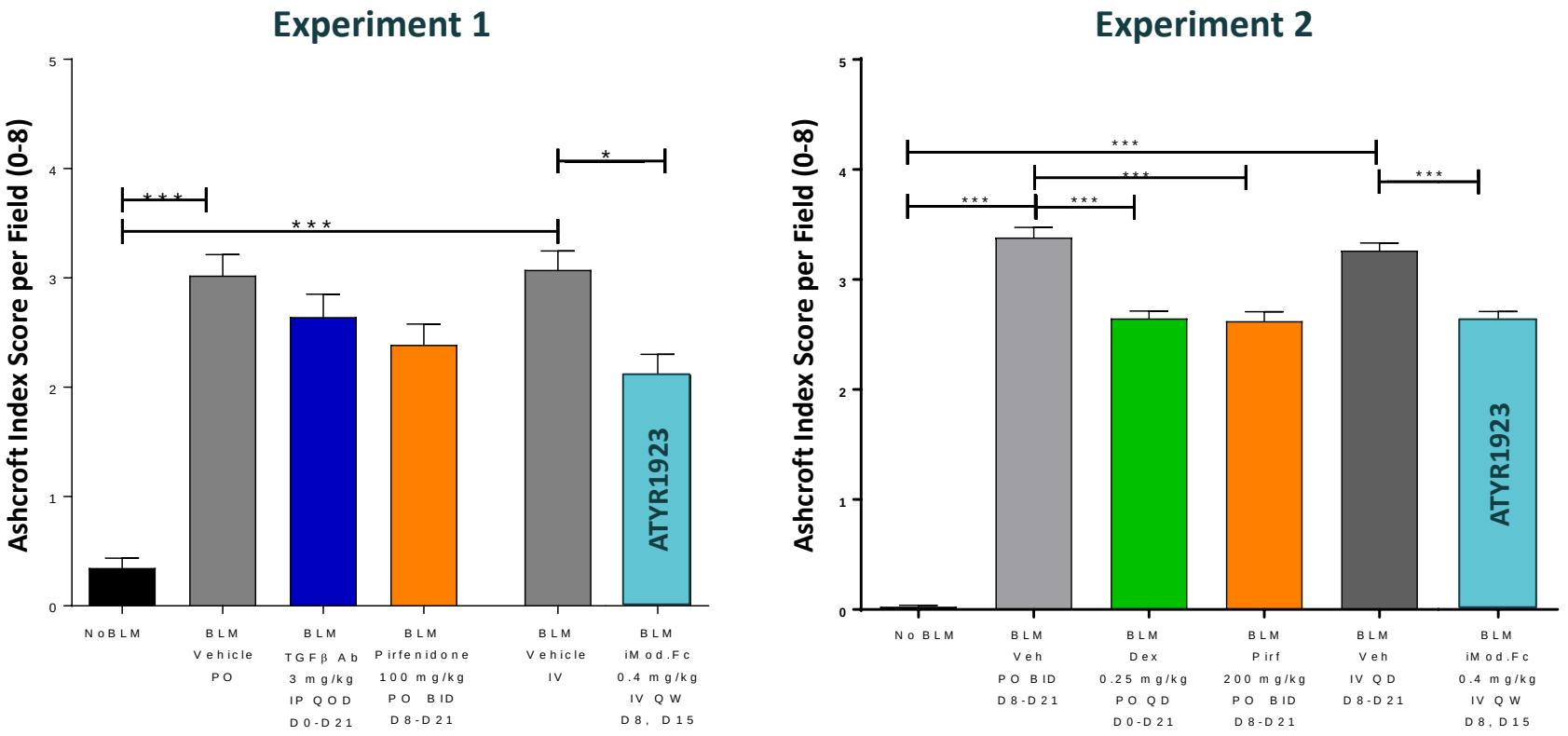
Sarcoidosis

Estimated ILD US Patient Populations



Slide adapted from Dr. Steven Nathan, Medical Director, Advanced Lung Disease and Transplant Program at Inova Fairfax Hospital, Falls Church, VA

ATYR1923 Ameliorates Fibrosis in Bleomycin-Induced Lung Injury



ATYR1923 (iMod.Fc) administered therapeutically at 0.4 mg/kg weekly drives efficacy comparable to or greater than Pirfenidone*, anti-TGF antibodies, and dexamethasone

Pirfenidone: *Current approved therapy for IPF patients (annual sales in 2016 ~ $830M)*

Note: *Bleomycin mouse model abstract presented as a poster at the American Thoracic Society in May 2017*

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ATYR1923 Clinical Development for Interstitial Lung Diseases

Clinical Overview
Randomized, double-blind, placebo-controlled studies to investigate the safety, tolerability, immunogenicity, pharmacokinetics and pharmacodynamics of intravenous ATYR1923 (iMod.Fc) in healthy volunteers and patients with interstitial lung disease.

Phase 1 - Healthy Volunteers:
- 36 subjects across 6 dose cohorts
- Dosing (single infusion):
  - 0.03 mg/kg up to potentially 5.0 mg/kg

✓ First subjects dosed in the fourth quarter of 2017
❑ Data expected in 2Q 2018

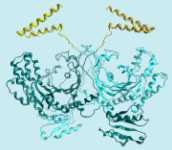
Phase 2 - Interstitial Lung Disease patients with an immune component:
- Collaborating with industry leading clinicians to develop patient trials for ATYR1923

ORCA – Targeting a Novel Immune Set Point for Cancer Patients

Antibodies to the Resokine Pathway

Regulating T Cells to Temper or Enhance Anti-Tumor Immunity

Resokine



"Agonist"

Regulates T cell activation with potential to ***temper*** immune system

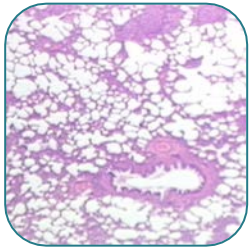
ORCA

"Antagonist"

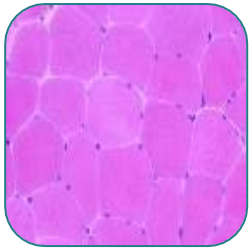
Unlocks T cell activity with potential to ***enhance*** *anti-tumor immunity*

Anti-Synthetase Syndrome: Evidence of Resokine Pathway Relevance in a Human Disease Setting

Healthy Tissue



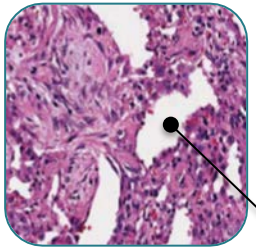
Healthy lung



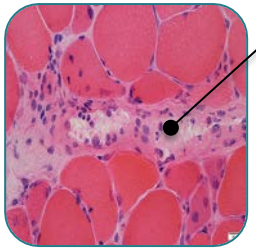
Healthy muscle

Resokine disruption via auto-antibodies

T Cells Mobilized in Tissue

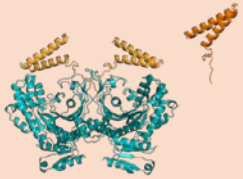


Interstitial Lung Disease

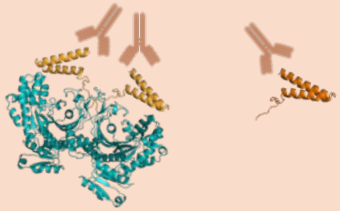


Inflammatory Myopathy

↑ Immune cell invasion/activity



Resokine acts as homeostatic regulator of immune activity



Antibodies to Resokine lower threshold for T cell activation

**100% (18 of 18) anti-synthetase syndrome patients tested positive for antibodies for Resokine proteins*

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ORCA Program: Snapshot

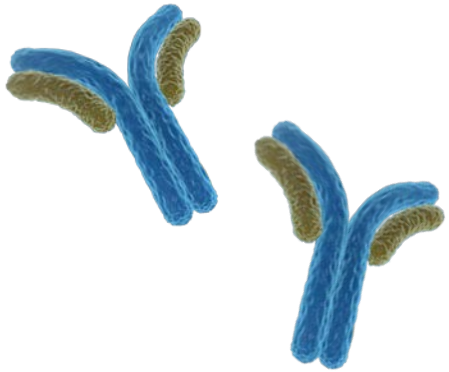
Patients:
Potentially all cancer types:

- >450 patient samples in over 10 tumor types tested
- ~95% of cancer patients tested positive for Resokine

Target:
Resokine pathway

Therapeutic Concept:
Antibody to block Resokine activity, increases T cell engagement

Rationale:
Human evidence of Resokine antibody changing T cell behavior (anti-synthetase syndrome patients)
Phenotype replicated in animal functional knock-out models



Biomarker:
Liquid biopsy correlates with tumor volume and efficacy

ORCA Program: Supportive *In Vivo* Data and Development Timelines

In Vivo Efficacy Data

Resokine Abs effective in multiple mouse syngeneic tumor models

- ✓ Outperformed checkpoint inhibitors (e.g. Abs to PD-1, PD-L1, CTLA-4) in various animal models

Resokine Abs effective alone and in combination

- ✓ Efficacy potential as monotherapy and with checkpoint inhibitors (based on tumor model data)

Development Timelines

Resokine antibody selection:

- ✓ Panel of antibodies selected and in IND enabling activities

Present Data at Scientific Conferences:

- ✓ Abstract at ASCO-SITC in January 2018
- ❑ Additional presentations in 2018

First clinical trial in patients:

- ❑ Initiate in 2019

Accelerating Value Creation from Novel Immune Pathways

2018 Strategic Goals:

Advance Clinical Development

- ATYR1923 Phase 1 ongoing with data in 2Q 2018

Advance Immuno-Oncology Program

- IND-enabling activities ongoing for patient trials in 2019

Discovery and Pipeline Enhancement

- Collaborating with academic institutions and ongoing internal programs to discover innovative therapeutic candidates from tRNA synthetase biology

Financials:

✓ **$85.1M*** cash and investments as of 12/31/17; cash runway into 3Q 2019

✓ Market capitalization as of closing price on 12/31/17: **~$144M****

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**Estimated cash, cash equivalents and investments provided pending completion of year-end financial close and external audit*
***Market capitalization calculated using all common shares outstanding and preferred class X shares on an if-converted basis for a total outstanding share count of 41.14M shares.*