aTyr Pharma
NASDAQ: LIFE

Translating New Immune Pathways into Meaningful Medicines

Jefferies 2018 Global Healthcare Conference
June 7, 2018

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Forward-Looking Statements

The following slides and any accompanying oral presentation contain forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. The use of words such as “may,” “might,” “will,” “should,” “expect,” “plan,” “anticipate,” “believe,” “estimate,” “project,” “intend,” “future,” “potential,” “opportunity,” or “continue,” and other similar expressions are intended to identify forward-looking statements. For example, all statements we make regarding the potential therapeutic benefits of proteins derived from tRNA synthetase genes and our product candidates, including ATYR1923 and any product candidates from our other pipeline programs, the ability to successfully advance our pipeline or product candidates, the timing within which we expect to initiate, receive and report data from, and complete our planned clinical trials, our ability to receive regulatory approvals for, and commercialize, our product candidates, our ability to identify and discover additional product candidates, and the ability of our intellectual property portfolio to provide protection are forward-looking statements. All forward-looking statements are based on estimates and assumptions by our management that, although we believe to be reasonable, are inherently uncertain. All forward-looking statements are subject to risks and uncertainties that may cause actual results to differ materially from those that we expected. These risks, uncertainties and other factors are more fully described in our filings with the U.S. Securities and Exchange Commission, including our Annual Report on Form 10-K, our Quarterly Reports on Form 10-Q, and in our other filings. The forward-looking statements in this presentation speak only as of the date of this presentation and neither we nor any other person assume responsibility for the accuracy and completeness of any forward-looking statement. We undertake no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future events or otherwise, except as required by law.

Accelerating Value Creation from Novel Immune Pathways

Research:

Discover innovative therapeutic candidates based on extracellular functionality of tRNA synthetases

Initial focus on Resokine Pathway

Lead Product Candidate: ATYR1923

Engineered Resokine protein for the treatment of inflammatory interstitial lung diseases

Financials:

Cash, cash equivalents and investments at $74.1M as of 3/31/2018

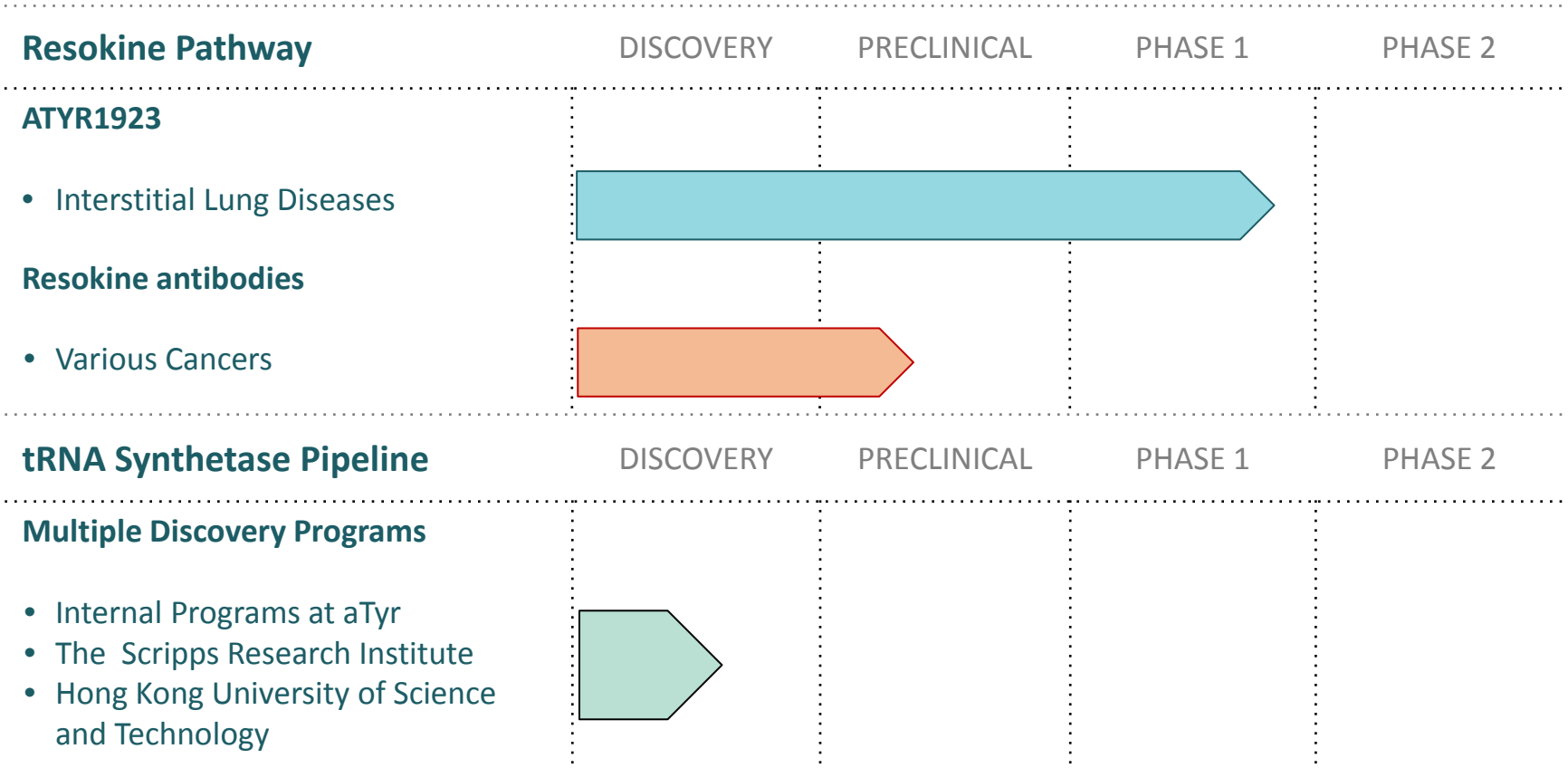
Upcoming Clinical Catalysts:

ATYR1923 Phase 1 data – 2Q 2018

Patient trial initiation – 4Q 2018

***Resokine Pathway:** Naturally secreted extracellular proteins derived from the histidyl-tRNA synthetase (HARS) gene

Therapeutic Candidate Pipeline



***ATYR1923:** Engineered fusion protein with histidyl-tRNA synthetase (HARS) splice variant

ATYR1923 for the Treatment of Interstitial Lung Diseases

Engineered HARS Splice Variant

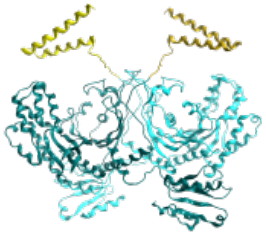
iMod: Extracellular Splice Variant Derived From HARS Gene

tRNA Synthetase Genes:

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

Intracellular
Protein Synthesis Function

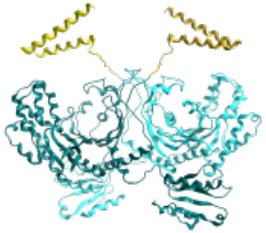
Histidyl-tRNA Synthetase (HARS)



Secretion
(non-canonical)

Extracellular
Immunomodulatory Function

Resokine (extracellular HARS and splice variants)



aTyr has identified the N-terminal domain of HARS as having an immunomodulatory function extracellularly (aTyr has named this the iMod Domain)

Immune Set Point Hypothesis: Resokine Pathway

Hypothesis: Resokine is part of a regulatory pathway that controls the immune set-point

- Sets the threshold of stimulation required for immune activation

Resokine inhibits T cell activation *in vitro*

- Inhibits release of inflammatory cytokines (e.g. IL-2, IFNγ) and effectors (e.g. granzyme B)
- Prevents up-regulation of cell-surface activation markers

Resokine has activity in a number of animal models of inflammatory disease

- TNBS-induced colitis, statin-induced myopathy, bleomycin-induced lung disease, IL-23 induced psoriasis, type-1 diabetes

Resokine circulates in healthy individuals

- Detectable levels in all healthy individuals tested
- Levels altered in some disease states

ATYR1923: Program Snapshot

ATYR1923:

Engineered Fc fusion protein with HARS splice variant

Refer to splice variant as the "iMod domain"

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

Mechanism:

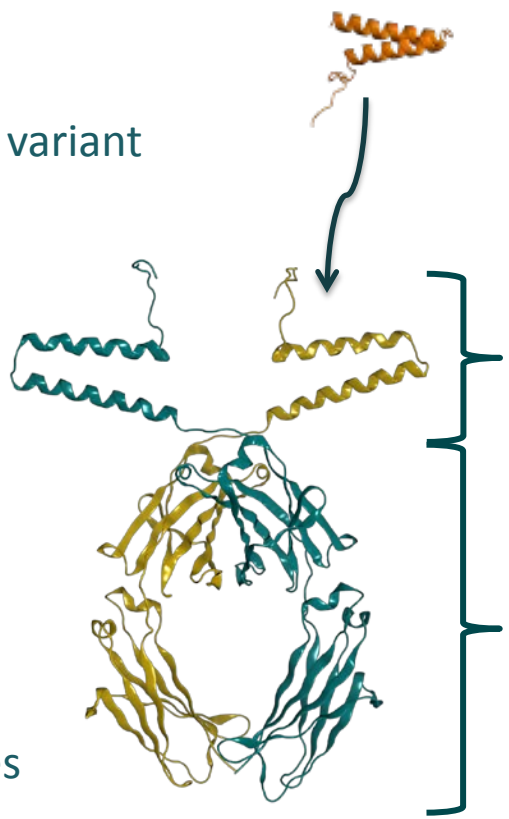
Regulation of immune system

Binds to Neuropilin-2 (NRP-2)

Target Population:

Primary: Inflammatory interstitial lung diseases

Secondary: Other inflammatory disorders

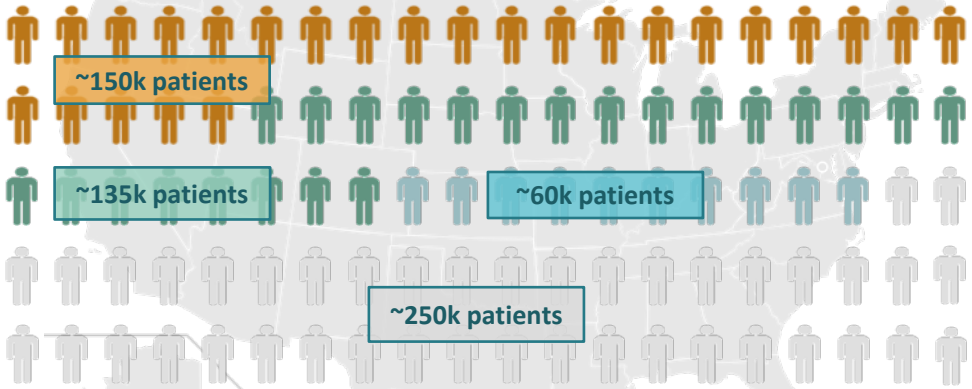


High Unmet Need in Multiple Interstitial Lung Diseases

Sarcoidosis
- **~150K patients in the U.S.**
- Systemic inflammatory disorder characterized by non-caseating granulomas (CD4+ T cell driven)
- Advanced pulmonary disease is leading cause of death
- ~30% of patients have chronic inflammation, unresponsive to steroid treatment

Chronic Hypersensitivity Pneumonitis (CHP)
- **~60K patients in the U.S.**
- Exaggerated immune response to environmental antigen
- Commonly misdiagnosed as IPF
- Median survival: 7 years
- No effective therapeutic options

Represents 1% of U.S. ILD population



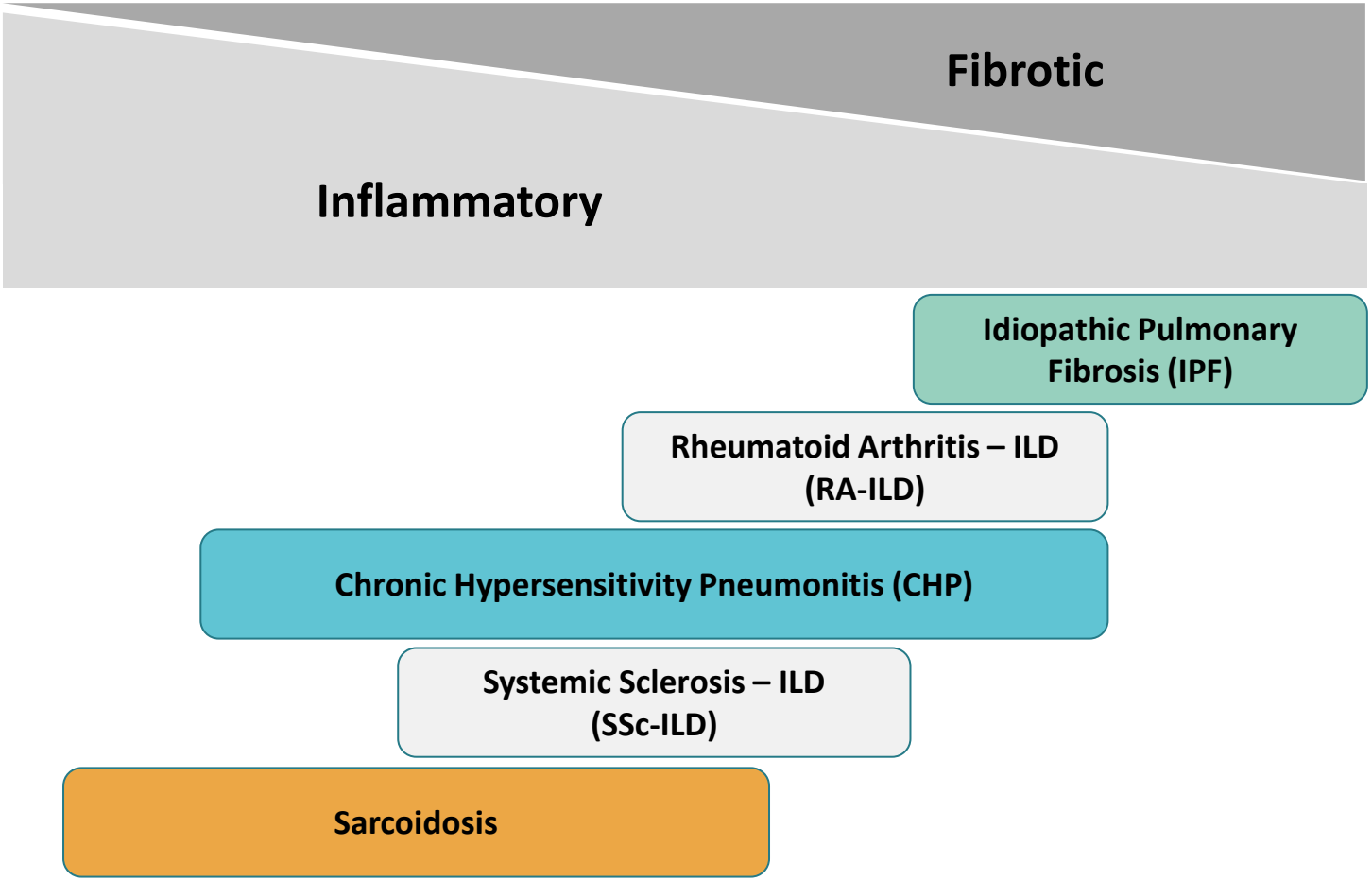
Idiopathic Pulmonary Fibrosis (IPF)
- **~135K patients in the U.S.**
- Irreversible, progressive disease with acute episodes
- Median survival: 3-5 years
- Current SOC: Nintedanib / pirfenidone slow functional loss but associated with significant side effects;
  - ➢ **~$2.0B+ combined sales in 2017 and growing**

Other ILDs (>100 disorders, ~250K patients in the U.S.)
- Many secondary to other disease **(e.g. SSc-ILD, RA-ILD)**
- All share underlying inflammatory insult

Large unmet medical need
- Many have grave prognosis
- SOC has limited evidence of safety or efficacy

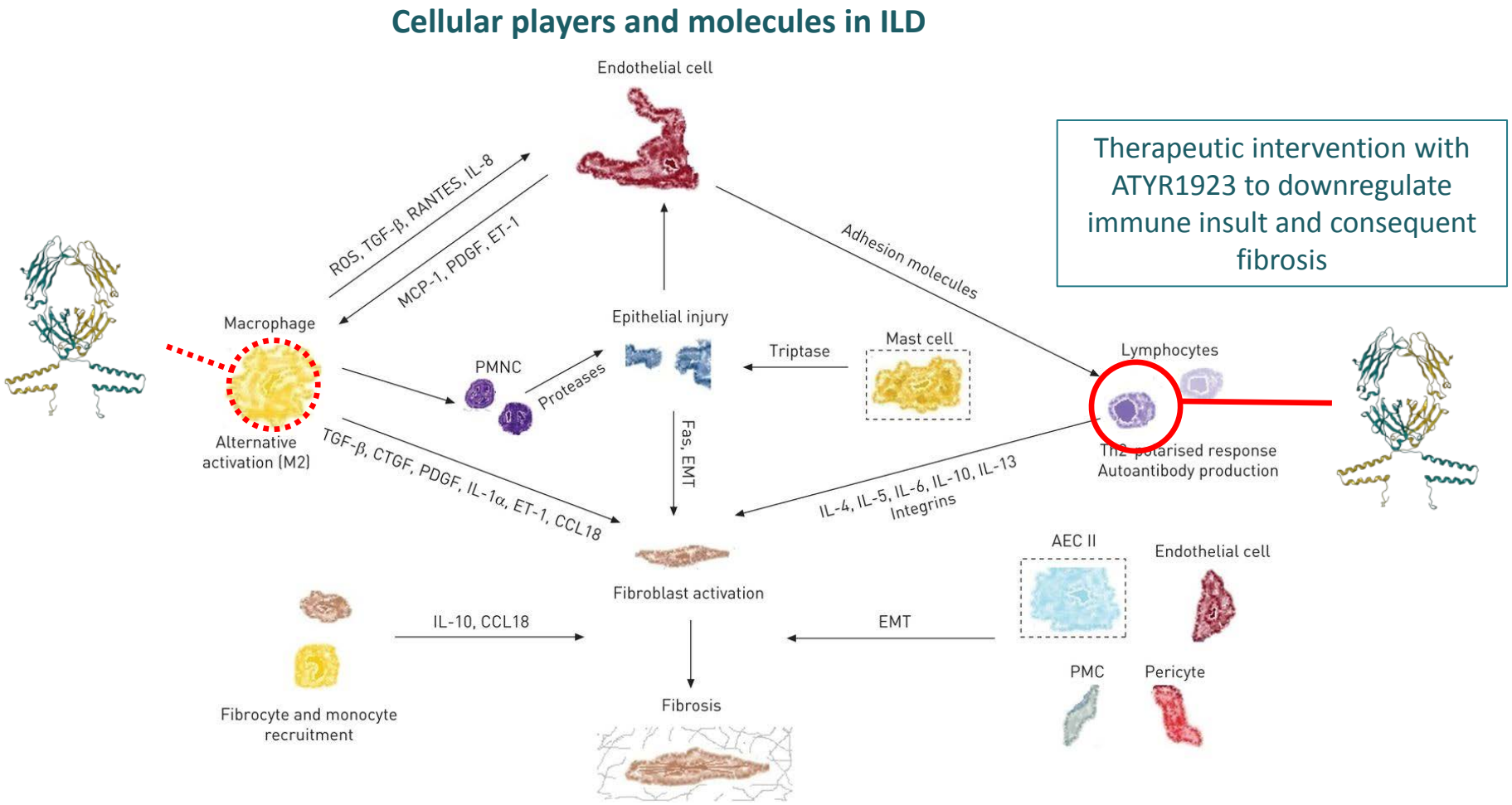
2017 annual sales of Ofev® (nintedanib) ~920 Euros, 52.3% increase YoY
2017 annual sales of Esbriet® (pirfenidone) ~869 CHF, 13% increase YoY

Interstitial Lung Diseases Share Persistent Immune Engagement



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

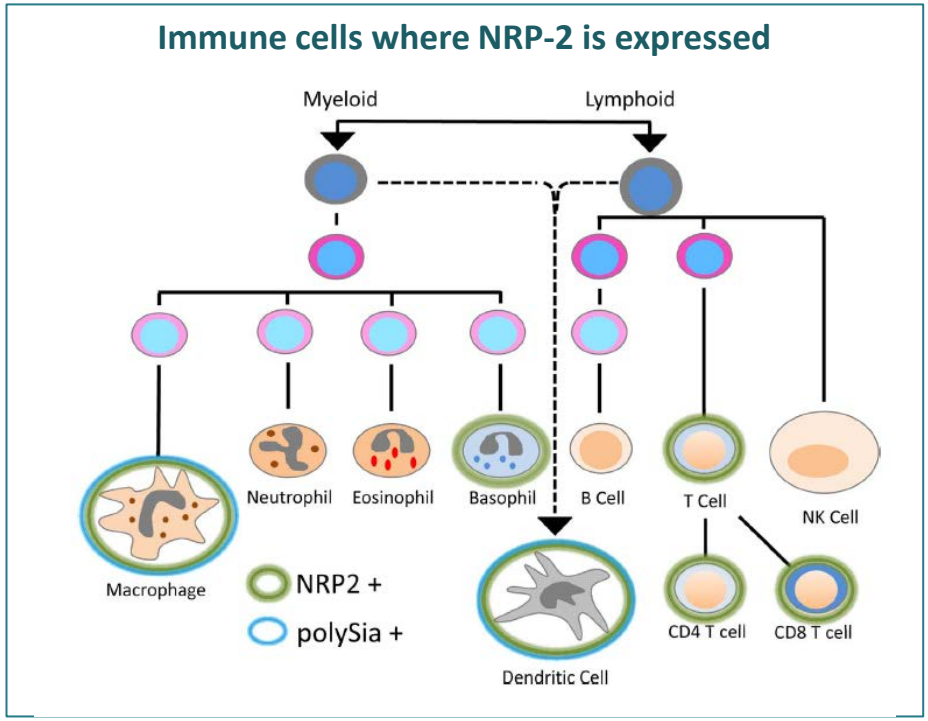
ATYR1923 MOA Overlaps with ILD Pathogenesis



Bagnoto, Harari, *European Respiratory Review*, 2015

Neuropilin-2 (NRP-2) Identified as a Binding Partner for ATYR1923

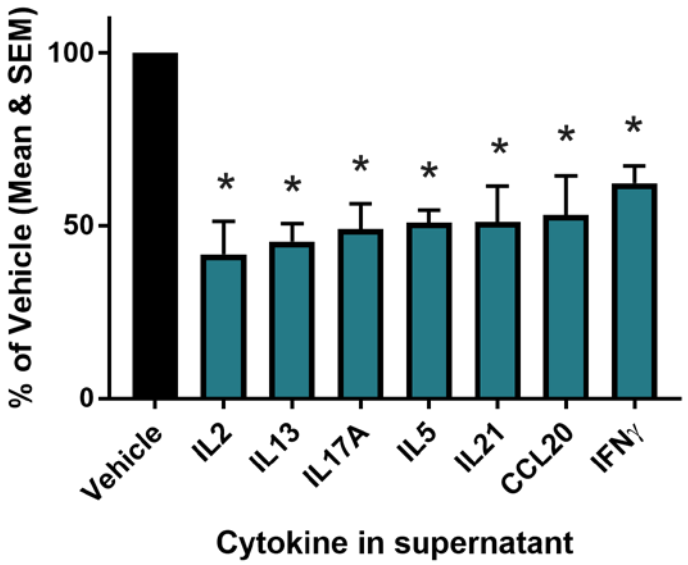
- Pleiotropic receptor that can bind to a number of different ligands
- Well-established role in the development of the neural and lymphatic systems
- Emerging role in the immune system; present on a number of immune cell types
- Expressed on alveolar macrophages and may play role in regulating lung inflammation



Schellenberg et al. *Role of Neuropilin-2 in the immune system.* Mol. Immunol. 90, 239-244. 2017

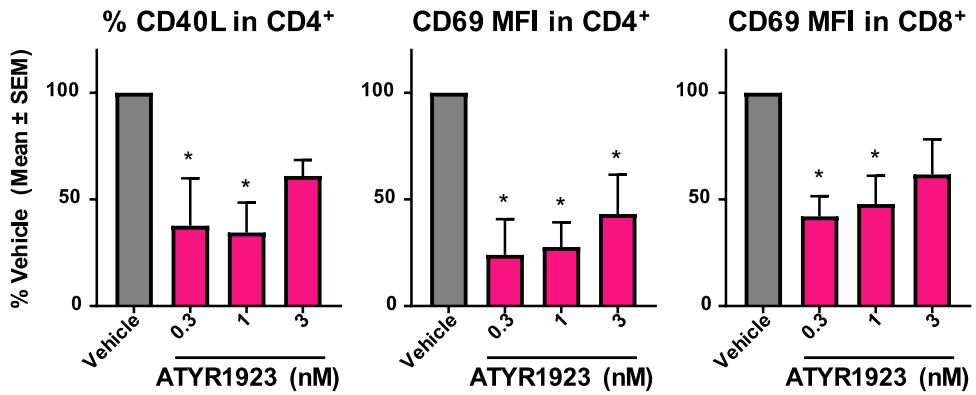
ATYR1923 Inhibits T Cell Activation In Vitro

Effect of 0.3 nM ATYR1923 on T Cell Cytokine Release



Mean response from 3 donors

Effect of ATYR1923 on T Cell Activation Markers

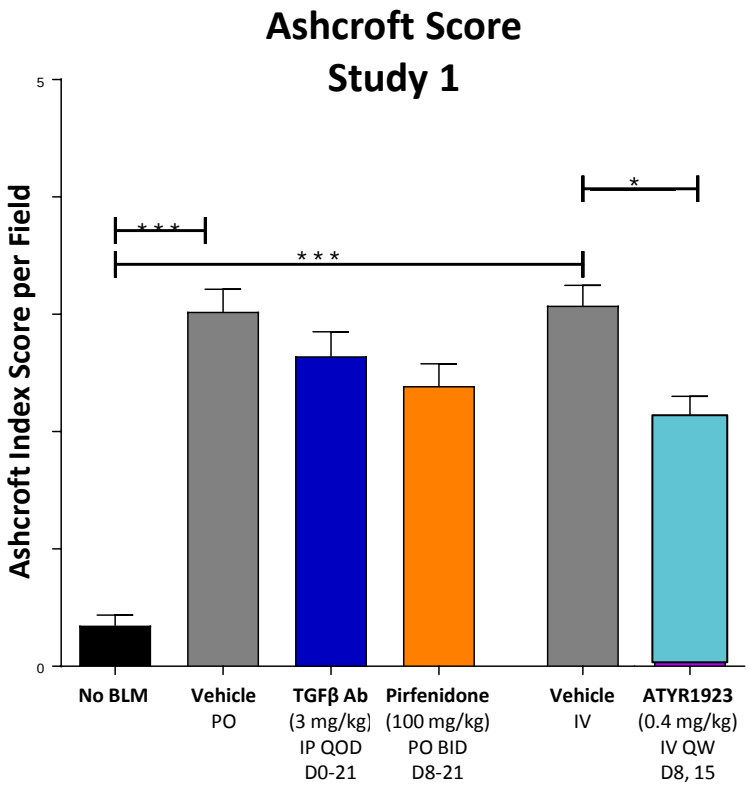


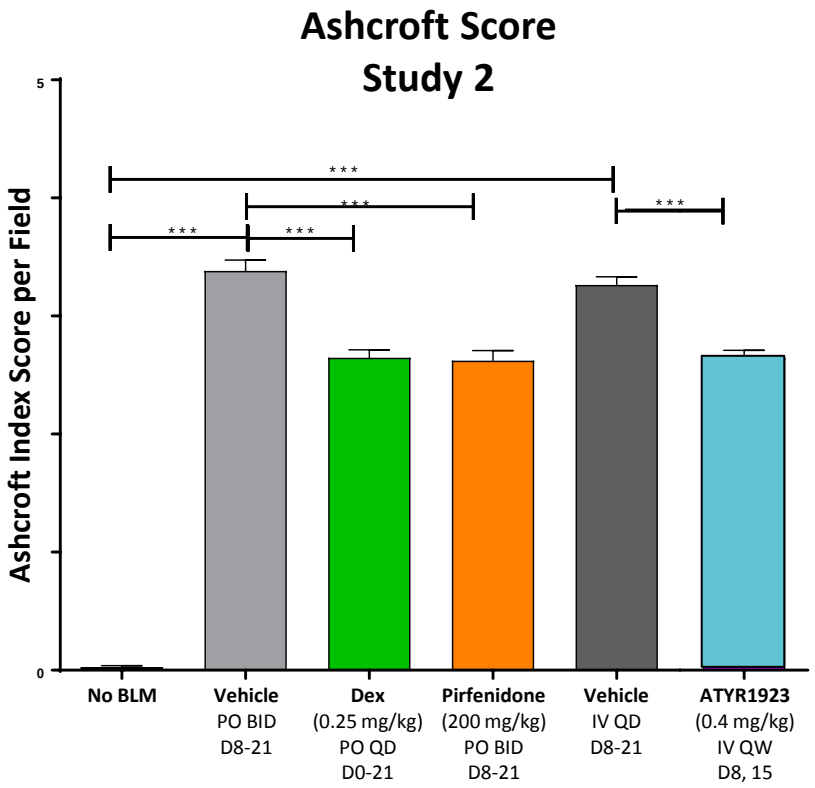
aTyr is currently exploring the interaction with ATYR1923 and NRP-2 across multiple immune cell types

*$P < 0.05$

Note: *Presented in a poster at the American Academy of Immunology Annual Meeting in May 2018*

Weekly Therapeutic Dosing of ATYR1923 Reduces Fibrosis in Mouse Bleomycin Model



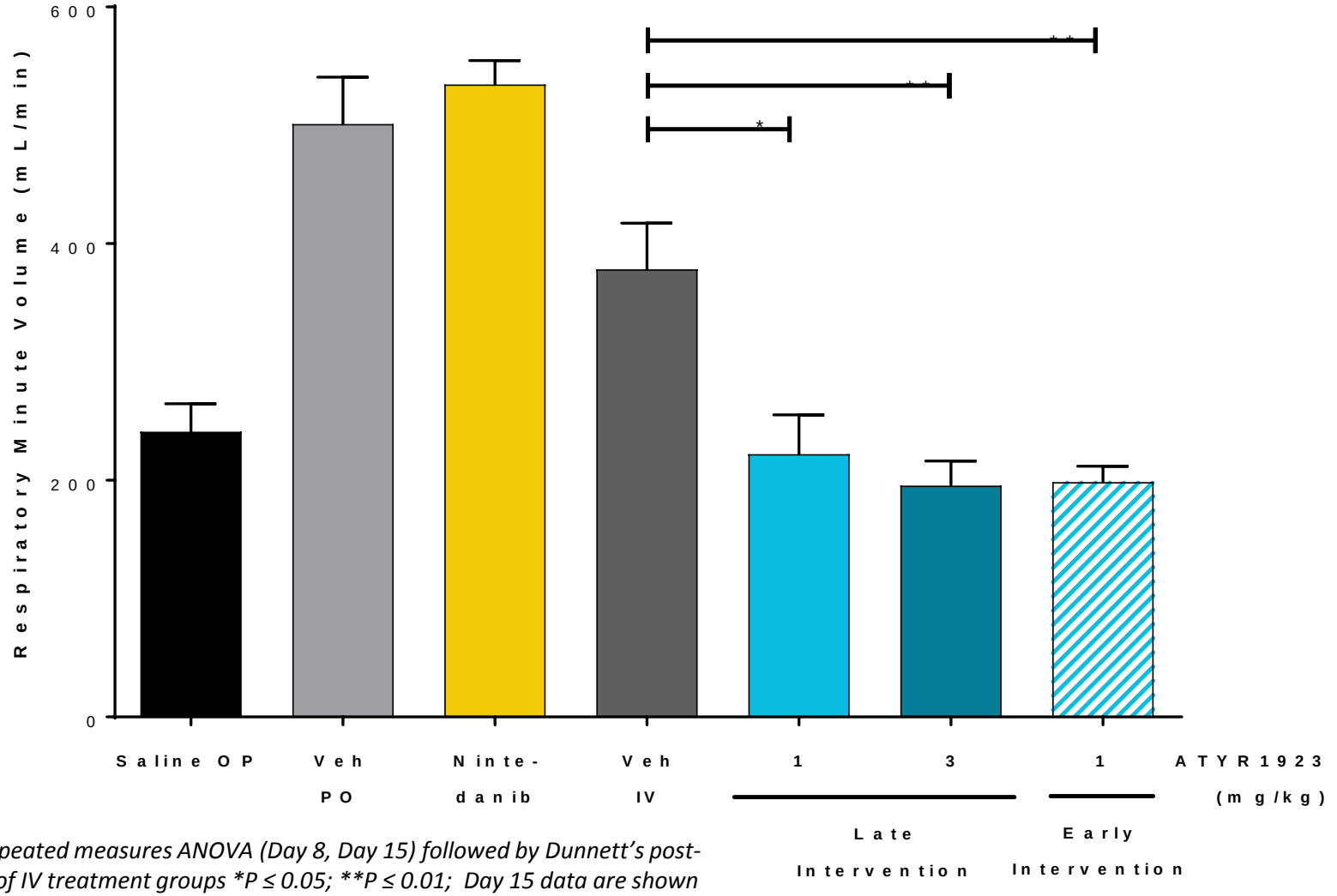


ATYR1923 administered therapeutically at 0.4 mg/kg QW reduces histological fibrosis comparable to or greater than pirfenidone, anti-TGF antibodies, and dexamethasone

****P ≤ 0.001; *P < 0.05*

Note: *Presented in a poster at the American Thoracic Society International Conference in May 2017*

ATYR1923 Returns Breathing to Normal in Rat Bleomycin Model



*2-way repeated measures ANOVA (Day 8, Day 15) followed by Dunnett's post-hoc test of IV treatment groups *P ≤ 0.05; **P ≤ 0.01; Day 15 data are shown*

Late and early intervention commenced on Days 9 and 2, respectively
Respiratory Volume = amount of air inhaled/exhaled/min; Nintedanib dosed daily (Days 9-21)
Note: *Presented in a poster at the American Thoracic Society International Conference in May 2018*

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Favorable Safety Profile Observed in 1- and 3- Month GLP Toxicology Studies

Nonhuman Primates

2 weekly IV doses of 3 mg/kg

- No increase in ~30 serum immune markers

1- and 3-month weekly IV dose

at 0, 10, 30, and 60 mg/kg

- No adverse test article–related findings
- Systemic exposure increased with increasing dose and did not appear to change with repeated dosing
- Anti-drug antibodies (ADA) did not appear to have an impact on systemic exposure
- No-observed-adverse-effect level (NOAEL) = 60 mg/kg (C_{trough} = 228 nM)

6-Month GLP study ongoing in nonhuman primates

Rodents

1- and 3-month weekly IV dose

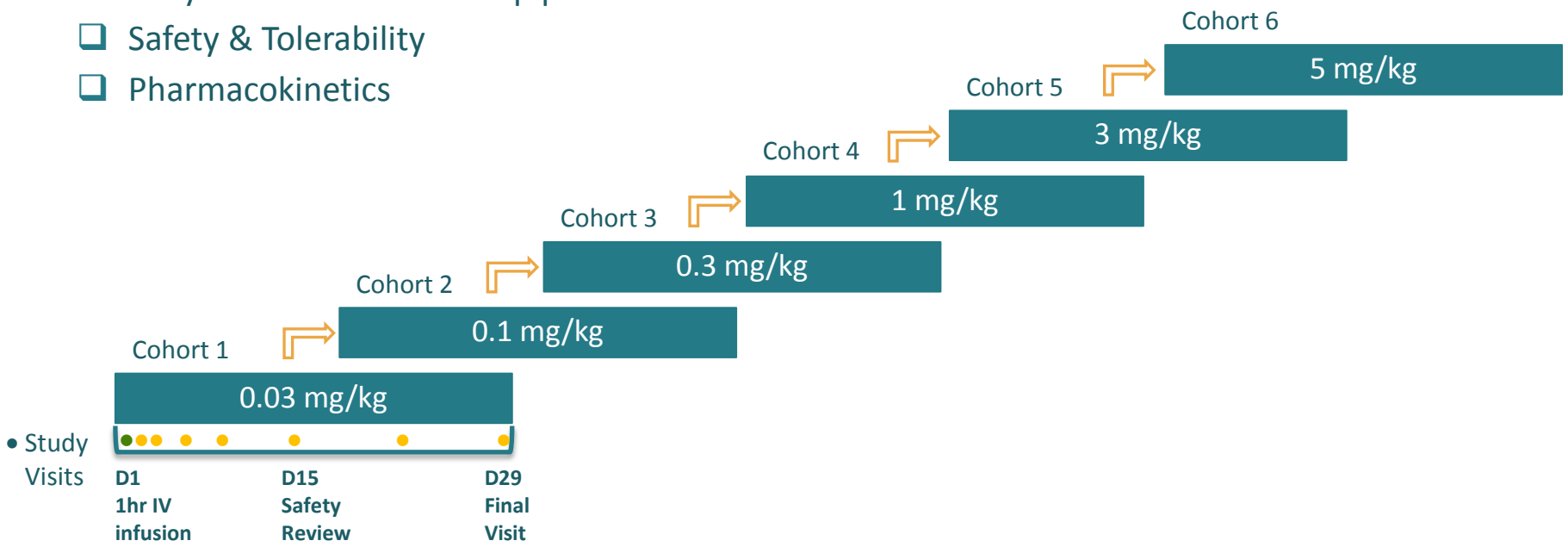
at 0, 10, 30, and 60 mg/kg

- No adverse test article–related findings
- Systemic exposure increased with increasing dose and did not appear to change with repeated dosing
- ADA did not appear to have an impact on systemic exposure
- NOAEL = 60 mg/kg

Note: *Presented in a poster at the American Thoracic Society International Conference in May 2018*

ATYR1923 Phase I Healthy Volunteer Study

- Randomized, double-blind, placebo-controlled, single-ascending-dose
- 6 Cohorts; 6 healthy volunteers/cohort; 2:1 randomization (N=36 HVs total)
- 30-day assessment-follow-up period
  - ❑ Safety & Tolerability
  - ❑ Pharmacokinetics



- Dose escalation proceeded through Cohort 6 (DRC review after each cohort)
- All participants completed study drug infusion in all cohorts
- Top-line data to be announced in June

*DRC = Data Review Committee reviews safety of each cohort before approving dose escalation

Strategic Focus to Create Long-Term Shareholder Value

Phase 2 Trial – Interstitial Lung Disease

1. Several translational animal studies ongoing to better inform clinical direction
2. Understanding the interaction of Neuropilin-2 as a binding receptor for ATYR1923
3. Collaborating with industry leading pulmonary clinicians to develop patient trials for ATYR1923

➢ Initiate patient trial in 4Q 2018

Discovery and Pipeline Enhancement

- Academic collaborations and ongoing internal programs to discover innovative therapeutic candidates from tRNA synthetase biology

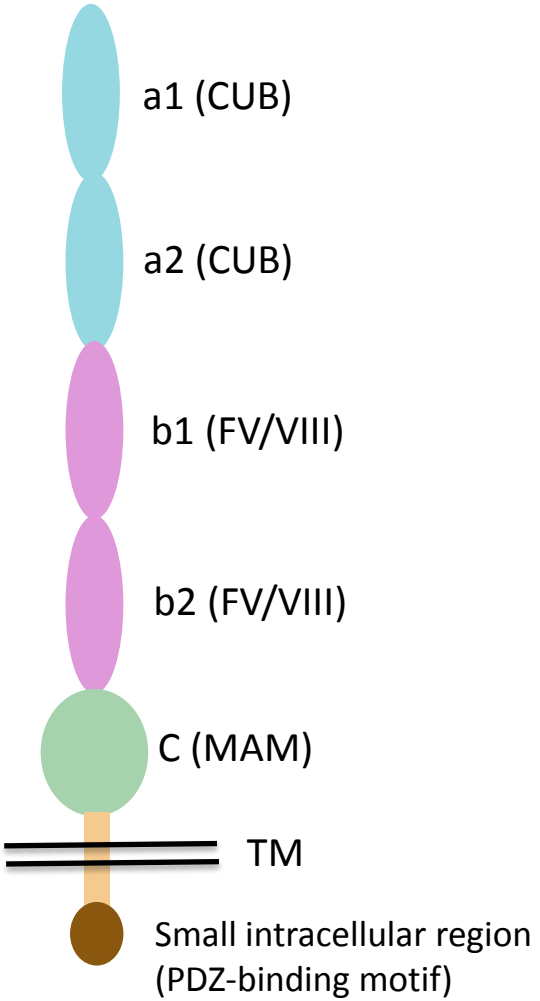
Financials

- **$74.1M** cash, cash equivalents and investments as of 3/31/18
- Market capitalization as of closing price on 6/1/18: **~$36M***

**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 41.3M shares.*

Appendix: Neuropilin-2 (NRP-2) Overview

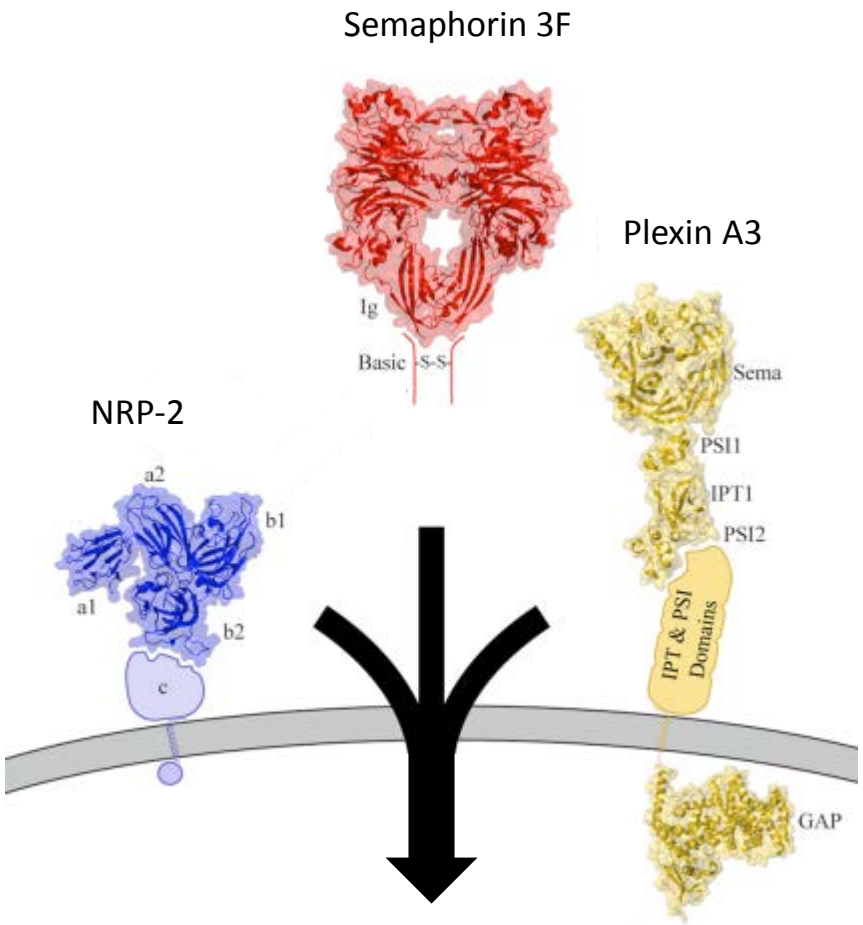
Neuropilin-2



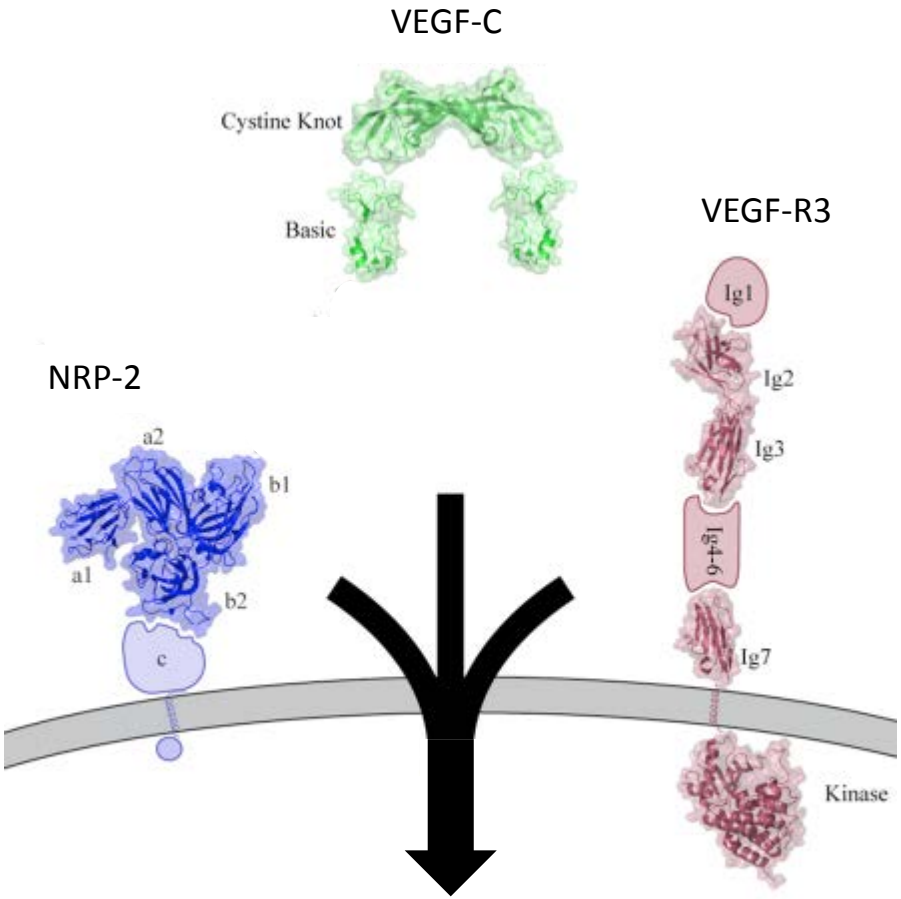
- Originally identified based on its role in axon guidance during neuronal development
- Subsequently shown to be a pleiotropic receptor that can regulate diverse pathways
  - Binds multiple ligands
  - Pairs with multiple co-receptors
- Widely distributed, though often held intracellularly and transported to the cell surface under specific stress/activation conditions
- Type I transmembrane glycoprotein of approx. 120kDa (926 amino acids)
- 5 defined extracellular domains
- Small intracellular domain (46 amino acids) has limited signaling ability

CUB: Complement C1r/s, UEGF, BMP-1 homology domain. FV/FIII: Factor V/VIII homology domain.
MAM: Meprin, A5, mu phosphatase homology domain

NRP-2 Utilizes Common Mechanisms to Regulate Diverse Pathways



Plexin driven signaling



VEGFR driven signaling

Adapted from Parker *et al.,* (2012) *Biochemistry* 51, 9437-9446

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NRP-2 is Highly Expressed in Alveolar Macrophages

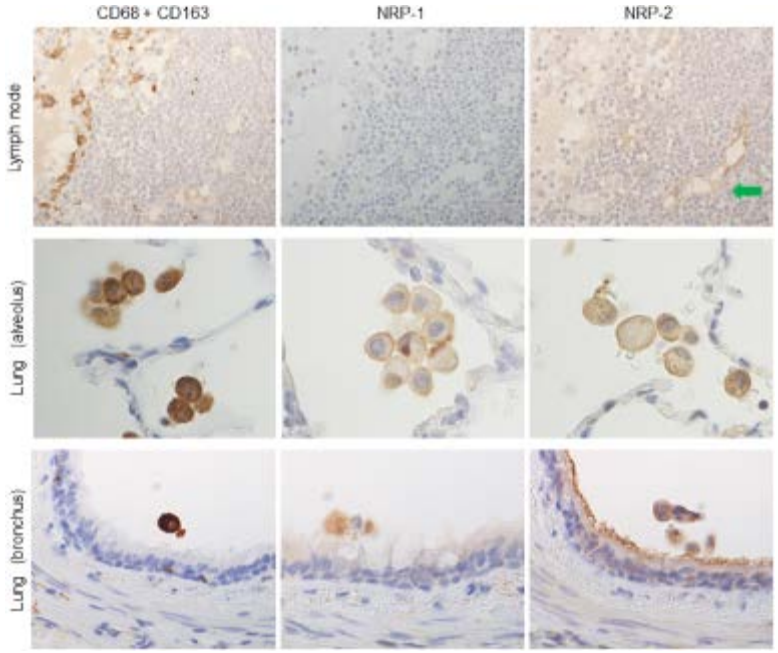

Fig 2. NRPs expression in tissue-specific macrophages compared to immunostaining with a cocktail of anti-CD68 and anti-CD163 antibodies. Expression was detected in alveolar macrophages in lung, but not in lymph node (sinus macrophages). And NRP-1 and NRP-2 also expressed on bronchial macrophages. Green arrow indicates NRP-2 expression on lymphatic vascular endothelium, used as positive control. Serial sections were counterstained with hematoxylin. NRP-1, neuropilin 1; NRP-2, neuropilin 2.

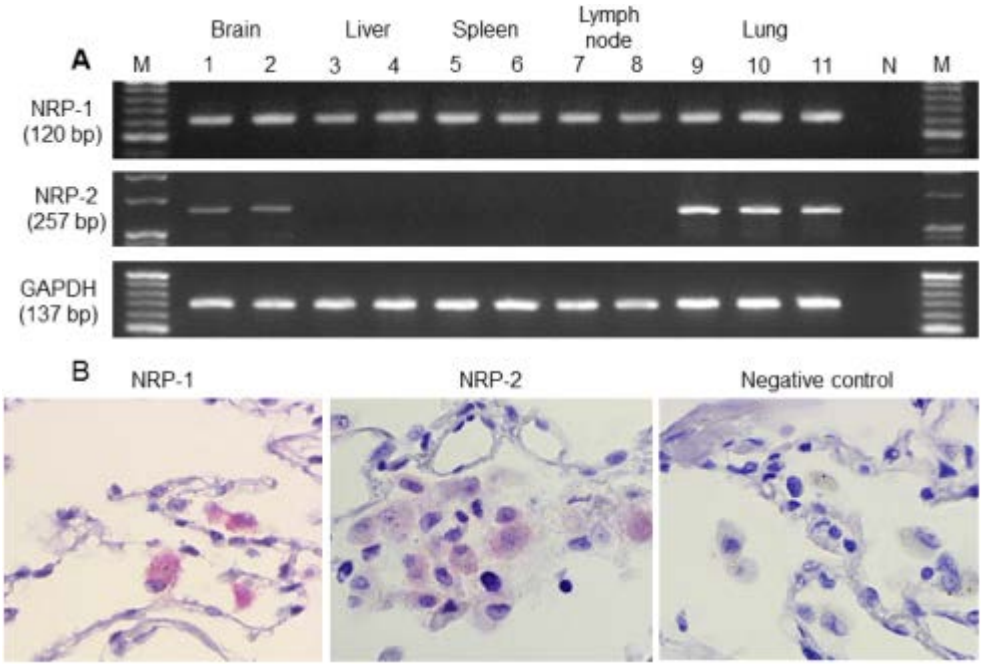

Fig 4. NRPs mRNAs expression in normal tissues (RT-PCR) and on alveolar macrophages in physiologically normal lung (in situ-PCR). (A) By reverse transcriptase polymerase chain reaction (RT-PCR), N represents the negative control, and M represents the 20 base-pair DNA ladder. (B) NRP-1 and NRP-2 mRNAs of alveolar macrophages inphysiologically normal lung by in situ-polymerase chain reaction (in situ-PCR). NRP-1, neuropilin 1; NRP-2,neuropilin 2; GAPDH, glyceraldehyde-3-phosphate dehydrogenase.

Table 3. Comparison of neuropilin-1 (NRP-1) and neuropilin-2 (NRP-2) expression on alveolar macrophages in lung cancer adjacent to the cancer margin, lung inflammation and lung tissue remote to the cancer nest (physiologically normal lung).

Cases/Diseases	Number of NRP-1 positive cells[A)] (mean ± SD)	Number of NRP-2 positive cells[A)] (mean ± SD)
Adenocarcinoma (n = 15)	38.3 ± 8.9[‡, #]	37.8 ± 9.20[‡, #]
Squamous cell carcinoma (n = 15)	46.7 ± 9.2[*, ***]	48.1 ± 10.7[*, ***]
Inflamed lung (n = 20)	25.1 ± 9.1[*, **, ‡]	24.5 ± 12.1[*, **, ‡]
Physiologically normal lung (n = 5)	9.2 ± 3.8[**, ***, #]	8.9 ± 3.9[**, ***, #]

Ye Aung *et al.*, (2016) PLOS One DOI:10.1371/journal.pone.0147358

Recent Publications

- Schellenberg et al. *Role of Neuropilin-2 in the Immune System.* Mol. Immunology. 2017
- Roy at al. *Multifaceted Role of Neuropilins in the Immune System: Potential Targets for Immunotherapy*. Frontiers in Immunology. 2017
- Immormino et al. *Neuropilin-2 Regulates Airway Inflammatory Responses to Inhaled Lipopolysaccharide*. Am J of Physiology. 2018
- Mucka et al. *Inflammation and Lymphedema Are Exacerbated and Prolonged by Neuropilin 2 Deficiency*. Am J of Pathology. 2016