SYNACT PHARMA

SynAct Pharma AB

Transforming the Treatment of Severe Inflammatory Diseases

Kempen Life Sciences Conference

May 2021

SynAct Pharma – Highlights

- SynAct Pharma is focused on the development of novel and first in class agonists that target the melanocortin system
- Our lead drug candidate AP1189 is an oral selective melanocortin agonist that both elicits anti-inflammatory effects and stimulates the immune system's resolution mechanisms – immune resolution
- 2021 is a pivotal year for SynAct
- We began the year with a successful capital raise of EUR 8M
- We will complete our three AP1189 Phase 2a POC studies:
  - **2H21 – Rheumatoid Arthritis**
  - **2Q21 – COVID-19-induced ARDS**
  - **2H21 – idiopathic membranous nephropathy (iMN)**
- And we will prepare for the next phase of development of 1189 with a goal of study initiation in H1-2022

Facts and Figures

Founded in 2013

Listed on Spotlight exchange since 2016

Ticker: (SYNACT:SS)

Market cap: EUR 200 m

Last capital raise: EUR 8M in February 2021 including institutional investors

Management holds app. 20% ownership

More than 7000 shareholders

SynAct Pharma – Experienced Management

Jeppe Øvli Øvlesen, MBA – CEO

- >20 years of CEO experience
- Founding Board Member of more than 10 biotech/medtech companies
- Co-founder of e.g. TXP Pharma
- Former CFO & VP BD of Action Pharma

Henrik Stage, MsC – CFO

- >25 years experience from Biotech and financial industry
- Former CEO and CFO at Santaris Pharma sold to Roche for $450m
- >$150m from Big Pharma deals. Prepared Santaris for US Nasdaq IPO

Thomas Jonassen, MD – Co-founder & CSO

- Member, Board of Directors
- Associate Professor, KU in Denmark
- Visiting Professor, WHRI, UK
- Co-founder of TXP Pharma
- Co-founder and former CSO of Action Pharma

Thomas Boesen, PhD – COO

- 20 years experience from Biotech and Pharma Industry
- Inventor of several new chemical entities
- Co-Founder of TXP Pharma
- Former VP Discovery, Action Pharma

James Knight, CBO

- 25+ years of experience in biotech ranging from R&D through commercial strategy and business development at Biogen, Dura, Elan, Questcor and BioTime
- Formally VP of Portfolio Strategy at Questcor Pharmaceuticals overseeing expansion Acthar promoted indications, growing sales from $110M to $1B

SynAct Pharma – Board of Directors

Torbjørn Bjerke, MD – Chairman

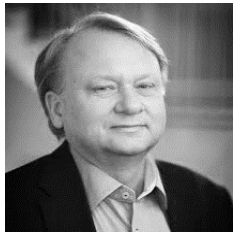
- >25 years track record from Pharma industry as Head R&D and CEO (private & public)
- Co-founder of Action Pharma, TXP Pharma and Arctic Aurora Life Science
- Member, BoD for DBV Technologies

Thomas Jonassen, MD – Co-founder & CSO

- Member, Board of Directors
- Associate Professor, KU in Denmark
- Visiting Professor, WHRI, UK
- Co-founder of TXP Pharma
- Co-founder and former CSO of Action Pharma

John Haurum, MD – Board Member

- Former CEO of F-star (UK) with deal flow in excess of €200m
- Co Founder and former CSO of Symphogen
- Member of the board in a number of European biotech companies



Terje Kelland, MD – Board Member

- Former Executive positions in Novo Nordisk, SOBI, and Pharmacia
- Former Vice VD of Karolinska Dev.
- Background as a professor at Lunds U.

Uli Hacksell, PhD – Board Member

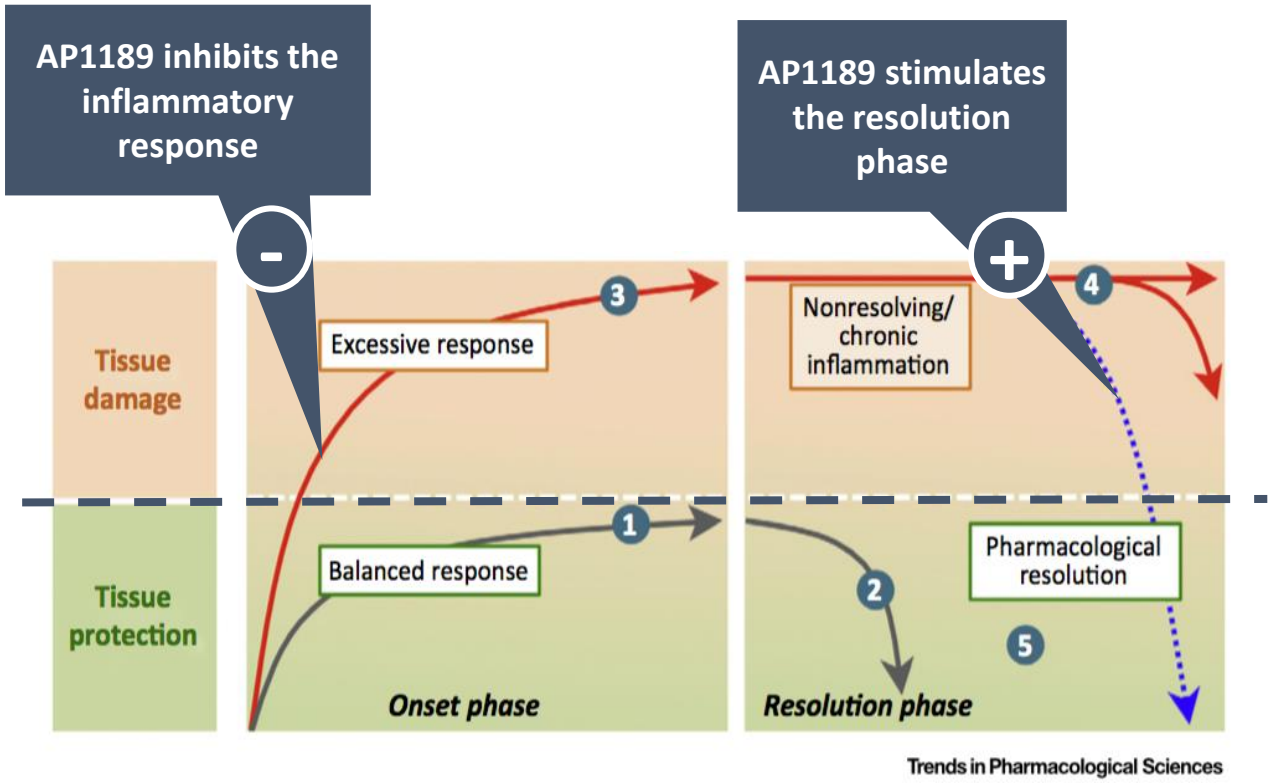
- Former CEO of Medivir
- Former CEO of Acadia Pharmaceuticals, took it from private startup to multibillion USD public company
- Board member of many other Life Sciences companies

SynAct Pharma – Pipeline Overview

Asset	Indication	Preclinical	Phase I	Phase IIa	Phase IIb	Phase III	Next milestone
AP1189	Rheumatoid Arthritis						Q321 Top Line
	Nephrotic Syndrome						2H21 Top Line
	COVID-19-induced acute respiratory distress syndrome						2Q21 Top Line
	Psoriatic Arthritis*						
Pharmacology program							

* Phase II development to await data from RA study

Inflammation Resolution – A New Frontier



The Inflammatory Response

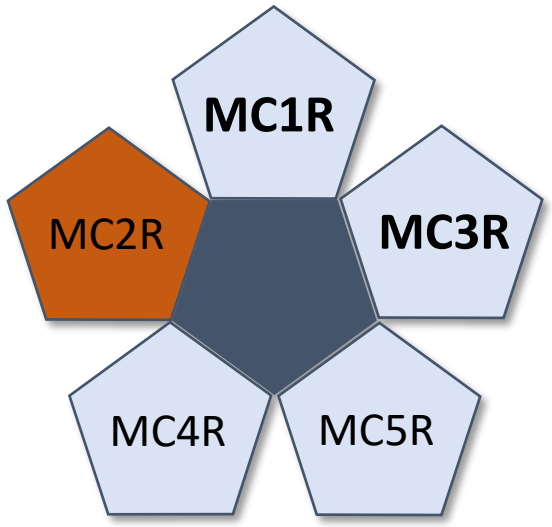
1. Inflammatory response effectively controlled in extent and time – protects tissues and limits damage
2. Pathways activated to safely terminate the inflammatory response and promote healing
3. Exaggerated response to inflammatory stimuli – can have detrimental consequences and harm tissues
4. Failure to achieve resolution of inflammation can result in chronic inflammation
5. Activation of endogenous resolution pathways has the potential to restore tissues and function

Resolution therapy holds promise to correct dysregulated or chronic inflammation in many pathological settings

Compared to most current therapeutic approaches Resolution Therapy does not induce immuno-suppression

The Melanocortin System and its Role in Inflammation

Melanocortin Receptor Family

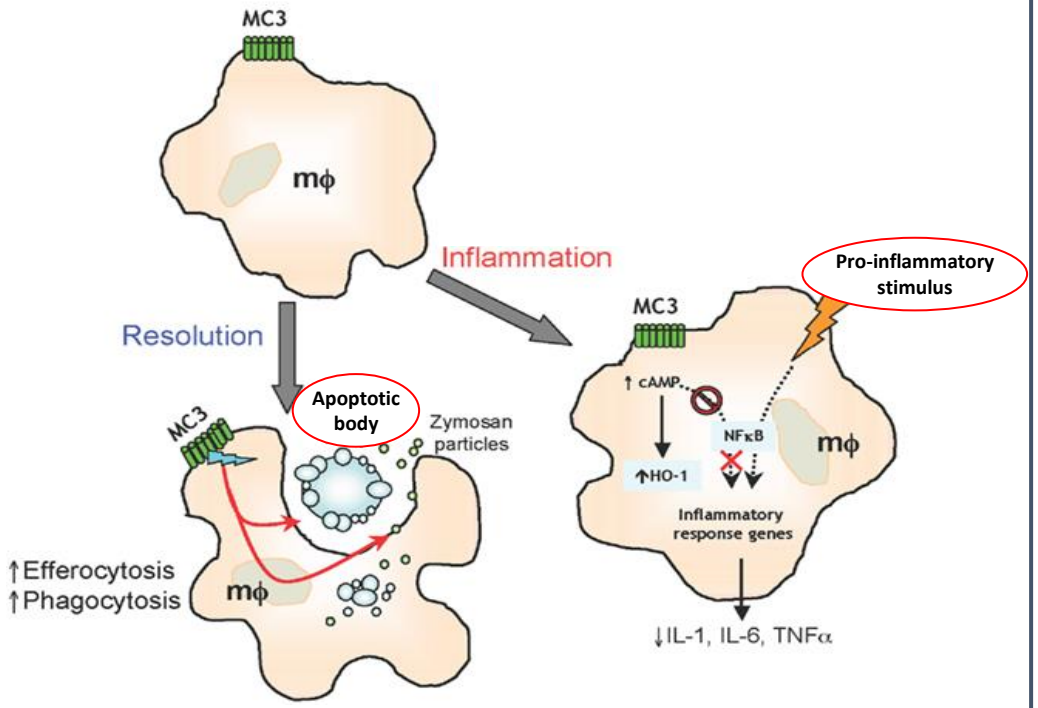


Steroid dependent effects Steroid independent effects

Discovery of a family of 5 melanocortin receptors has led to the discovery of direct steroid independent effects

MC1R and MC3R are believed to be the key receptors involved in immunomodulation

Melanocortin is activated in inflammatory diseases



Melanocortins are endogenous peptides released during the inflammatory process

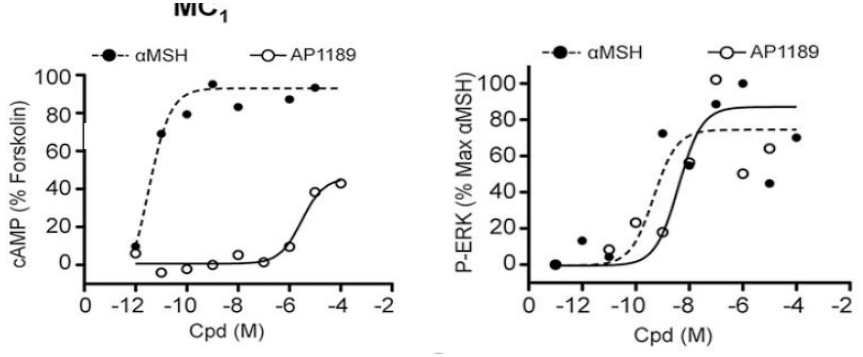
Stimulation of MC1R and MC3R promote naturally occurring resolution processes to fight excessive inflammation

AP1189 – First-in-Class Selective and Biased MCR 1 and 3 Agonist

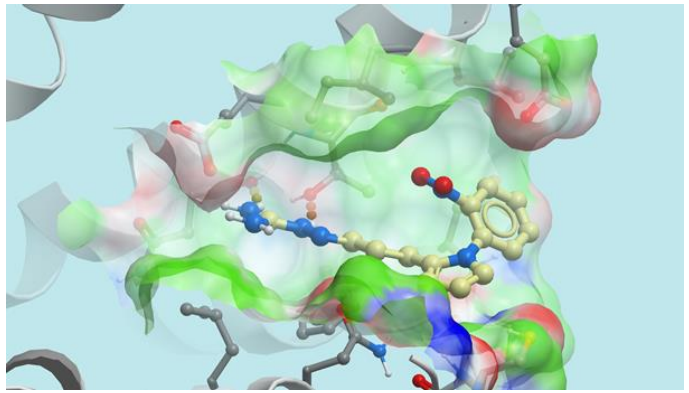
AP1189

- AP1189 was designed to preferentially activate melanocortin receptors 1 and 3 (MC1R and MC3R) which are believed to be responsible for direct immunomodulatory effects
- Importantly, AP1189 does not activate MC2R which is found on the adrenal gland and is responsible for the release of cortisol and the subsequent steroid side effect and tolerability issues that are associated with ACTH therapies
- AP1189 is also a biased agonist at MC1R and MC3R where it stimulates the ERK pathway over the canonical cAMP pathway which could lead to fewer off target effects including skin pigmentation

MC1 receptor activation in transfected cells[1]



AP1189 selectively engages ERK Pathway



Proposed binding mode of AP1189

1. Montero-Melendez et al: J Immunol. 194:3381-8, 2015; 2. Data from Completed Phase 1 study in healthy volunteers; 2. Yu, J. *et al.* Determination of the melanocortin-4 receptor structure identifies Ca as a cofactor for ligand binding. *Science* **368** , 428–433 (2020).

AP1189: Oral Convenience and Targeted Selectivity Within a Proven Mechanism

- Melanocortin therapies have reported efficacy in refractory patients across a range of diseases and systems
- Despite this promising activity, significant limitations around access/pricing, side effects and route of administration significantly limit utilization
- AP1189 was designed to overcome the limitations of ACTH therapy and unlock the full potential of melanocortin therapies

Key Features	AP1189	Acthar Gel & Generics
Melanocortin specificity	Melanocortin receptors 1 & 3	None
Safety profile	Well-tolerated in clinical experience so far	Similar to steroids
Potentially steroid sparing?	✓	✗
Presentation	Once a day oral	Intramuscular injection
Source/Underlying material	Small molecule	Porcine pituitary extract
Positioning	Potential flexibility in the treatment paradigm	Late-stage patients with severe disease

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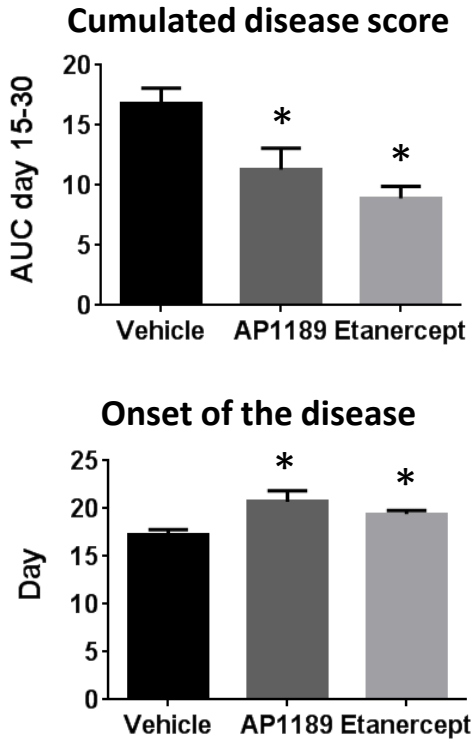
AP1189 – Rheumatoid Arthritis

Immune Resolution Without Immunosuppressive and Steroid Safety Issues

AP1189 for Rheumatoid Arthritis: Pre-Clinical Dataset Supports Clinical Development

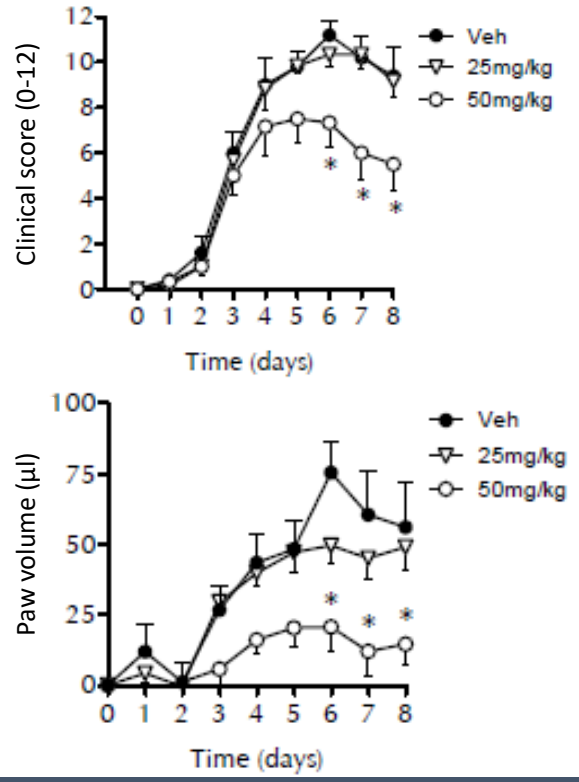
Collagen-induced arthritis
(30mg/kg, p.o.)



*Unpublished data: n=10, *: p < 0.05 vs Vehicle*

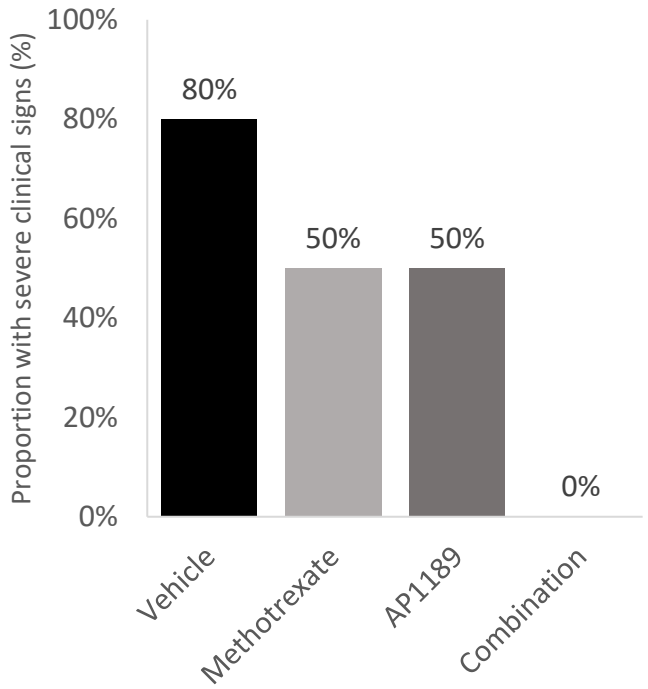
AP1189 provided a significant reduction in disease score as well as delay in onset

K/BxN-induced arthritis
(25/50mg/kg, i.p.)



AP1189 provided a dose-dependent result in K/BxN-induced arthritis

Combination Treatment with Methotrexate

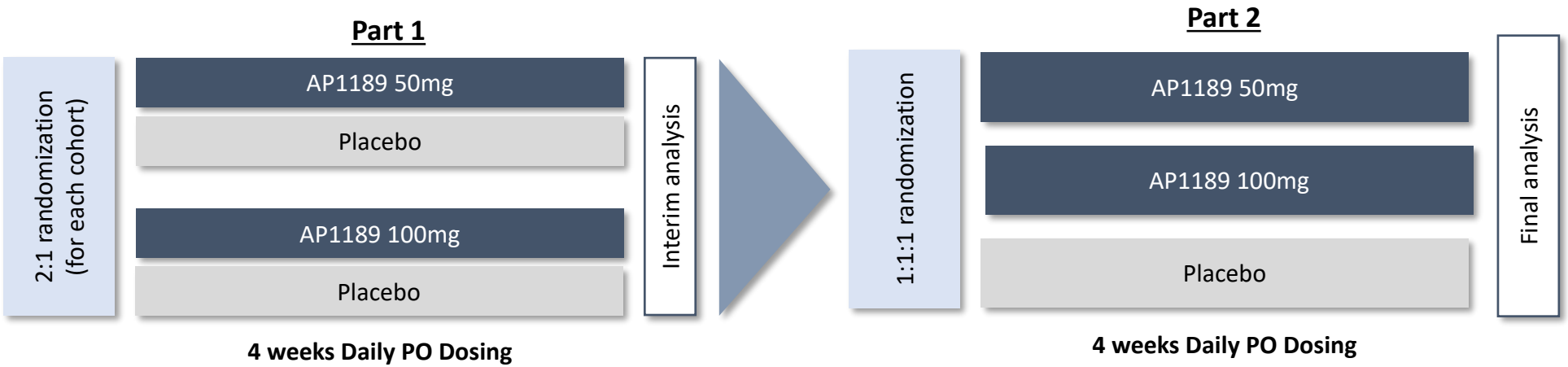


n=6 per group

Incidence of severe clinical signs in K/BxN induced arthritis

Montero-Melendez et al: J Immunol. 194:3381-8, 2015, PCT/EP2019/066578

RA P2a POC Study:
Phase 2a Study in Early RA Patients With Severe Disease Activity



Key inclusion criteria:

- Severe RA (severe CDAI score of >22)
- Treatment naive
- Candidate for starting methotrexate treatment

Part 1: n=29, interim assessment based on first 26 completed 11/20

Part 2: n=~76, target completion Q3/21

Clinical sites in Denmark; Sweden; Norway; Moldova and Bulgaria added from 03/21

Primary endpoint: CDAI Response Rate Vs placebo at 4 weeks (From Severe to at least Moderate, CDAI ≦ 22)

Secondary endpoints:

- Swollen and tender joints
- CDAI score
- DAS28 score
- HAQ-DI score
- FACIT-Fatigue score
- ACR response
- Reduction is key circulating cytokines (exploratory)

Evaluation of clinical activity relative to MC1r polymorphism

RA P2a POC Study:
Phase 2a Part 1 – Up to 75% Week 4 Response Rate

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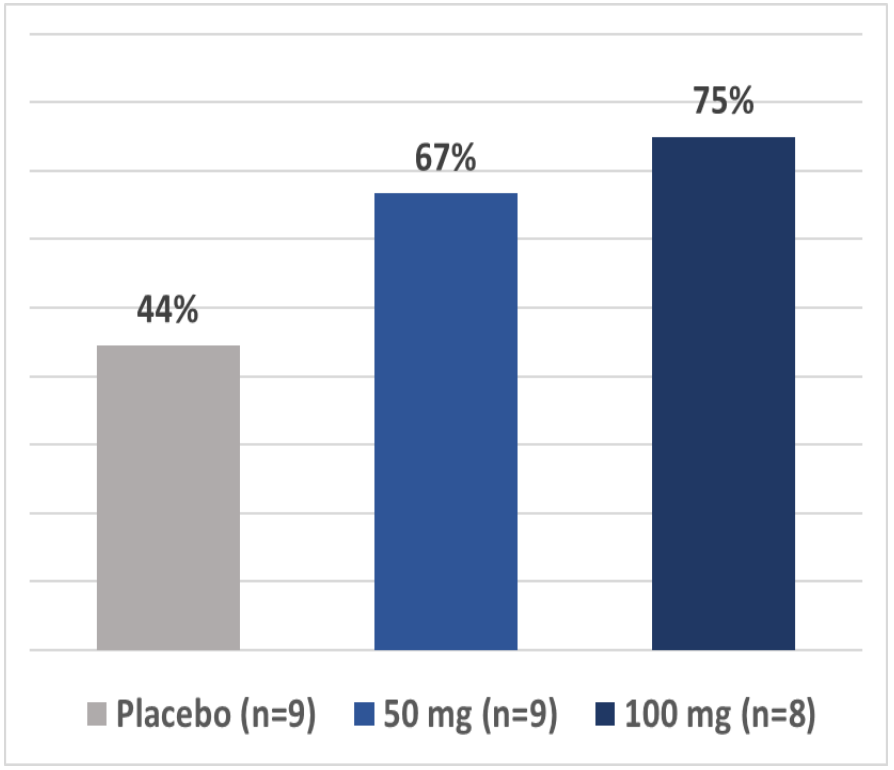
Response Rate on at 4 Weeks



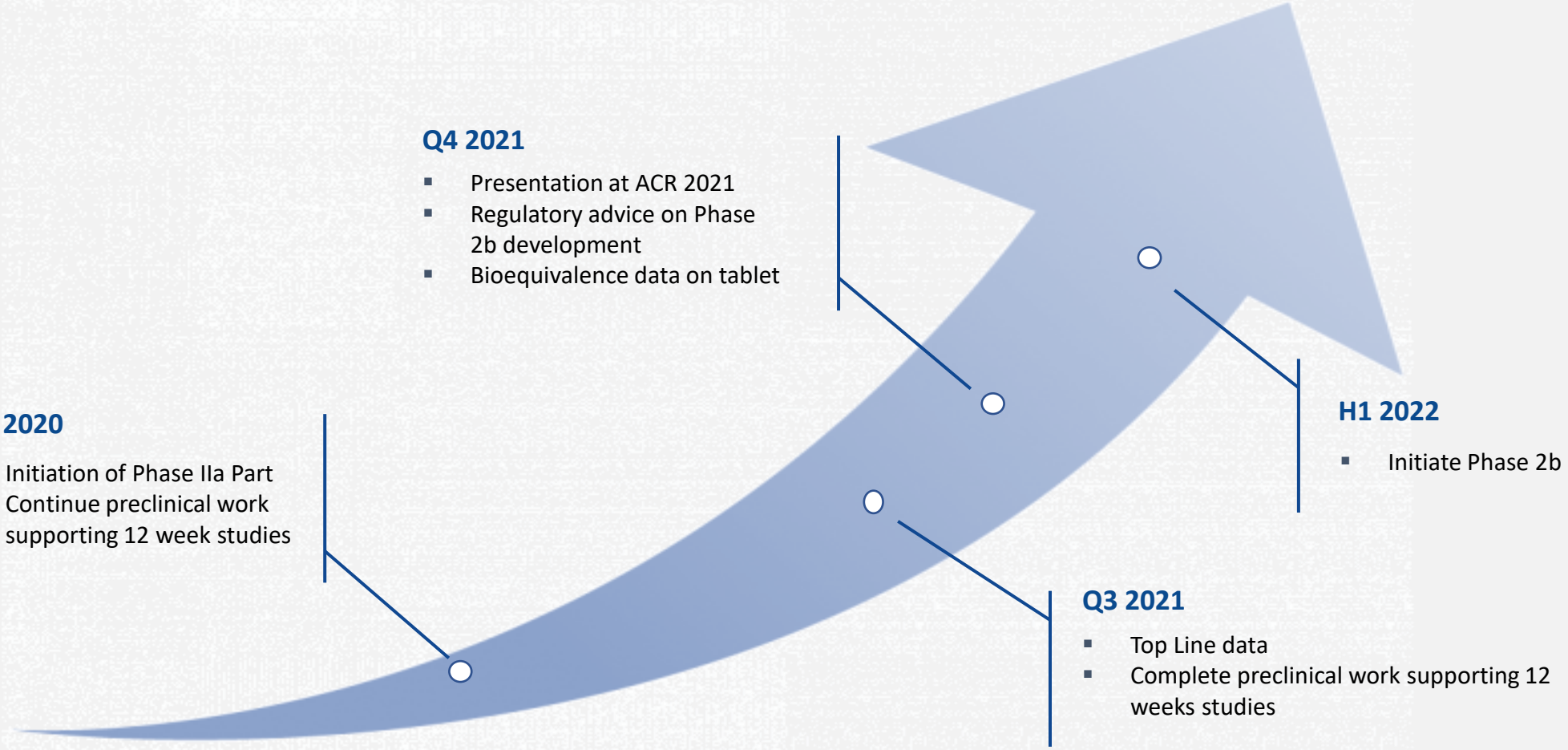
More patients treated with AP1189 achieved a CDAI score ≦ 22

Observations from the DSMB

- No concerns about safety with no reports of any serious adverse events
- The overall frequency of adverse events is comparable between the two treatment groups and slightly higher for AP1189
- The most common adverse event was nausea
- A greater number of patients treated with AP1189 achieved CDAI scores below 22 at the end of treatment
- The number of patients going from severe to moderate CDAI score was higher in both treatment groups than in the placebo group
- The small number of patients precluded any statistical evaluation of significant differences

Part 1 patient population: 19 Women/10 Men, Median age 57 years (span 27-77), Median baseline CDAI 34 (span 23-49)
Clinical Disease Activity Index (CDAI): >22=severe, 11-22=moderate, 2.9-10=low, ≦2.8=remission

RA P2a POC Study:
Study to be completed and reported in H2, 2021



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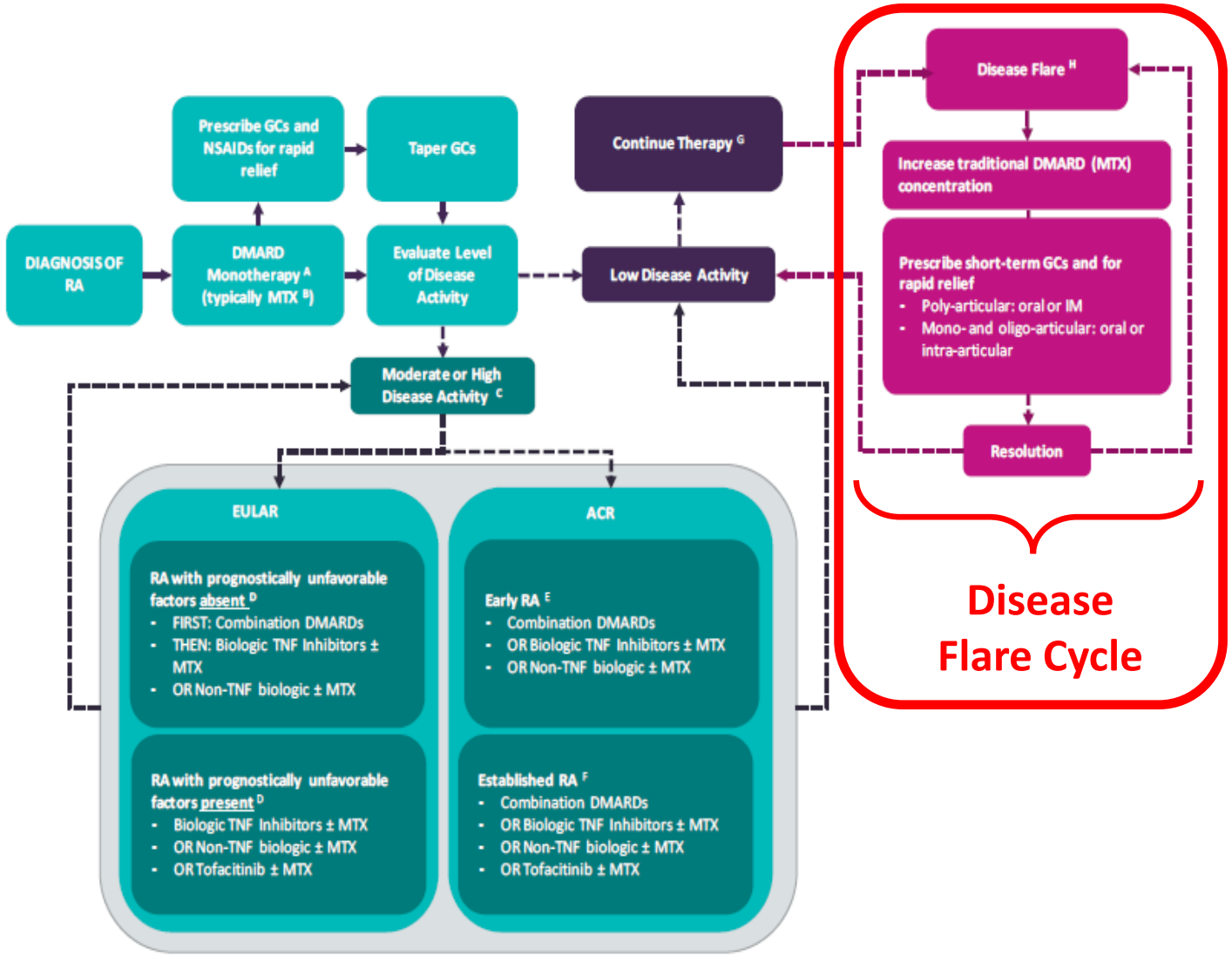
AP1189 – Big Market Opportunity in the Treatment of Flares in RA

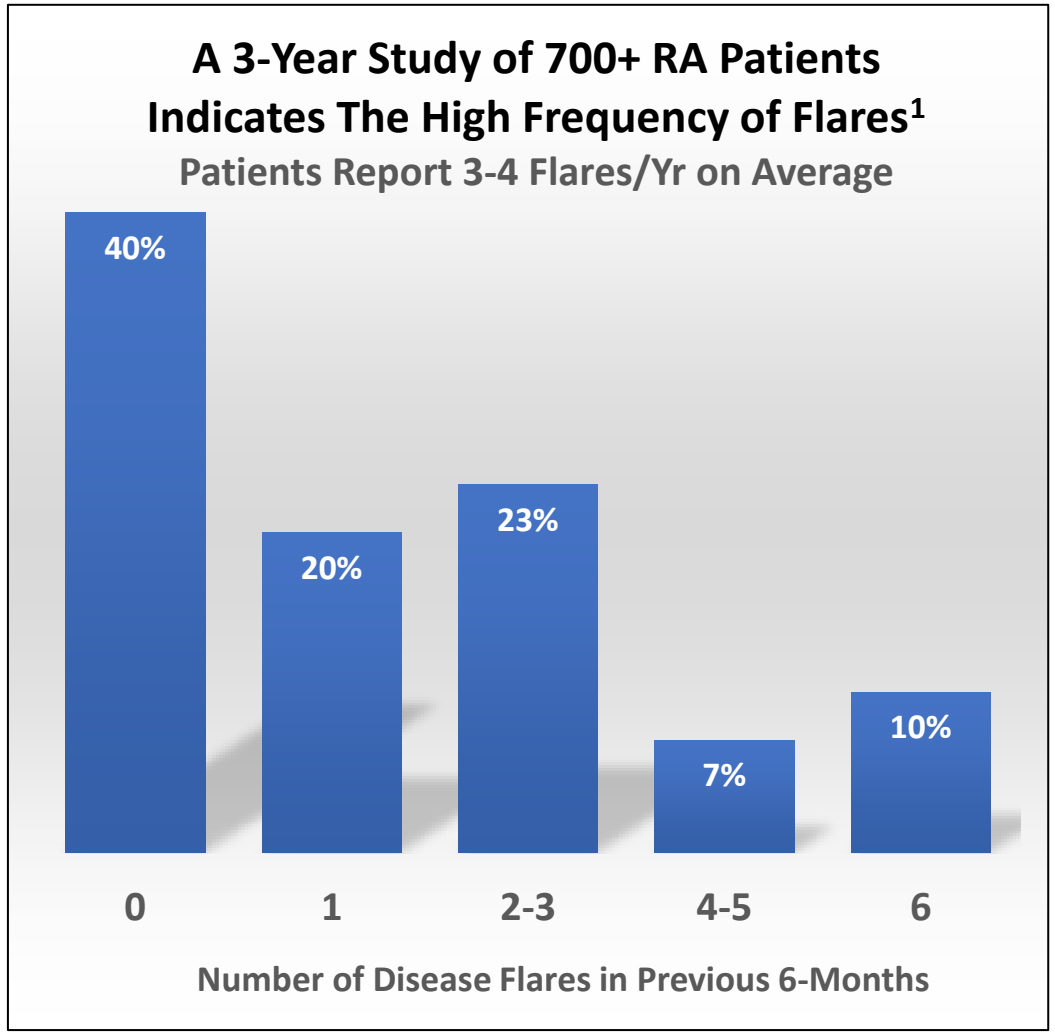
RA Tx Armamentarium is Broad But Remission Can Be Elusive and Short-Lived



- **Despite having numerous biologics with multiple MoAs, JAK inhibitors, immunosuppressives and steroids, RA treatment is still an art form**
- **Rheumatologists tend to treat aggressively but will cycle within class and to new MoAs as patients experience continued disease flares and progression**
- **Despite all these therapies, remission remains elusive**
- **In a study of 700+ RA patients followed for 3 years[2]:**
  - 47% never achieved remission,
  - 19% achieved remission once,
  - 17% achieved remission twice
  - Only 12% were noted to be in remission at each visit

Figure taken from Global Data *RA: Global Drug Forecast and Market Analysis to 2027*, 2019; (2) Byerk et al., J Rheumatol 2014;41:227–34

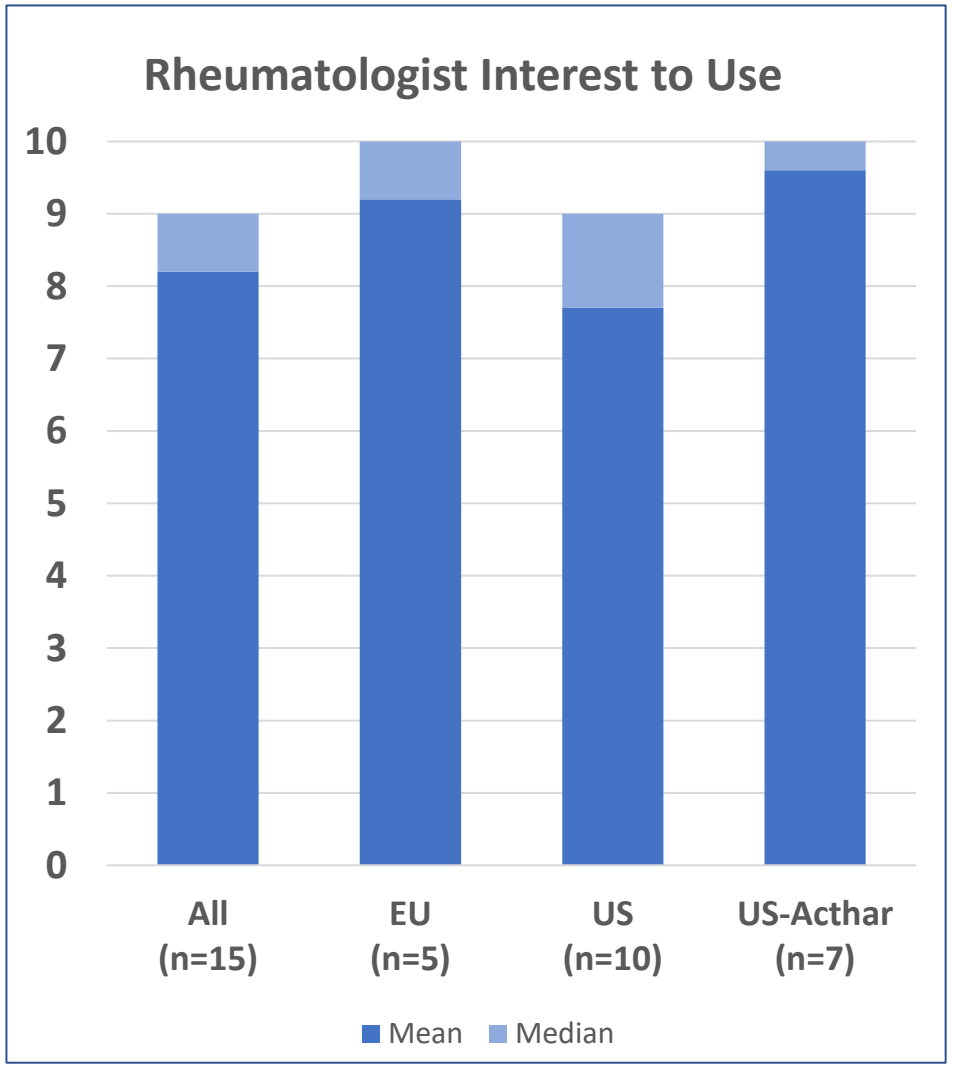
Tx Changes in RA are Driven by Periods of Acute Disease Activity –Disease Flares



- While 'Treat to Target' is remission, periods of acute disease activity or flares are common
- Rheumatologists try to treat patients with maintenance therapy to achieve no disease activity (remission) but will look to change therapy when a patient experiences acute moderate or severe flare activity
- In a study of 700+ RA patients followed for 3 years 76% of flares were treated by either adjusting the dose of current meds or starting a new therapy[1]
- Most often, physicians report either prescribing steroids or increasing the background dose of steroids to address disease flares[1]
- Disease and flare activity drives Tx choices for both treating the flare as well as changes or adjustments to the maintenance Tx regimen

(1) Figure adapted from Byerk et al., J Rheumatol 2014;41:227–34

Rheumatologists Express a High Degree of Interest in 1189 to Treat RA Flares



- **We conducted 1:1 interviews with high patient volume rheumatologists to explore unmet needs around the treatment of RA disease flares**
- **US respondents were familiar with melanocortin MoA and 7/10 have used Acthar over the last 12 months**
  - Great enthusiasm and support for melanocortin MoA and efficacy experienced with Acthar but negative views on Acthar pricing and access
- **Rheumatologists reacted very favorably to a product profile for 1189 that was based upon the P2a Part 1 data**
  - Median and mean product interest was high in both US and EU
  - Interest was highest among US Rheums with recent Achar experience
- **Stated intent to use was in 15-80% of their RA patients**

GlobalData RA Primary Research Project, 12/2020

Rheumatologists Described 2 Target Patient Segments For 1189

Segment	Description	7 MM Segment Size
Frequently Flaring	• Patients who experience multiple flares per year (4+) • Typically experience low disease activity between flares • Can be on long-term steroids	• ~15% of patients[1] • >2M flares/year[2]
Other Moderate to Severe Flares	• Moderate to severe systemic flares affecting average daily functions characterized by significant synovitis • Excludes 'Frequently Flaring' patients	• ~55% of patients[2] • ~4M flares/year[2]

- **Both patient segments have high unmet need for the treatment of acute disease particularly without the tolerability and safety issues associated with steroids[1]**
- **Both segments represent significant $1B+ commercial opportunities with realistic use and pricing assumptions[2]**
- **The interviewed rheumatologists also identified additional flare opportunities in other rheumatic conditions[1]**
  - Acthar users were interested in potential usage in other conditions where they also have had success with Acthar

1 GlobalData RA Primary Research Project, 12/2020; 2 Internal assessments

AP1189 for Rheumatoid Arthritis: Several Positioning and Development Strategies

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Current P2a POC Study in Treatment Naive

- 4-week trial in treatment naive patients experiencing severe acute disease activity
- Activity seen in P2a POC Part 1 suggests early onset of action – to be confirmed in Part 2
- Supports potential development as:
  - first line (add on) treatment in previous treatment naive pts
  - treatment option for flares
  - treatment option in conventional or biologic DMARD incomplete responders

Acute Use 'Flare' Positioning

- Target patients with flares experiencing severe acute disease activity or refractory patients with ongoing chronic disease activity
- Own market research support positioning in flares
- Shorter 8-12 weeks treatment duration
- Possibility to make adaptive study designs for early entering of clinical Phase III

Frist line treatment in previous treatment naïve patients

- Safety, including lack of immunosuppression, thus far supports early line positioning
- Aim to induce recovery within 3 months dosing as first line (add on) treatment

DMARD-IR Positioning

- Positioning as second line treatment in patients with incomplete responses or who are refractory to traditional or biologic DMARDs
- To control disease activity

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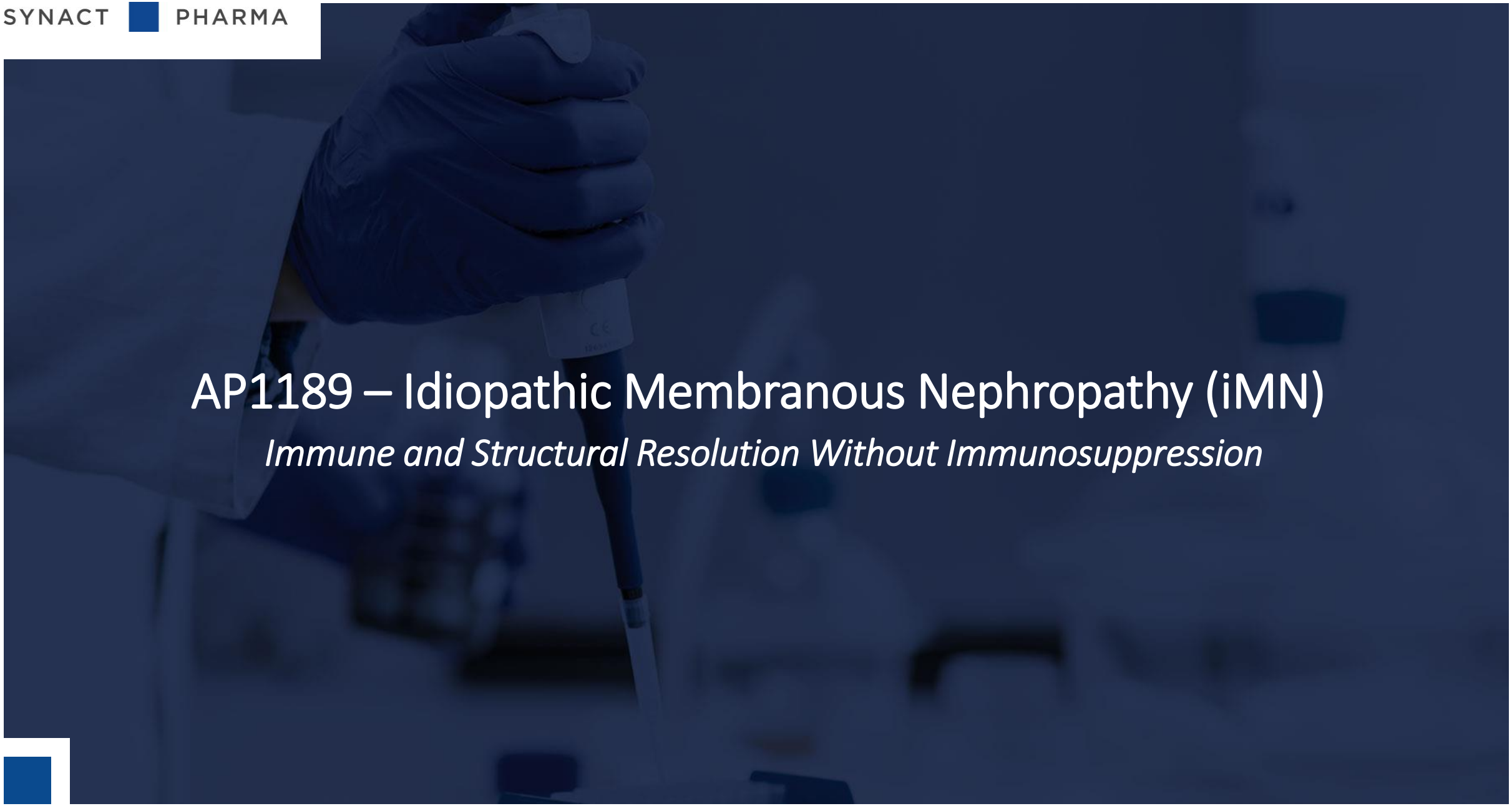
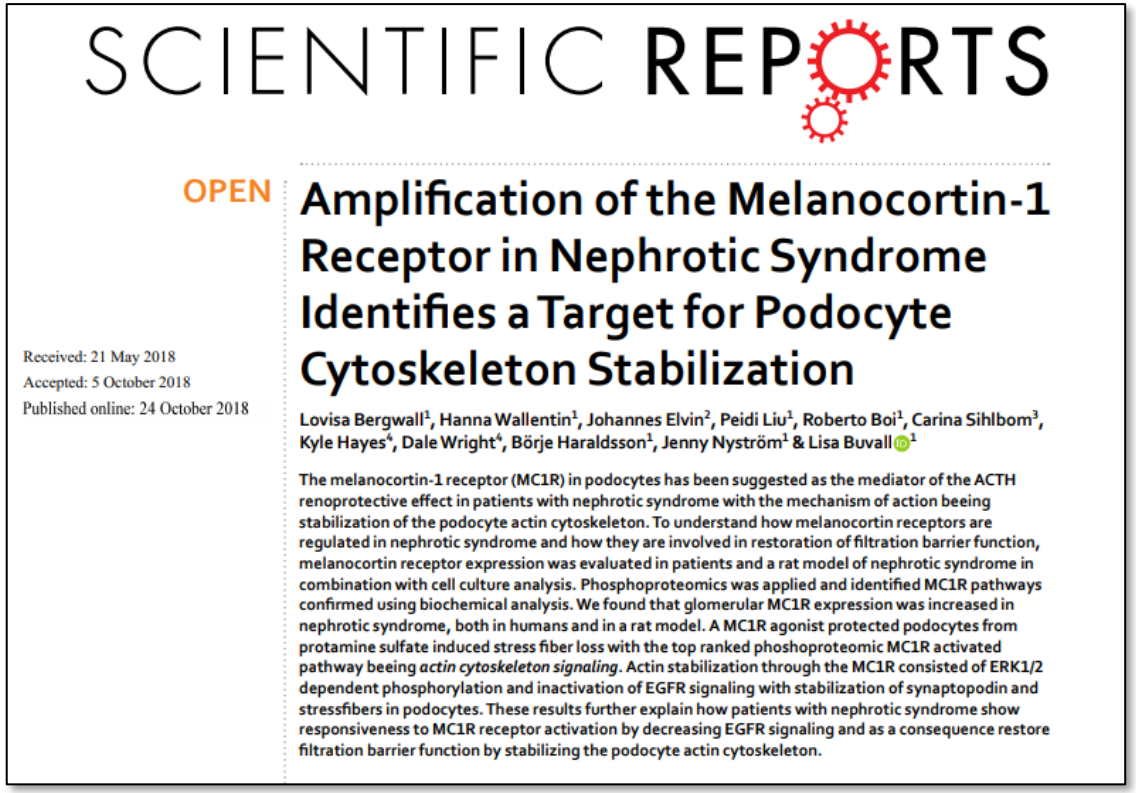


AP1189 – Idiopathic Membranous Nephropathy (iMN)

Immune and Structural Resolution Without Immunosuppression

iMN P2a POC Study:
Melanocortins Directly Improve Podocyte Architecture



SCIENTIFIC REPORTS

OPEN

Amplification of the Melanocortin-1 Receptor in Nephrotic Syndrome Identifies a Target for Podocyte Cytoskeleton Stabilization

Received: 21 May 2018
Accepted: 5 October 2018
Published online: 24 October 2018

Lovisa Bergwall[1], Hanna Wallentin[1], Johannes Elvin[2], Peidi Liu[1], Roberto Boi[1], Carina Sihlbom[3], Kyle Hayes[4], Dale Wright[4], Börje Haraldsson[1], Jenny Nyström[1] & Lisa Buvall[1]

The melanocortin-1 receptor (MC1R) in podocytes has been suggested as the mediator of the ACTH renoprotective effect in patients with nephrotic syndrome with the mechanism of action beeing stabilization of the podocyte actin cytoskeleton. To understand how melanocortin receptors are regulated in nephrotic syndrome and how they are involved in restoration of filtration barrier function, melanocortin receptor expression was evaluated in patients and a rat model of nephrotic syndrome in combination with cell culture analysis. Phosphoproteomics was applied and identified MC1R pathways confirmed using biochemical analysis. We found that glomerular MC1R expression was increased in nephrotic syndrome, both in humans and in a rat model. A MC1R agonist protected podocytes from protamine sulfate induced stress fiber loss with the top ranked phoshoproteomic MC1R activated pathway beeing *actin cytoskeleton signaling*. Actin stabilization through the MC1R consisted of ERK1/2 dependent phosphorylation and inactivation of EGFR signaling with stabilization of synaptopodin and stressfibers in podocytes. These results further explain how patients with nephrotic syndrome show responsiveness to MC1R receptor activation by decreasing EGFR signaling and as a consequence restore filtration barrier function by stabilizing the podocyte actin cytoskeleton.

MC1R & Nephrotic Syndrome

- MC1R expression is increased in nephrotic syndrome, both in rat models and in humans
- MC1R agonism induced protection of podocytes from stress fiber loss
- Actin stabilization through the MC1R consisted of ERK1/2 dependent phosphorylation and inactivation of EGFR signaling with stabilization of synaptopodin and stress fibers in podocytes
- Patients with nephrotic syndrome show responsiveness to MC1R receptor activation by decreasing EGFR signaling (though ERK dependent Phosphorylation) and as a consequence restore filtration barrier function by stabilizing the podocyte actin cytoskeleton

AP1189 induces its pharmacological effects though MC1R and MC3R-mediated ERK dependent phosphorylation

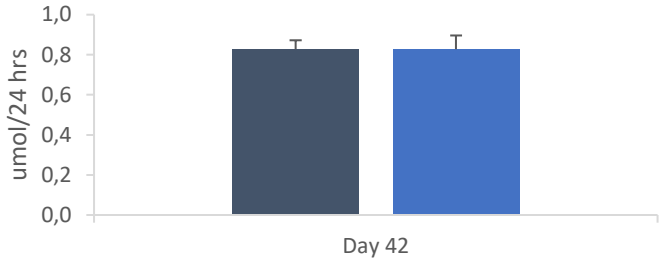
Sci Rep. 2018 Oct 24;8(1):15731

iMN P2a POC Study:
Pre-Clinical Dataset Supports Clinical Development

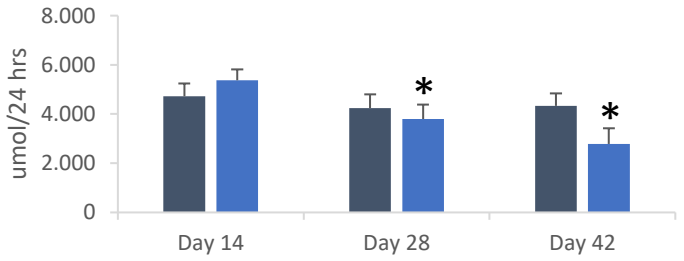
Vehicle (n=12)
AP1189 (n=12)

Membranous nephropathy rat model (passive Heymann Nephritis)

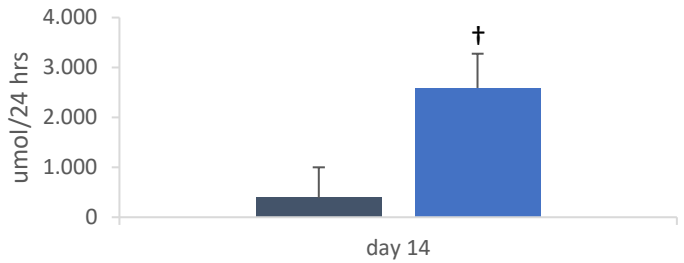
Creatinine Clearance (ml/min/g KW)



Albumin excretion rate



Reduction in AER (day 14-42)

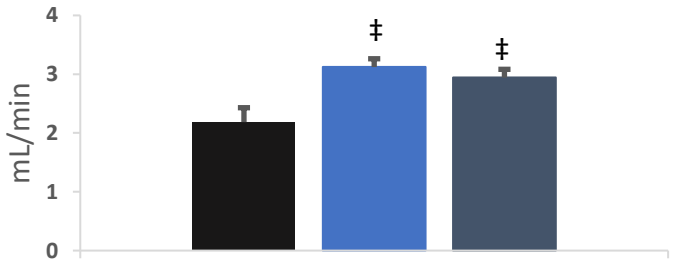


AP1189 showed no effect on creatinine clearance where albumin excretion decreased significantly

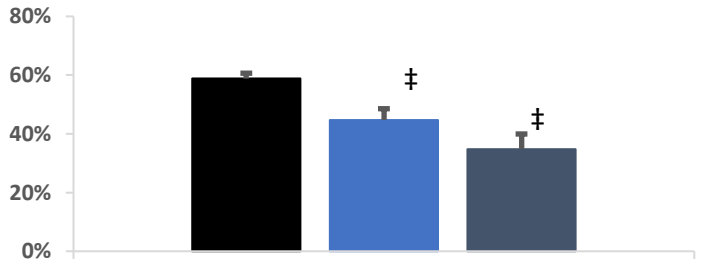
ACTH (n=6)
AP1189 20mg/kg (n=8)
AP1189 40mg/kg (n=8)

AP1189 vs ACTH in a model of Nephrotic Syndrome

Creatinine Clearance



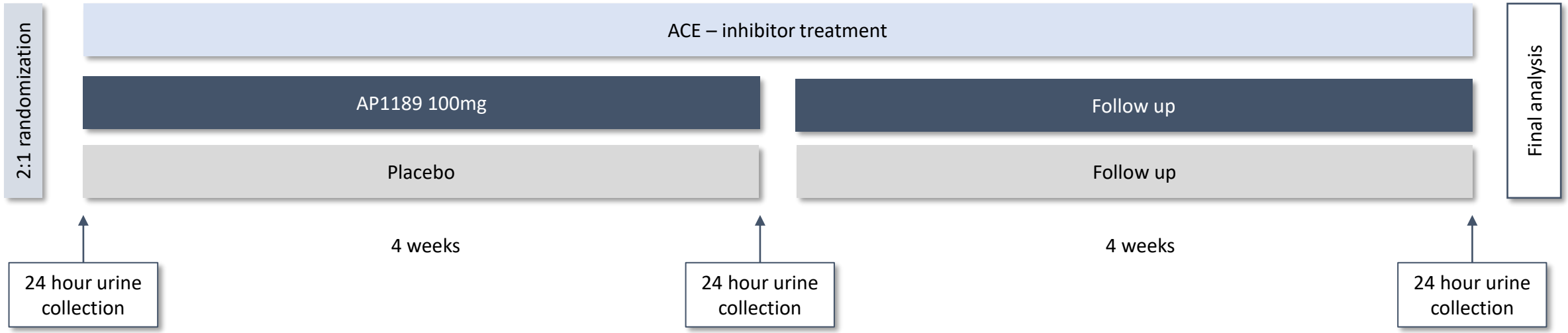
Fractional Albumin Excretion



AP1189 preserved creatinine clearance and dose-dependently reduced the fractional albumin excretion relative to ACTH

*p<0.05 vs. Day 14; † p<0.05 vs. vehicle; ‡ p<0.01 vs. ACTH; data from PCT/EP2019/066578. Model adapted from Lindskog et al, J Am Soc Nephrol. 2010; 21:1290-1298

iMN P2a POC Study:
Targeting Proteinuria in Moderate-to-Severe iMN Patients



Key inclusion criteria:

- Moderate-to-severe nephrotic syndrome
- Patients on stable dose of ACE inhibitors
- Patients are experiencing controlled blood pressure yet continued proteinuria

Primary endpoint: Change in 24 hour protein excretion following 4 weeks of treatment relative to baseline compared to placebo

Secondary endpoints include:

- Change in 24 hour albumin excretion following 4 weeks of treatment relative to baseline compared to placebo
- Change in plasma albumin from baseline to the end of the four week treatment period
- The number of subjects who show partial or complete remission in proteinuria on the last day of treatment and four weeks after the last dose is administered

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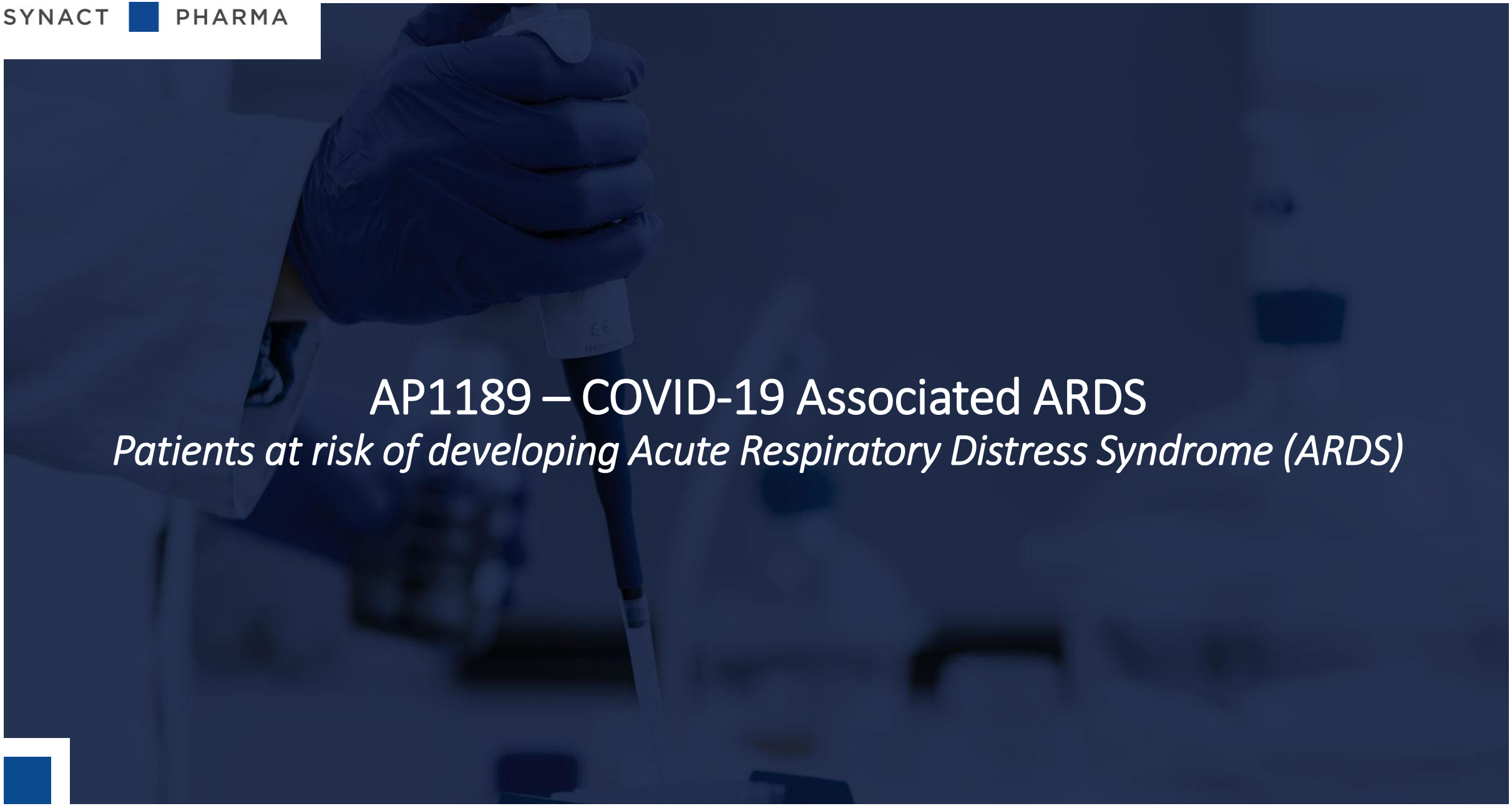
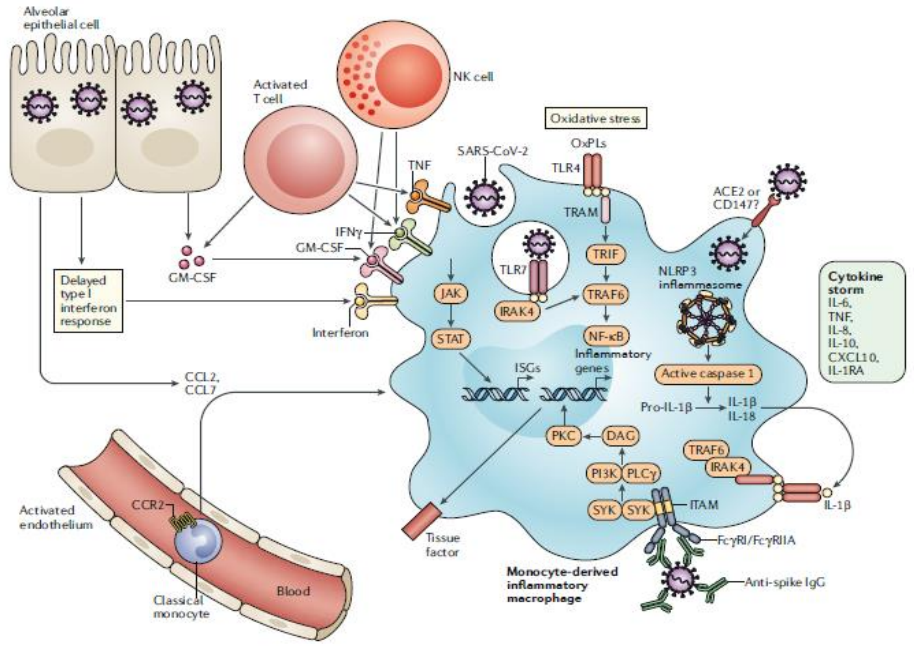


AP1189 – COVID-19 Associated ARDS

Patients at risk of developing Acute Respiratory Distress Syndrome (ARDS)

Macrophages as a potential target for AP1189 treatment in Covid-19 infection
(and other viral infections associated with hyper-inflammatory responses)

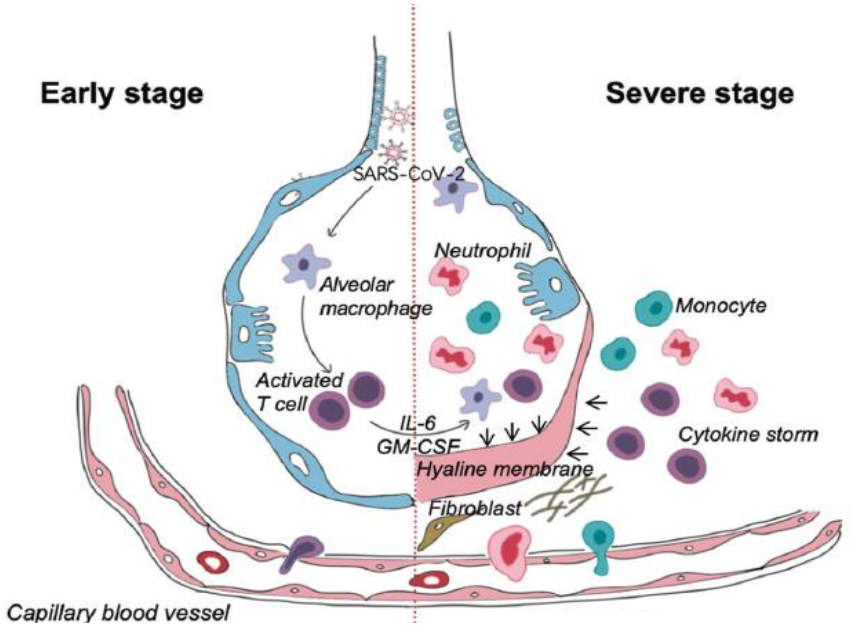
Macrophages play a role in COVID-19 hyper-inflammation



COVID-19 infection is associated with severe pneumonia that if left untreated can develop into ARDS due to an exacerbated inflammatory response

Hyperactivation of monocyte-derived macrophages is a key event leading to development of life-threatening ARDS

AP1189 targets key pathways in hyper-inflammation

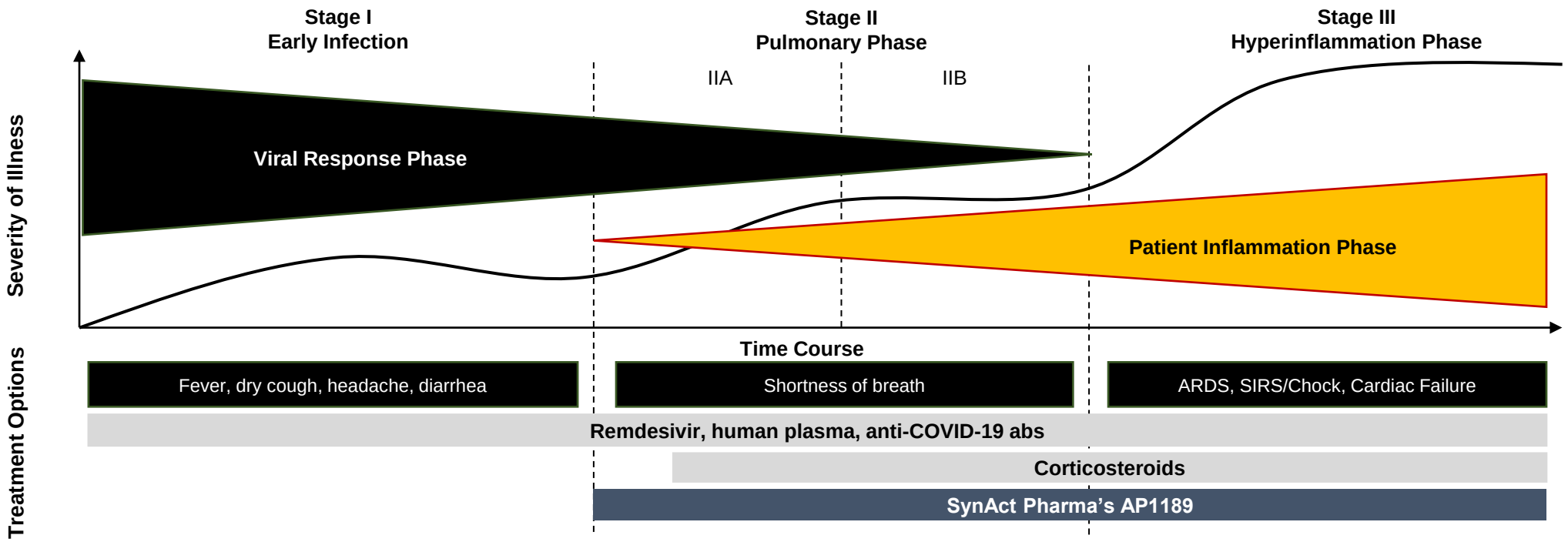


AP1189 induces inflammatory resolution by reducing pro-inflammatory pathways

Shifts the phenotype of macrophages from pro-inflammatory type 1 to a type 2 phenotype with marked pro-resolving capabilities

Nature Reviews Immunology, May 2020; Cell Death & Differentiation, March 2020

COVID-19: Disease development and AP1189's fit in treatment



AP1189's anti-inflammatory properties provide strong rationale to explore its potential utilization in COVID-19 infections

AP1189 as an add-on therapy in COVID-19 infected patients

Key inclusion criteria:

- Positive COVID-19 infection
- Need for supportive respiratory assist[1]

Primary endpoint: Time to respiratory recovery defined as the time from initiation of treatment to the time when the patient's SpO2 is ≥93% determined by pulse oximetry in the patient on ambient air for a minimum of 30 minutes

Key secondary endpoints:

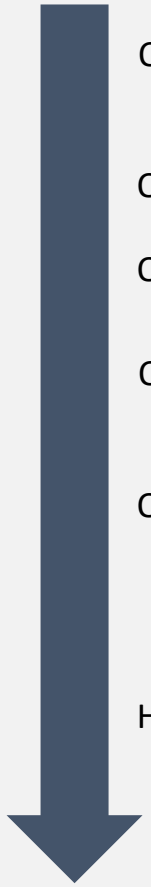
- Rate of ICU admission during the treatment period
- Rate of patients that go to mechanical ventilation at any time during hospitalization
- Rate of patients discharged at Day 14 or before
- Rate of mortality at Day 28
- Length of hospitalization
- Length of stay in the ICU
- Number of supplementary oxygen-free days on Day 28

1. Defined as either SpO2 < 93% without supportive oxygen treatment or PaO2/ FiO2 <300 mmHg despite supportive oxygen treatment

SynAct Pharma Highlights

- Company strategy is focused to become the leader within inflammation resolution to treat inflammatory and autoimmune diseases with significant medical need
- AP1189 is an oral selective melanocortin agonist that both elicits anti-inflammatory effects and stimulates the immune system's resolution mechanisms – immune resolution
- Next generation of compounds will be diversified from AP1189 to target more diseases
- Great focus on BD and investor relations
- Uplift to Nasdaq Stockholm in ultimo 2021 to attract more specialist and institutional shareholders

Milestones



Q4 2020	▪ Reporting of interim data Phase IIa data RA ▪ Initiation of Phase IIa Part 2 RA
Q1 2021	▪ Raised 8 M €
Q2 2021	▪ Complete Phase IIa COVID-19-induced ARDS study
Q3 2021	▪ Complete Phase IIa RA study ▪ Tablet for BE study released and CTA filed
Q4 2021	▪ Presentation of RA study at ACR meeting ▪ Completion of Phase IIa in NS ▪ Uplift to Main Market
H1 2022	▪ Start Phase IIb in RA following Scientific advice from FDA/EMA ▪ End of Phase IIa meeting NS

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