

# SynAct Pharma AB

Resolving Inflammation Through  
Melanocortin Biology

December 2021



# Forward Looking Statements

Certain information set forth in this presentation contains “forward-looking information”, including “future-oriented financial information” and “financial outlook”, under applicable securities laws (collectively referred to herein as forward-looking statements). Except for statements of historical fact, the information contained herein constitutes forward-looking statements and may include, but is not limited to, the (i) projected financial performance of the Company; (ii) completion of, and the use of proceeds from, the sale of the shares being offered hereunder; (iii) the expected development of the Company’s business, projects, and joint ventures; (iv) execution of the Company’s vision and growth strategy, including with respect to future M&A activity and global growth; (v) sources and availability of third-party financing for the Company’s projects; (vi) completion of the Company’s projects that are currently underway, in development or otherwise under consideration; (vi) renewal of the Company’s current customer, supplier and other material agreements; and (vii) future liquidity, working capital, and capital requirements. Forward-looking statements are provided to allow potential investors the opportunity to understand management’s beliefs and opinions in respect of the future so that they may use such beliefs and opinions as one factor in evaluating an investment.

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# SynAct Pharma – Highlights

- SynAct Pharma is focused on the development of novel and first-in-class agonists that target the melanocortin system
- There is high unmet need in autoimmune and inflammatory diseases for efficacious and safe therapies – current therapies can present significant benefit Vs risk challenges
- Lead drug candidate, AP1189, is currently in Phase II development for various indications with inflammatory manifestations
- Several near-term value inflection points for AP1189:
  - 2Q22 – Initiation of confirmatory COVID-19 study
  - 1H22 – Envisaged uplist to Nasdaq Stockholm Main Market
  - 2022 – Phase IIb initiation in RA
  - 2022 – Initiate re-designed Phase IIa in Nephrotic Syndrome
  - 2022 – Discovery results of new compounds targeting MC1R and MC3R
- Management and Board of Directors possesses a strong track record in global pharmaceutical development, business development and science

## Facts and figures

**Founded in 2013**

**Listed on Spotlight Stock Market with plan to uplist to Nasdaq Stockholm Main Market**

**Ticker:** (SYNACT:SS)

**Market cap:** c. SEK 3.3b/€325m

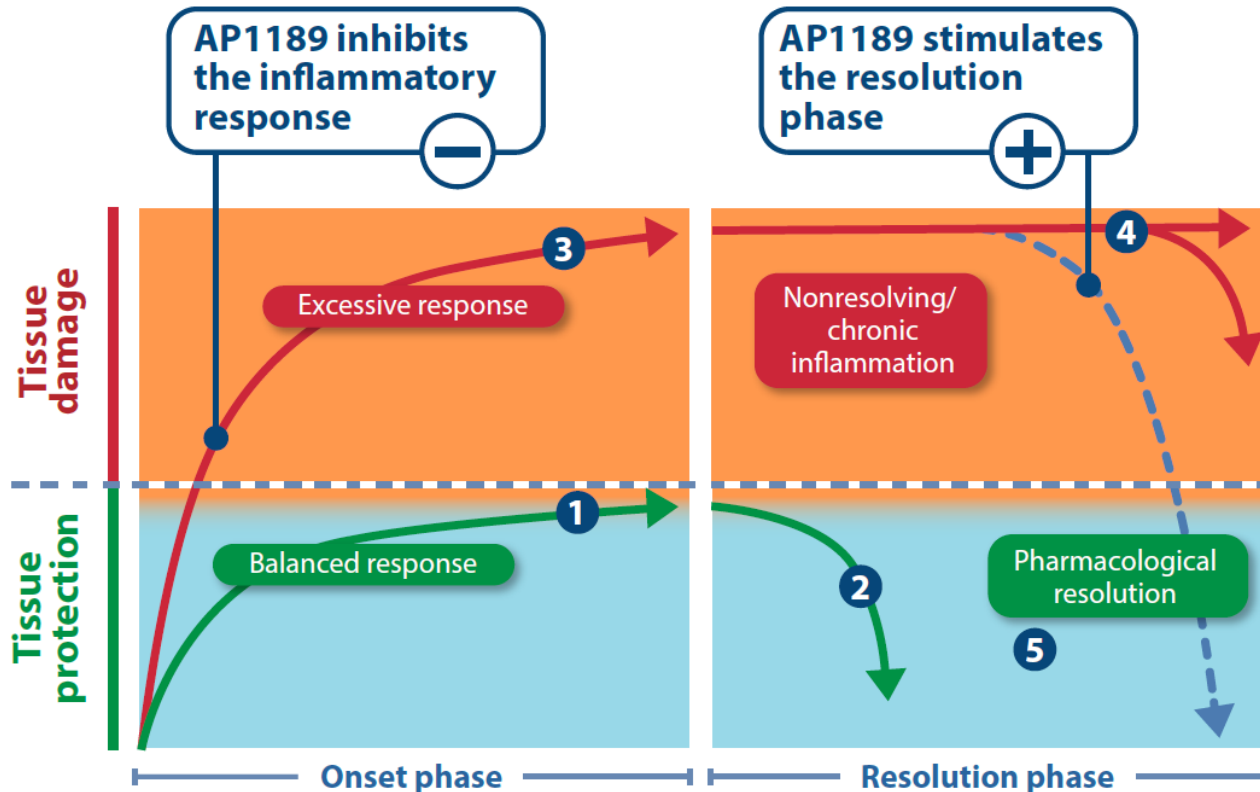
**Cash balance:** SEK 44.4m/€4.4m  
(30 September 2021)

**Management holds c. 20% ownership**

# SynAct Pharma – Pipeline overview

Asset	Indication	Preclinical	Phase I	Phase IIa	Phase IIb	Phase III	Next milestone
AP1189	Rheumatoid arthritis	▶					IND filing with FDA
	Nephrotic syndrome	▶					Ongoing Phase IIa being re-designed
	Virus-induced respiratory insufficiency	▶					Initiate confirmatory trial
	Next indication	▶					
Next generation of compounds	Inflammatory diseases	▶					

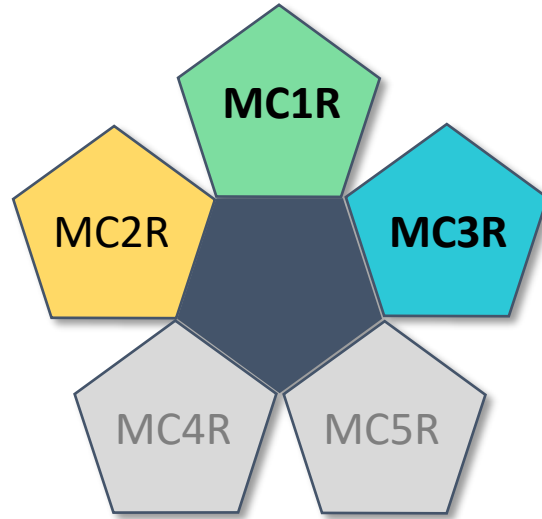
# Inflammation Resolution can correct dysregulated inflammation without inducing immunosuppression



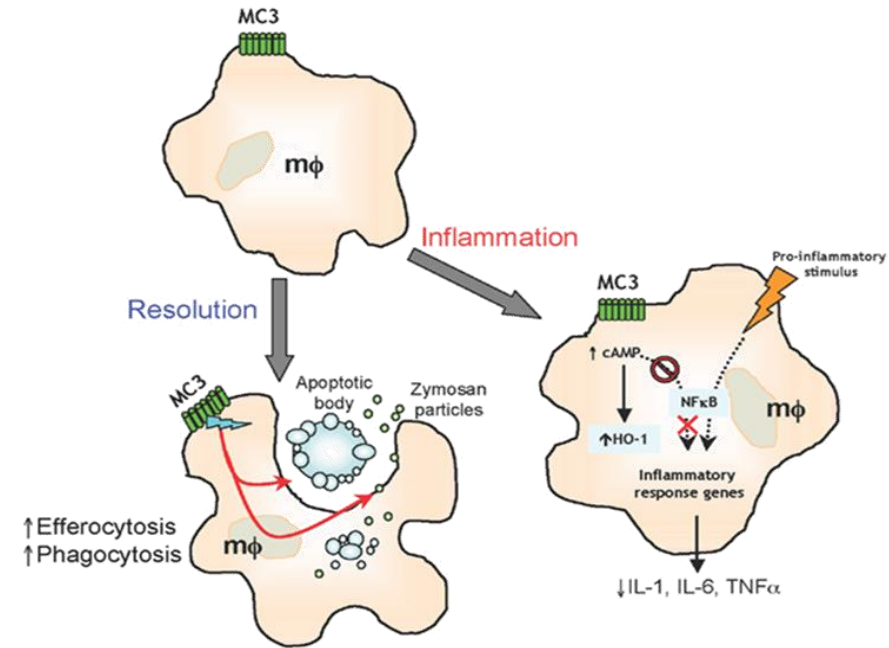
## The inflammatory response

- 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

# AP1189: A First-in-Class Selective Melanocortin Receptor 1 and 3 Agonist



■ Steroid dependent effects    ■ Targeted by AP1189



- AP1189 was designed to 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 glands and is responsible for the release of cortisol and the subsequent steroid side effects and tolerability issues that are associated with ACTH therapies

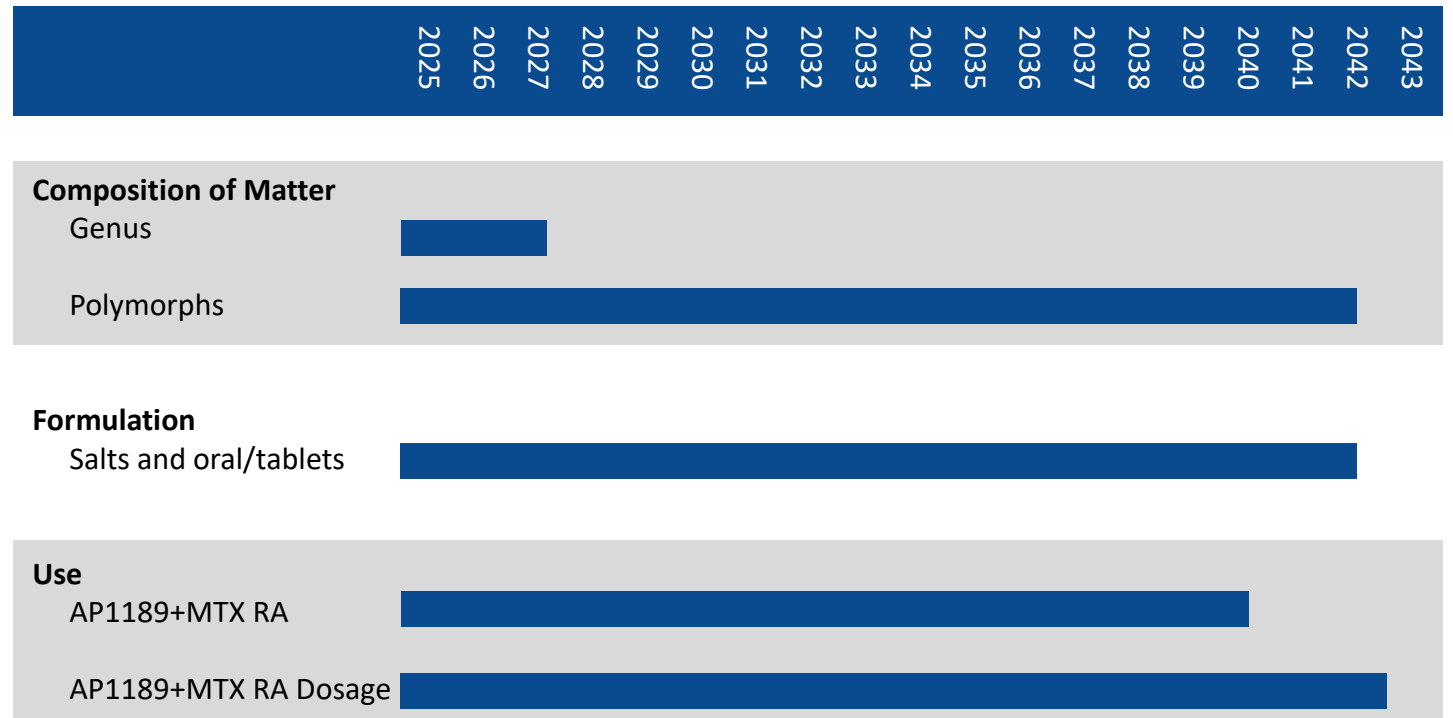
- AP1189 exhibits anti-inflammatory activity through stimulation of MC1R and MC3R on target cells – lowering pro-inflammatory cytokines
- AP1189 promotes pro-resolution pathways following stimulation of MC1R and MC3R on target cells – such as increasing efferocytosis in macrophages

# SynAct Pharma Has Executed an IP Strategy to Safeguard AP1189 through 2042 with Several Layers of Protection

## IP Strategy

- Critical composition of matter coverage directed toward the genus of AP1189 expires in 2027, excluding PTE and data exclusivity
- Filings directed toward the AP1189 salt forms provide extended coverage beyond composition of matter patent on the AP1189 genus, with potential for PTE extensions (PTE extensions not included in the graph)
- Filings directed toward method of use for AP1189 provide further life cycle management

## AP1189 Patent Portfolio with focus on RA<sup>1</sup>





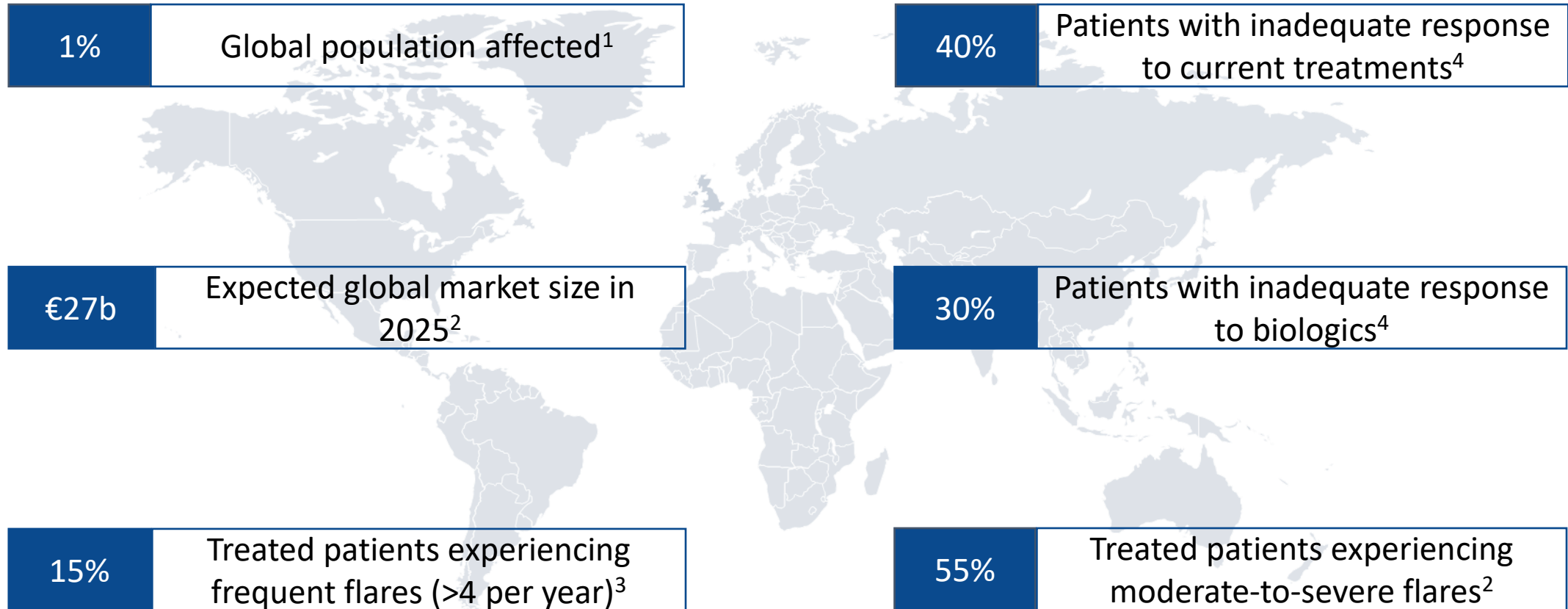
# AP1189 – Rheumatoid Arthritis

Immune Resolution without Immunosuppression

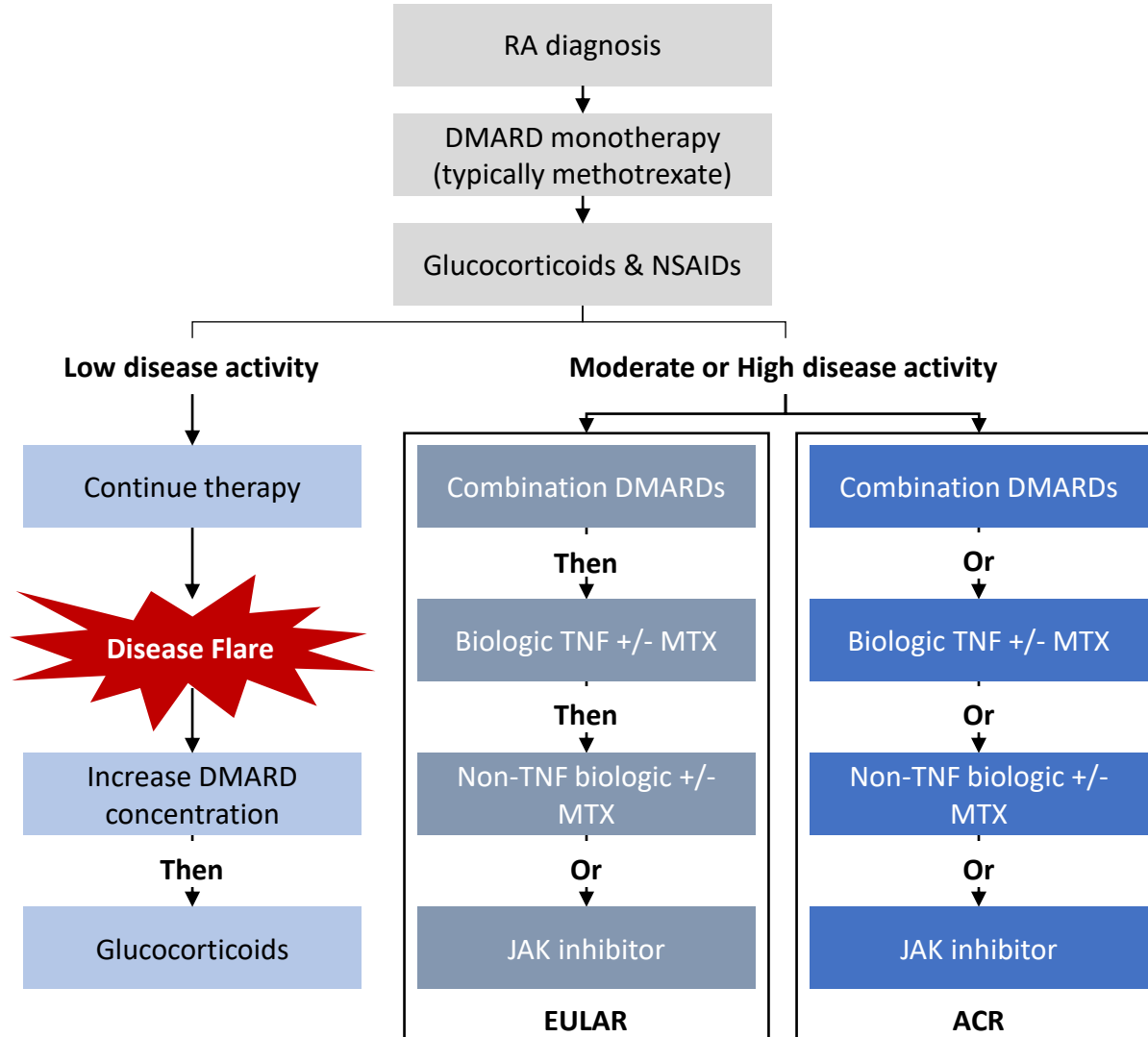




# AP1189 has potential to safely treat and attenuate RA symptoms and decrease time to inflammation resolution



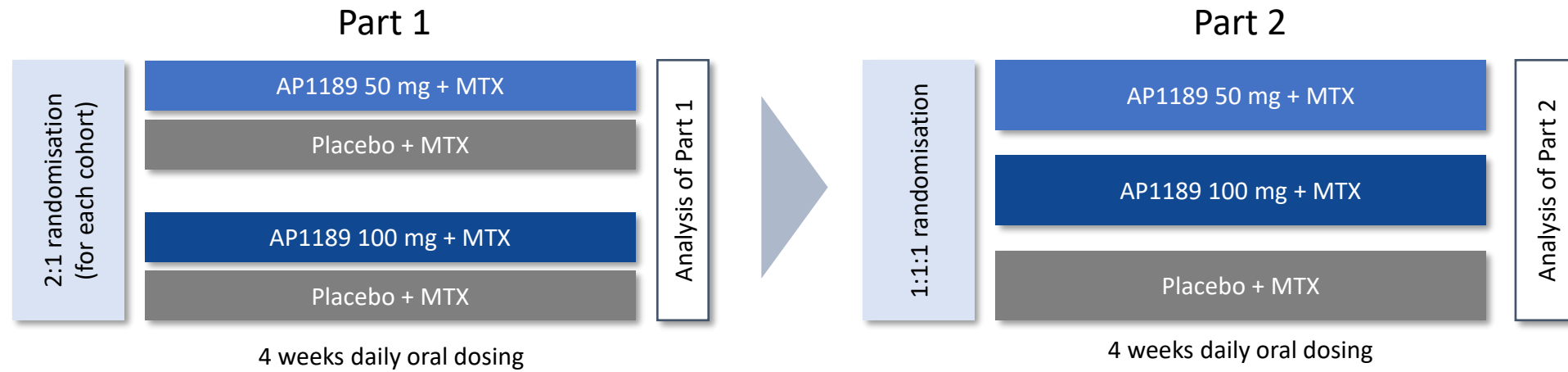
# The current treatment paradigm for RA leaves significant potential for new meaningful therapies



## Unmet need in the RA treatment paradigm

- Rheumatologists tend to treat aggressively with the variety of treatment options available, but RA treatment is still largely an art form
- DMARDs and biologics are well established in the treatment paradigm but don't work for all patients
- Despite a large variety of treatment options, remission remains elusive. In a study of 700+ RA patients followed for 3 years, 47% never achieved remission<sup>1</sup>
- The FDA has placed boxed warnings on the package inserts of JAK inhibitors over increased risks for serious opportunistic infections, cancer, and serious cardiovascular events
- Shortcomings of currently available treatment options create significant opportunity for new modalities that can safely treat RA

# Phase IIa BEGIN study in patients with early RA with severe disease activity



## Key inclusion criteria

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

**Part 1:** n=29, interim assessment based on first 26 completed

**Part 2:** n=105

**Clinical site locations:** Denmark, Sweden, Norway  
Moldova and Bulgaria added as of March 2021

## Primary endpoint

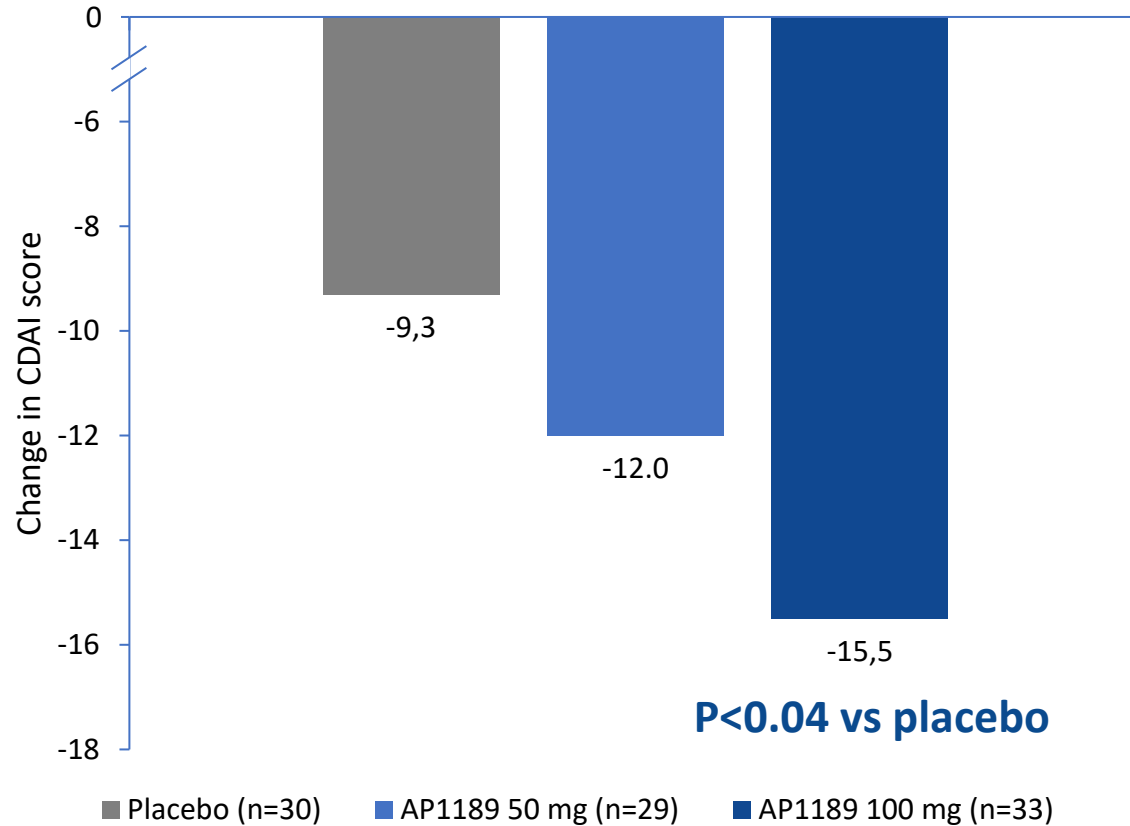
Absolute change in CDAI and response rate (severe to moderate) vs. placebo at 4 weeks

## Secondary endpoints

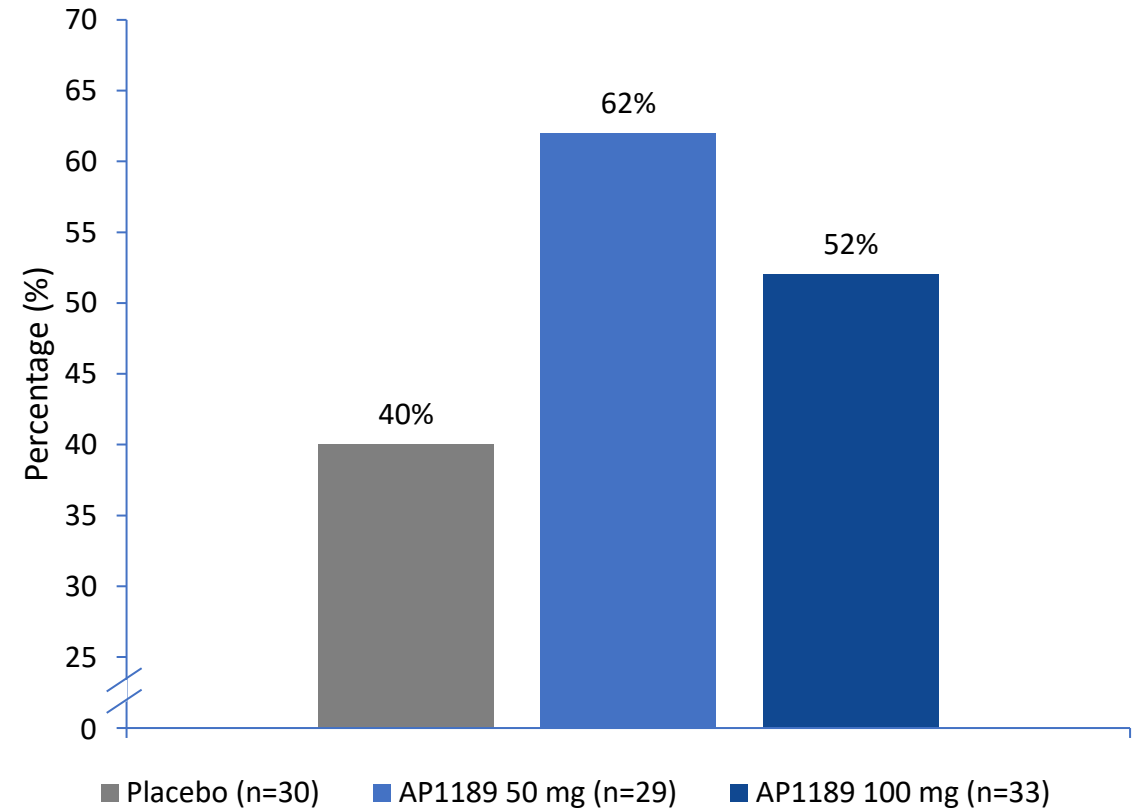
- Swollen and tender joints
- CDAI score
- DAS28 score
- HAQ-DI score
- FACIT-Fatigue score
- ACR response
- Reduction in key circulating cytokines (exploratory)
- Evaluation of clinical activity relative to MC1R polymorphism

# Phase IIa BEGIN: Change in Clinical Disease Activity Index (CDAI)

Mean change in CDAI from baseline to Week 4

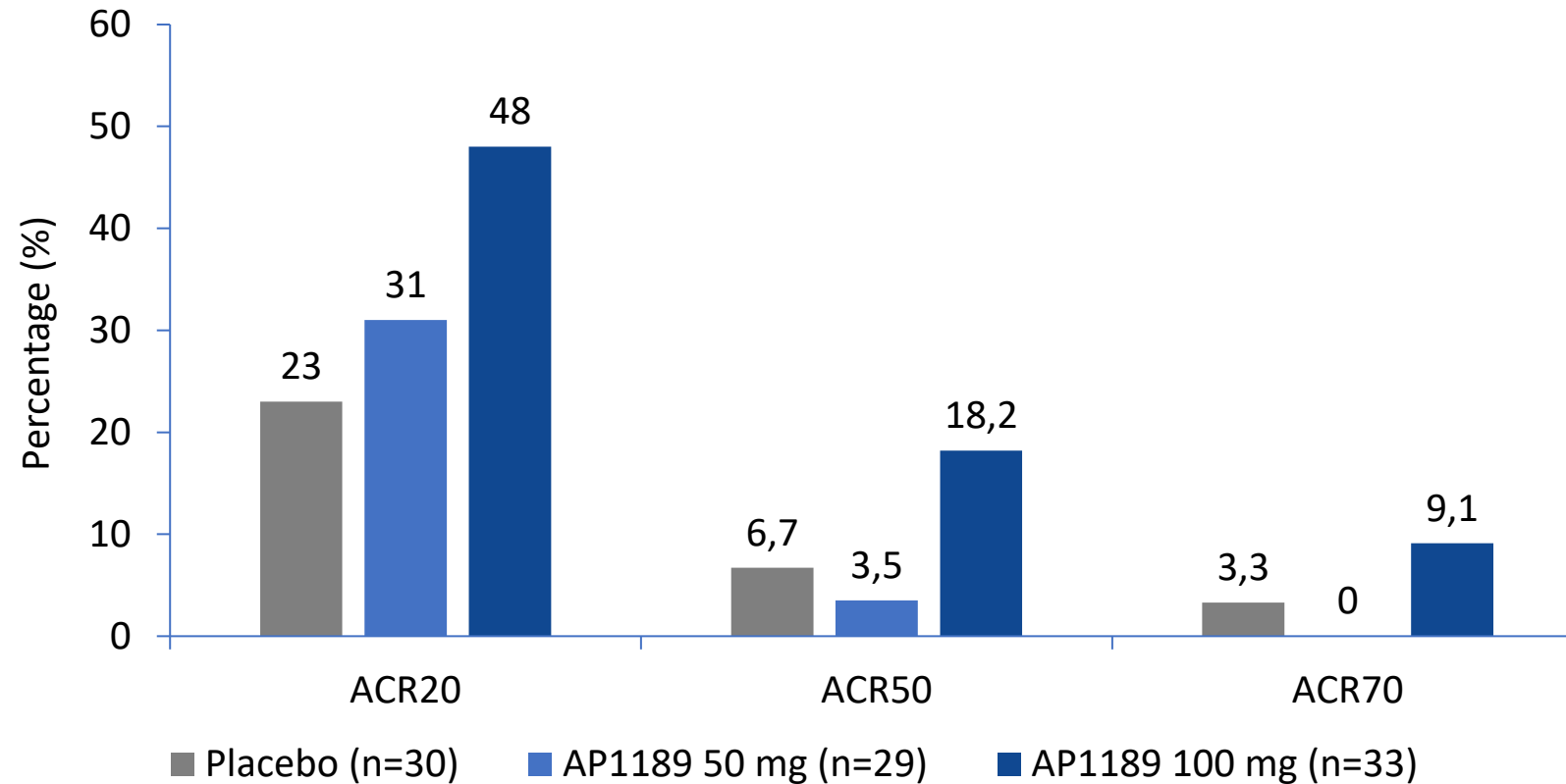


Proportion of subjects with a change in CDAI score from severe (CDAI > 22) to moderate (CDAI ≤ 22) at Week 4 vs. baseline



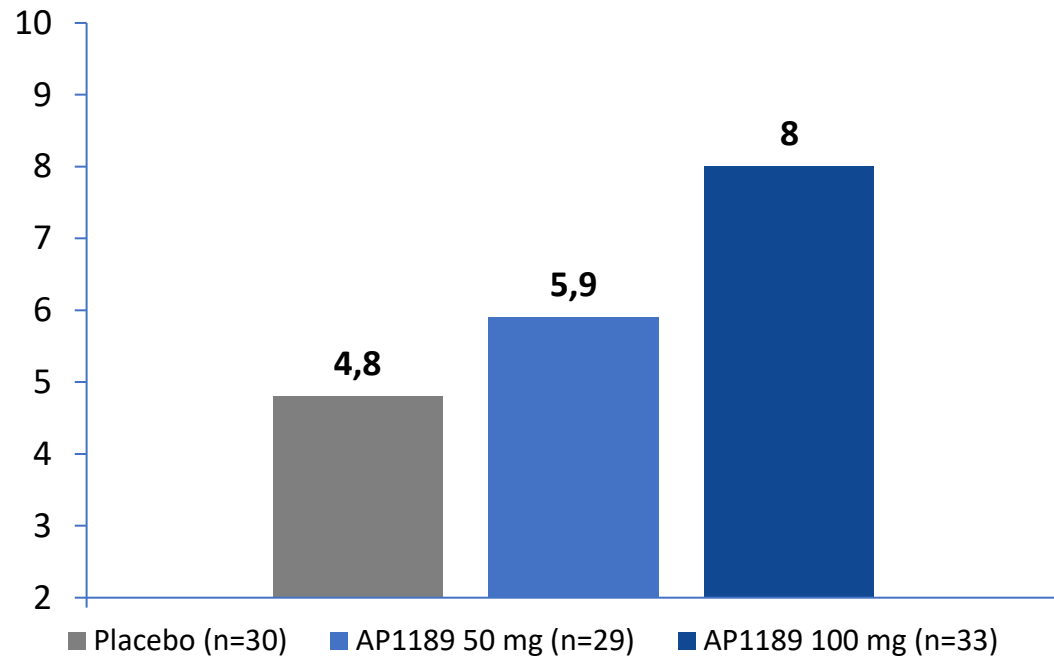
# Phase IIa BEGIN: Change in ACR20/50/70

Proportion of subjects achieving a minimum 20/50/70% improvement in disease activity after 4 weeks of treatment compared with baseline

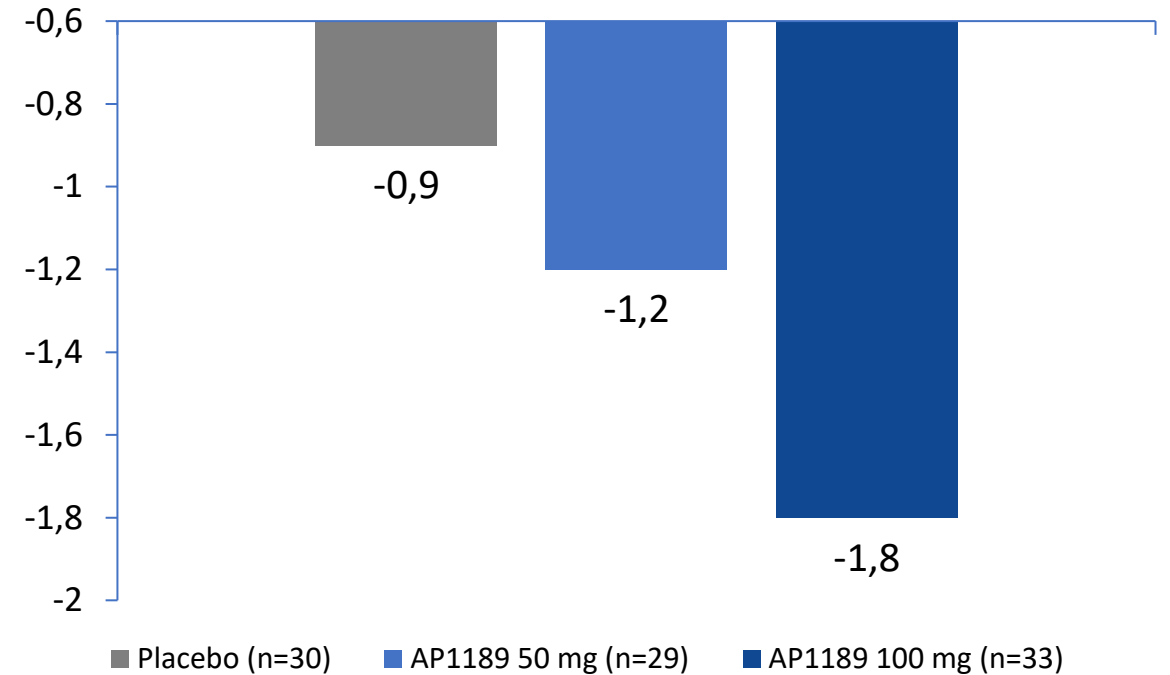


# Phase IIa BEGIN: AP1189 reduced patient fatigue and pain

Mean improvement in Fatigue (FACIT Score)



Mean reduction in pain (VAS-score)



# Phase IIa BEGIN: AP1189 demonstrated a benign safety profile

	Placebo (n=32)	AP1189 50 mg (n=31)	AP1189 100 mg (n=35)	Total (n=98)
Serious Adverse Events, n (%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
AEs, n reported from baseline	21	38	27	86
AE severity (mild/moderate/severe)	18/2/1	26/12/0	22/5/0	66/19/1
Discontinuation due to IMP-related AEs, n (%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Discontinuation due to MTX-related AEs, n (%)	1 (3%)	0 (0%)	0 (0%)	1 (1%)
AEs occurring in >5% patients:				
Nausea, n	4	3	4	11
Increase in aminotransferases, n/clinically significant	3/2	6/2	0/0	9/4
Gastrointestinal AEs other than nausea, n	2	3	7	12

# Phase IIa BEGIN: Conclusions

- In this 4 week study, patients treated once daily with 100 mg AP1189 achieved a statistically significantly greater reduction in mean CDAI as compared with placebo
- Change in disease activity from severe to moderate was numerically higher in groups treated with AP1189 as compared with placebo
- Consistent dose-dependent effects were also seen across secondary endpoints including DAS28, ACR20/50/70 scores, FACIT-fatigue score and pain.
- AP1189 was well-tolerated and presented with a favourable safety profile. No serious adverse events were reported in the study

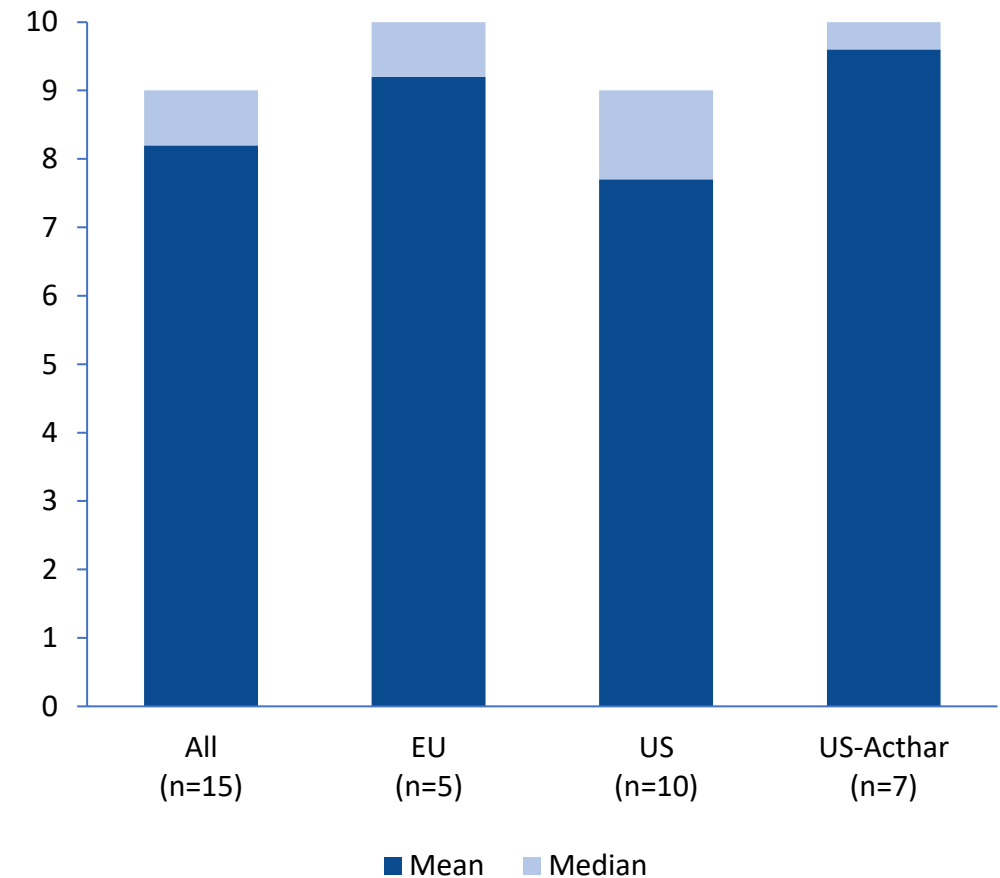
**Based on the positive results, SynAct Pharma will seek scientific advice and open an IND with the FDA to prepare for Phase IIb**



# Rheumatologists express high degree of interest in AP1189 based on the BEGIN Part 1 data

- Rheumatologists reacted very favourably to the product profile for AP1189 based on Part 1 data from BEGIN
- 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® despite negative views on Acthar® pricing and access
- Median and mean product interest was high in both the US and the EU
- Interest was highest among US rheumatologists with recent Acthar® experience
- Stated intent to use in 15%–80% of their patients with RA


Rheumatologist interest to use AP1189 on a scale of 1 to 10



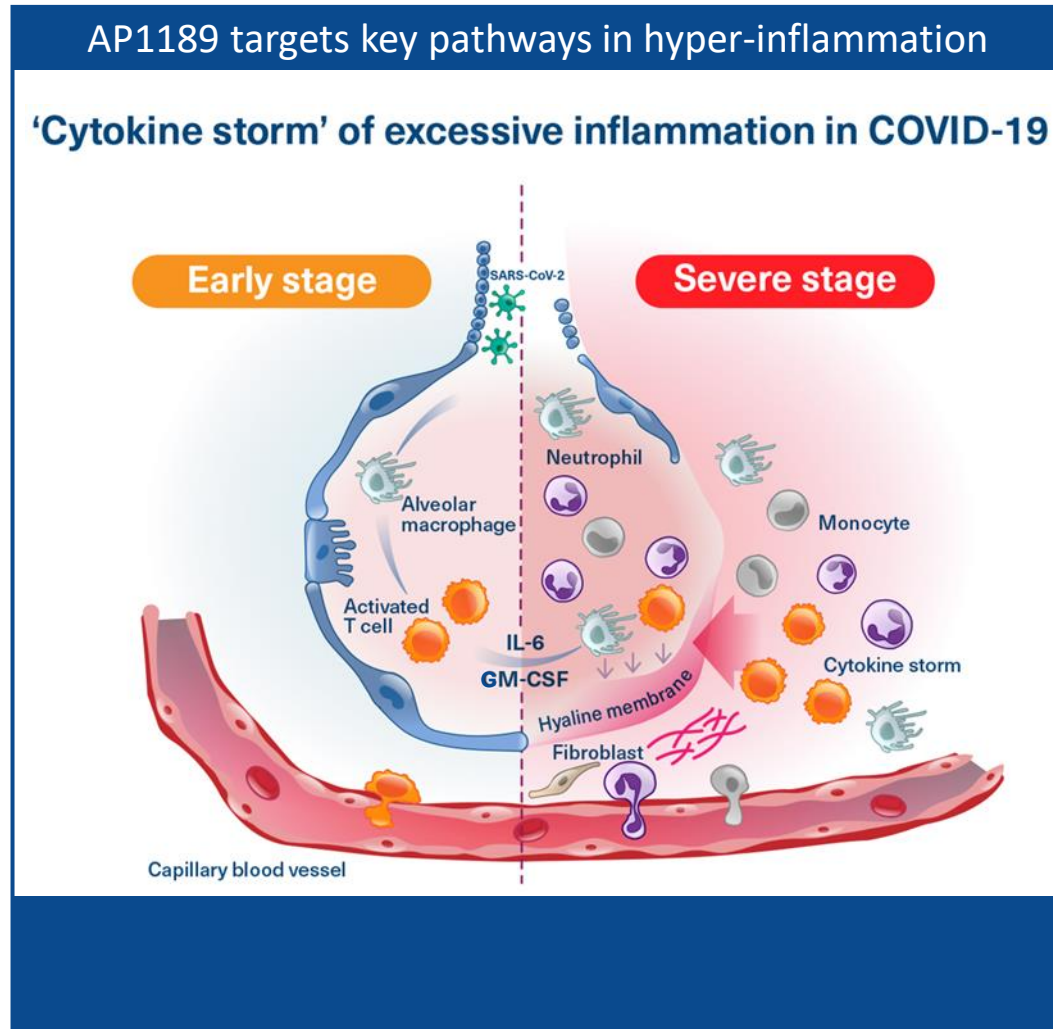


**AP1189 in Virus-induced Respiratory  
Insufficiency**

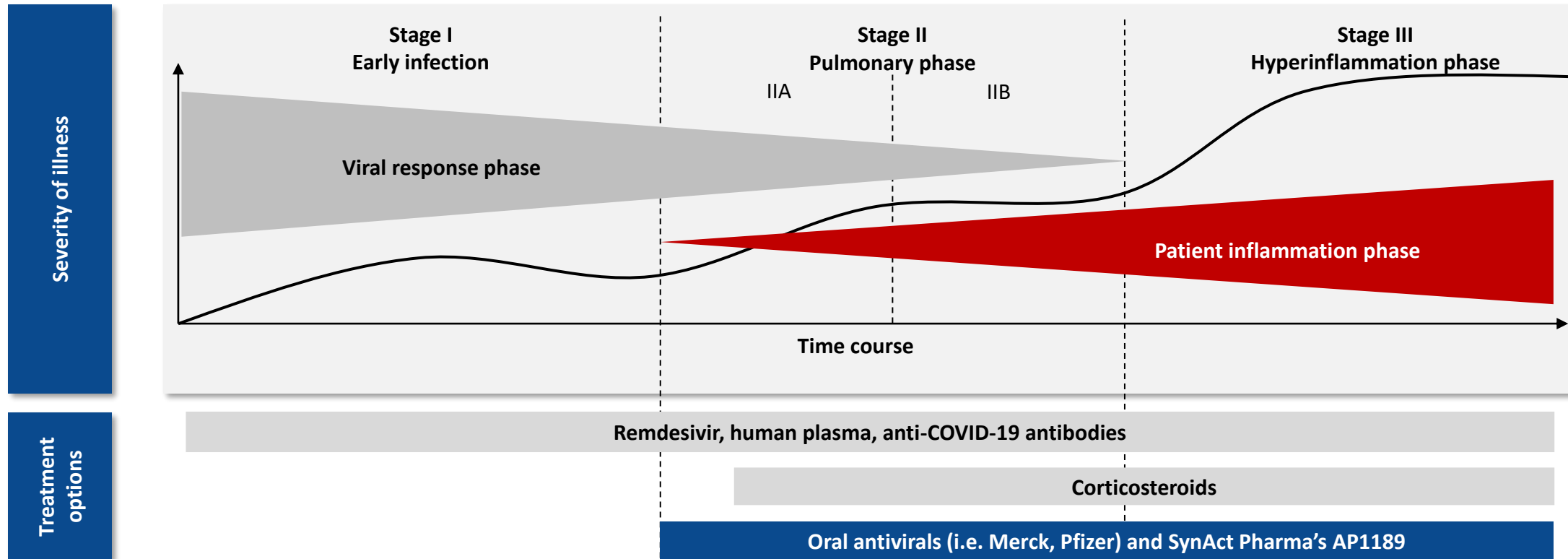
**Leveraging AP1189's MoA to Treat  
Viral-Induced Pulmonary Hyperinflammation**



# Virus-induced Respiratory Insufficiency: AP1189's MoA on macrophages can resolve hyper-inflammation of the lungs

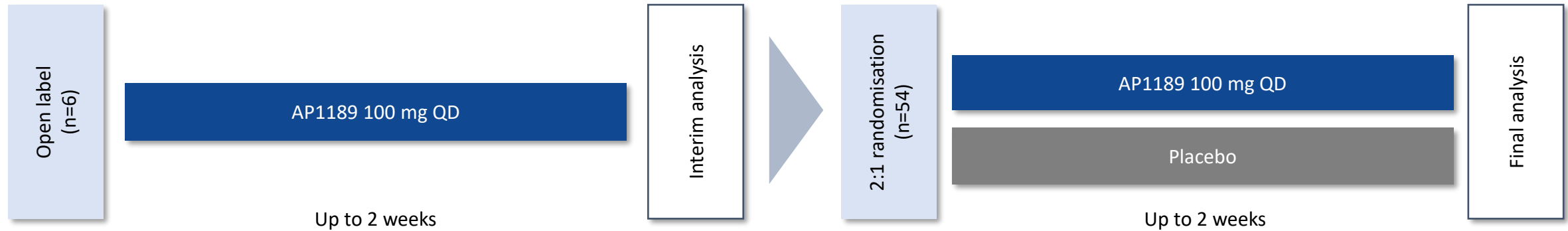


# COVID-19: AP1189's anti-inflammatory properties provide strong rationale to explore its potential utilization in COVID-19 infections



- The anti-inflammatory properties and tolerability profile of AP1189 create potential for it to become a part of the treatment paradigm for COVID-19
- As a tablet, AP1189 can provide convenience and cost advantages over infused treatment options, also in the outpatient setting
- AP1189 is not an antiviral, providing a differentiated mechanism compared to other oral antivirals currently available or in development

# RESOVIR-1: AP1189 versus placebo in patients with COVID-19 with respiratory insufficiency



## Key inclusion criteria

- Positive COVID-19 infection
- Need for supportive respiratory assist\*

## Primary endpoint

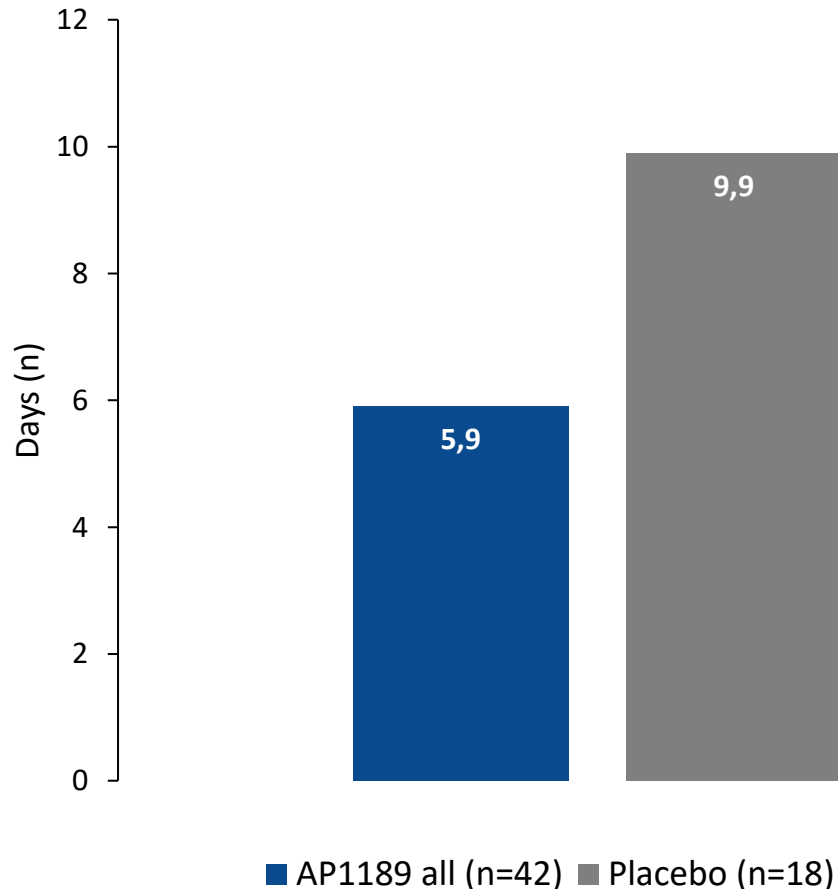
Time to respiratory recovery, defined as the time from initiation of treatment to the time when the patient's SpO<sub>2</sub> is ≥93% determined by pulse oximetry in the patient on ambient air for a minimum of 30 minutes

## Key secondary endpoints

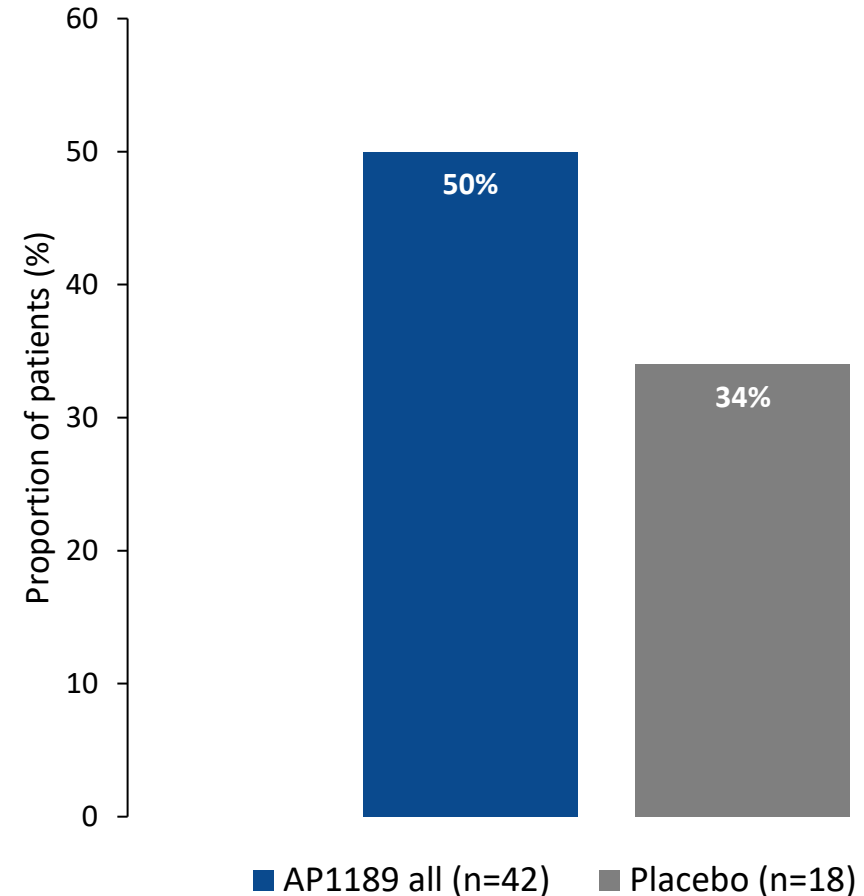
- Rate of ICU admission during the treatment period
- Proportion of patients who go to mechanical ventilation at any time during hospitalisation
- Proportion of patients discharged at Day 14 or before
- Rate of mortality at Day 28
- Length of hospitalisation
- Length of stay in the ICU
- Number of supplementary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

# RESOVIR-1: Treatment with AP1189 resulted in a greater proportion of patients achieving respiratory recovery at a faster pace

Average respiratory recovery time\*

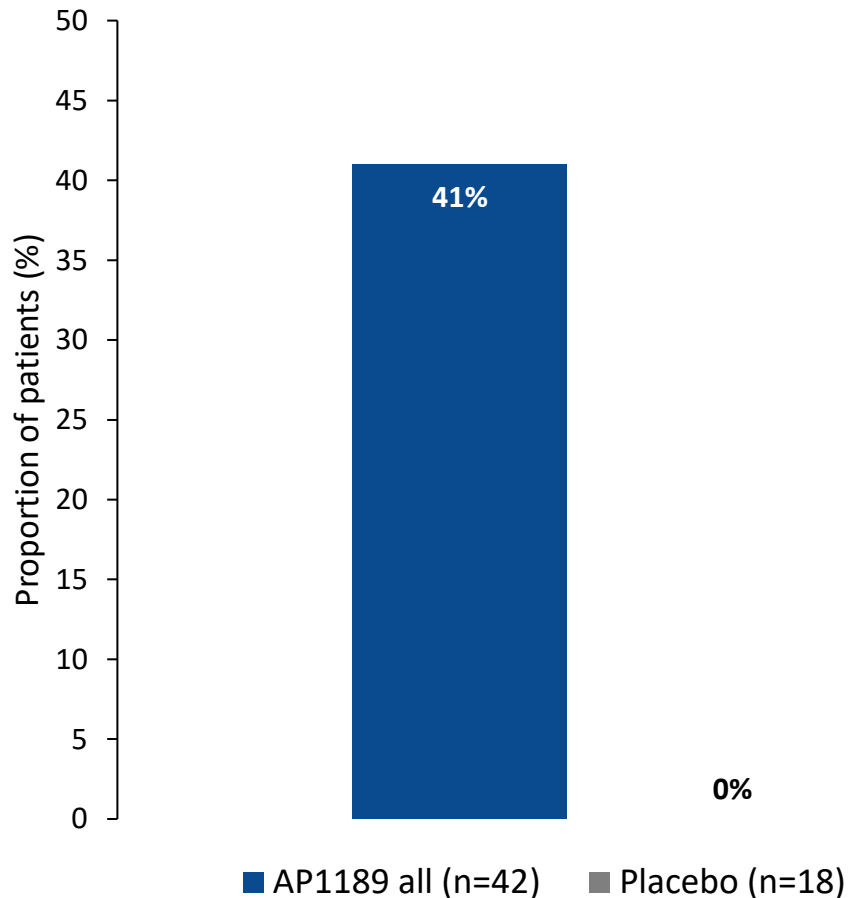


Cumulative respiratory recovery by Day 4\*

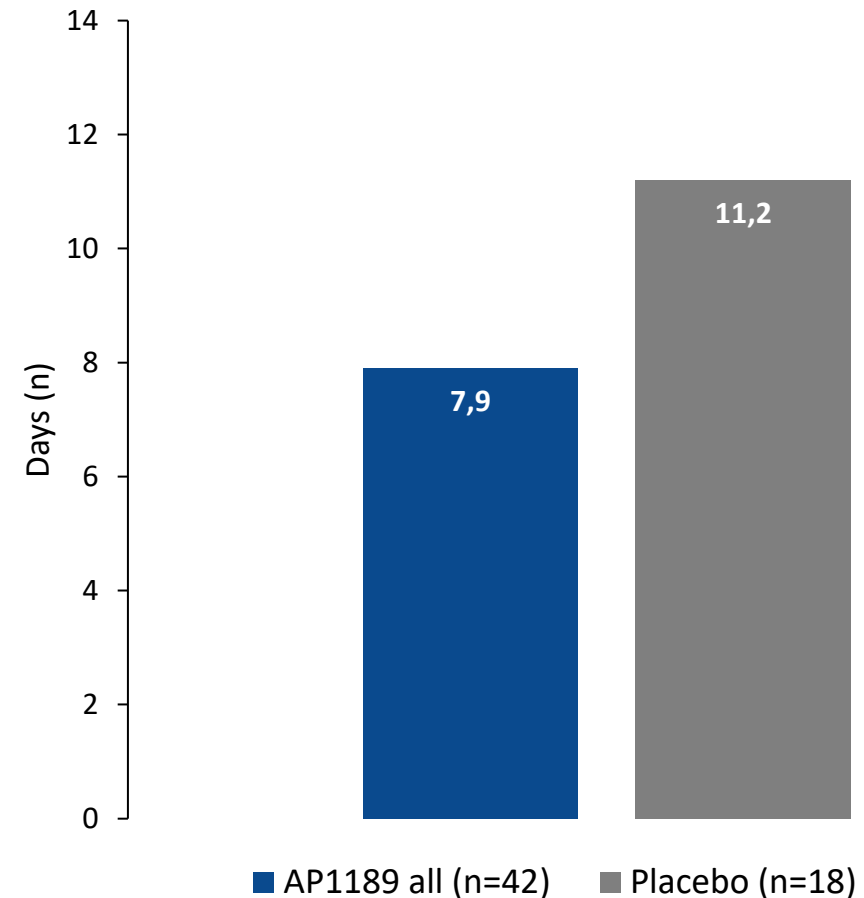


# RESOVIR-1: Patients treated with AP1189 were discharged from hospital faster than those receiving placebo

### Hospital discharge by Day 4



### Average hospital discharge time



# RESOVIR-1: AP1189 Continued to Demonstrate a Well-Tolerated Profile



## Observed safety profile

- The overall frequency of adverse events was higher in the AP1189-treated than the placebo-treated group
- Reported adverse events:
  - Nausea
  - Vomiting
  - Dyspepsia
  - Diarrhoea
  - Cough
  - Increase in transaminases
- GI-related adverse events were the most common
- The adverse event profile was comparable to that seen in previously reported studies conducted in healthy volunteers as well as in the BEGIN trial in RA



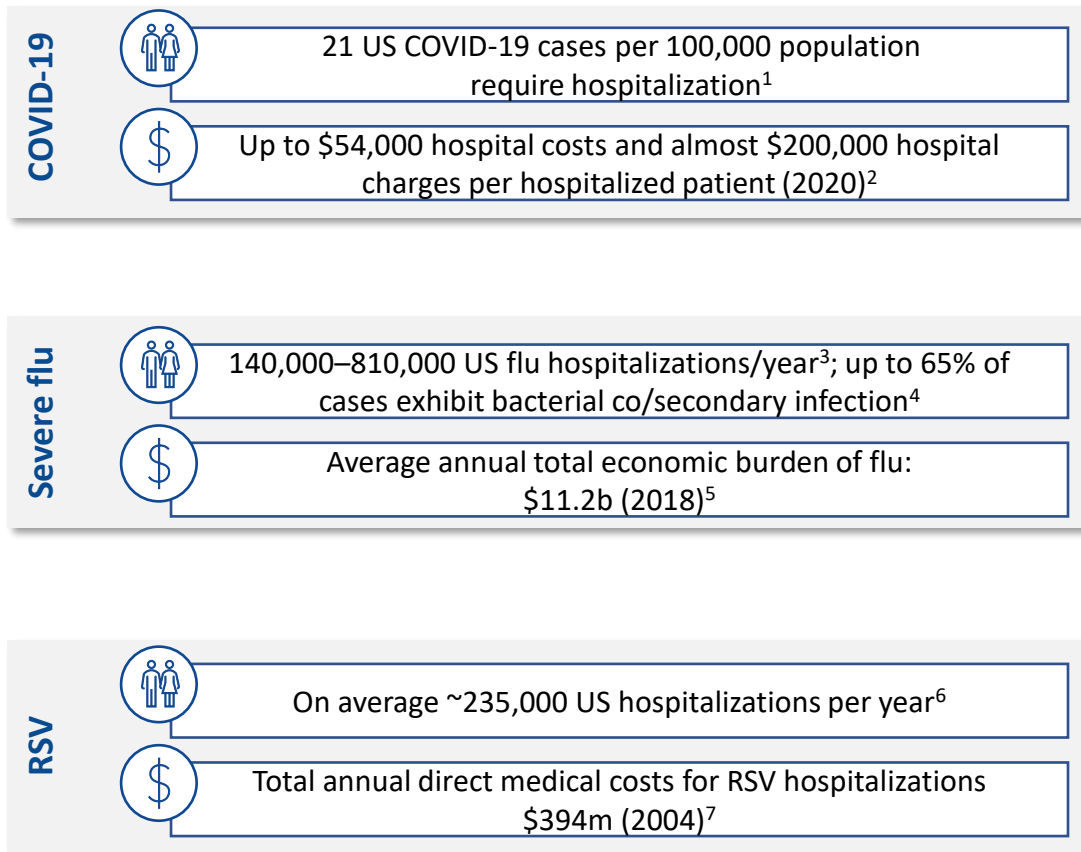
# RESOVIR-1: Conclusions

## Conclusions

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- Significantly reduced time to respiratory recovery by 4 days compared with placebo
- Reduced time to discharge from hospital by c. 3 days compared to placebo
- Facilitated early discharge from hospital with 33% of all AP1189-treated patients discharged following 4 days of treatment compared with 0% of placebo-treated patients
- Was associated with a greatly reduced proportion of patients who developed need for mechanical ventilation and reduced proportion of patients who developed acute kidney injury
- No treatment-limiting adverse events attributable to AP1189 were observed

# AP1189's broad anti-inflammatory mechanism can target Viral-Induced Respiratory Insufficiency in and beyond COVID-19



**Respiratory insufficiency, potentially developing into ARDS**



# Leadership



# SynAct Pharma – Experienced Management

## Jeppé Øvli Øvlesen, MBA – CEO



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



## Henrik Stage, MSc – CFO



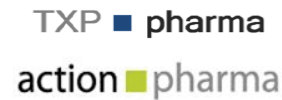
- >25 years' experience in biotech and financial industry
- Former CEO and CFO at Santaris Pharma, sold to Roche for \$450m
- >\$150m from Big Pharma deals; prepared Santaris for US Nasdaq IPO



## Thomas Jonassen, MD – Co-founder and CSO



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



## Thomas Boesen, PhD – COO



- 20 years' experience in biotech and pharma industry
- Inventor of several new chemical entities
- Co-founder of TXP Pharma
- Former VP Discovery, Action Pharma



## James Knight, MBA – CBO



- >25 years' experience in biotech ranging from R&D through commercial strategy and business development at Biogen, Dura, Elan, Questcor and BioTime
- Formerly VP of Portfolio Strategy at Questcor overseeing expansion of Acthar®-promoted indications, growing sales from \$110m to \$1b



## Anders Dyhr Toft, MD, PhD, eMBA – CMO



- Senior leadership roles in Medical Affairs, Operations and Commercial and has played key roles in multiple blockbuster launches of medicines for people living with chronic disease. Most recent role as Corporate VP heading up Commercial Innovation at Novo Nordisk HQ.



# SynAct Pharma – Board of Directors

## Torbjørn Bjerke, MD – Chairman



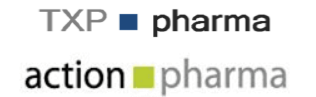
- >25 years track record from pharma industry as Head, R&D and CEO (private and public), BD
- Co-founder of Action Pharma, TXP Pharma, Arctic Aurora LifeScience and Biotech Select and Carelight Ltd
- Chairman TXP Pharma, Carelight Ltd



## Thomas Jonassen, MD – Board Member, Founder



- Associate Professor, KU in Denmark
- Visiting Professor, WHRI, UK
- Co-founder of TXP Pharma and Resother
- 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
- Board member of a number of European biotech companies



## Terje Kelland, MD, PhD – Board Member



- >30 years of international experience from management positions in the life science industry.
- SVP at Novo Nordisk A/S, head of research and development at Biovitrum AB (now SOBI AB), and has held various positions within Pharmacia AB.



## Uli Hacksell, PhD – Board Member



- Former CEO of Medivir
- Former CEO of Acadia Pharmaceuticals, taking it from private startup to multibillion USD public company
- Board member of many other life sciences companies



## Marina Bozilenko, BA, MA – Independent Board Member



- 30 years of investment banking and other healthcare industry expertise, including raising >\$30b in capital and executing numerous M&A transactions
- Strategic Advisor to William Blair & Company, having joined in 2010 as Head of Biotech & Pharma and Managing Director
- BA in molecular biology and MA in economic history from the University of Chicago



# Summary



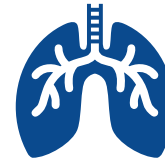
# SynAct Pharma – Investment highlights and upcoming news flow

- Focus on developing a novel treatment for inflammatory and autoimmune diseases targeting the melanocortin system
- Several near-term value inflection points from Phase II development and other corporate activities
- First-in-class compound with unique biology and once-daily dosing designed to have versatility across several indications
- Fortified IP portfolio providing protection until 2042
- Experienced management team and BoD with strong track record in drug development and deal making
- Continually evaluating compelling business development opportunities



RA

- Initiate Phase IIb programme



Virus-induced respiratory insufficiency

- Initiate confirmatory virus-induced respiratory insufficiency trial, paving the way for Emergency Use Approval in select countries



Nephrotic syndrome

- Complete Phase IIa in re-designed study



Corporate/other

- Uplist to Nasdaq Stockholm Main Market (1H22)
- Additional IP
- Discovery of new assets
- Potential business development

SYNACT



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# Appendix



# Safety Concerns That Have Arisen With JAK Inhibitors Create a Tangible Opportunity for AP1189 in RA

## Recent developments with JAK inhibitors

- Based on a review of a large randomized clinical trial, the FDA has concluded that there is an increased risk of serious cardiovascular-related events such as heart attack or stroke with tofacitinib, a JAK inhibitor
- Subsequently, the FDA has required similar safety warnings for two other approved JAK inhibitors, baricitinib and upadacitinib, since they share the same mechanism of action, even though these safety events have not been studied in similar large safety trials
- Boxed warnings have now been placed on the package inserts of each of the approved JAK inhibitors
- The FDA is now limiting all approved uses of tofacitinib, baricitinib and upadacitinib to certain patients who have not responded to or cannot tolerate one or more TNF inhibitors



### **WARNING: SERIOUS INFECTIONS, MALIGNANCY, AND THROMBOSIS**

*See full prescribing information for complete boxed warning.*

- **Serious infections leading to hospitalization or death, including tuberculosis and bacterial, invasive fungal, viral, and other opportunistic infections, have occurred in patients receiving OLUMIANT. (5.1)**
- **If a serious infection develops, interrupt OLUMIANT until the infection is controlled. (5.1)**
- **Prior to starting OLUMIANT, perform a test for latent tuberculosis; if it is positive, start treatment for tuberculosis prior to starting OLUMIANT. (5.1)**
- **Monitor all patients for active tuberculosis during treatment, even if the initial latent tuberculosis test is negative. (5.1)**
- **Lymphoma and other malignancies have been observed in patients treated with OLUMIANT. (5.2)**
- **Thrombosis, including deep venous thrombosis, pulmonary embolism, and arterial thrombosis, some fatal, have occurred in patients treated with OLUMIANT. Patients with symptoms of thrombosis should be evaluated promptly. (5.3)**

# Phase IIa BEGIN: Baseline Characteristics

	Placebo (n=34)	AP1189 50 mg (n=35)	AP1189 100 mg (n=36)
Female, %	79.4	77.1	77.8
Age (years)			
Mean±SD	56.4±13.1	56.4±13.1	55.3±13.9
Median (range)	61 (26–78)	57 (28–79)	56.5 (27–77)
18–64 years/65–84 years (%)	73.5/26.5	71.4/28.5	72.2/27.8
Race, White/Asian/Other (n)	34/0/0	34/1/0	35/0/1
Weight (kg)			
Mean±SD	75.2±19.7	75.9±17.7	79.3±16.7
Median (range)	71.6 (48–145)	75.3 (42–111)	76.6 (48–118)
Height (cm)			
Mean±SD	167.5±7.8	167.5±6.6	166.3±8.4
Median (range)	167 (155–185)	167 (157–183)	165.5 (151–183)
CDAI	36.3±8.6	36.1±11.0	39.0±9.0
DAS-28	5.5±1.0	5.4±0.9	5.7±0.9

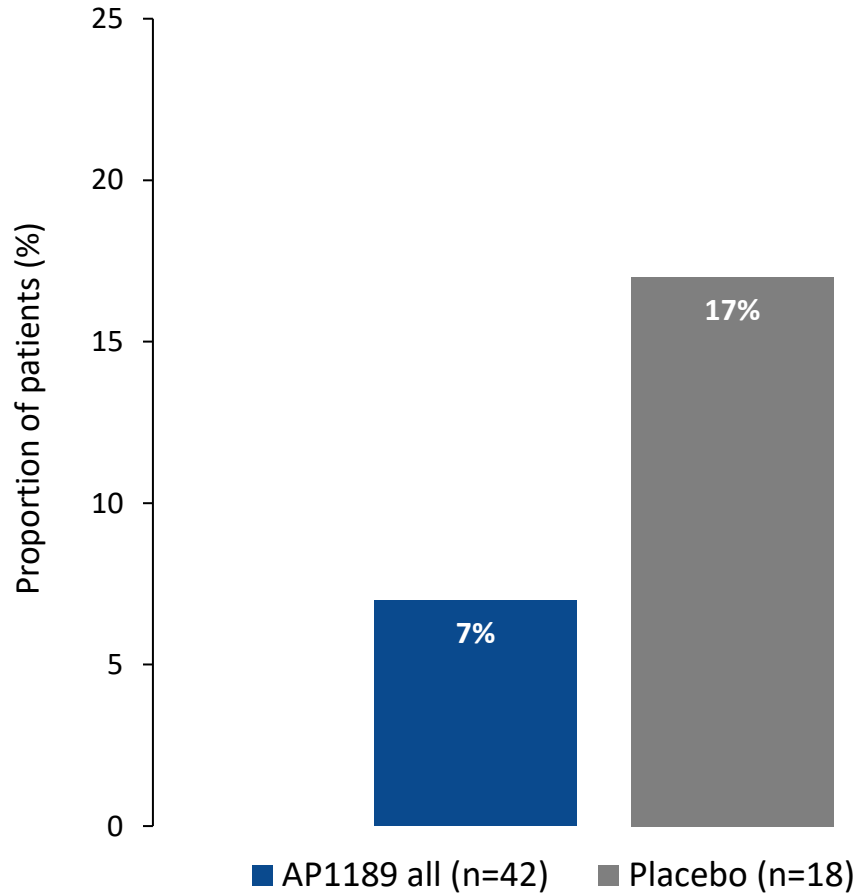
# Rheumatologists Describe Two Target Patient Segments for AP1189

Segment	Description	7 MM segment size
<b>Frequently flaring</b>	<ul style="list-style-type: none"> <li>Patients who experience multiple flares per year (&gt;4)</li> <li>Typically experience low disease activity between flares</li> <li>Can be receiving long-term steroids</li> </ul>	<ul style="list-style-type: none"> <li>~15% of patients<sup>1</sup></li> <li>&gt;2m flares/year<sup>2</sup></li> </ul>
<b>Other moderate-to-severe flares</b>	<ul style="list-style-type: none"> <li>Moderate-to-severe systemic flares affecting average daily functions characterized by significant synovitis</li> <li>Excludes 'frequently flaring' patients</li> </ul>	<ul style="list-style-type: none"> <li>~55% of patients<sup>2</sup></li> <li>~4m flares/year<sup>2</sup></li> </ul>

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

# RESOVIR-1: AP1189 treatment resulted in lower rates of both mechanical ventilation and development of Acute Kidney Injury

Mechanical ventilation up to Day 28



Acute kidney injury up to Day 28

