## SynAct Pharma AB

Resolving Inflammation Through Melanocortin Biology

March 2022

## **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.

These statements are not guarantees of future performance and undue reliance should not be placed on them. Such forward-looking statements necessarily involve known and unknown risks and uncertainties, which may cause actual performance and financial results in future periods to differ materially from any projections of future performance or result expressed or implied by such forward-looking statements.

Although forward-looking statements contained in this presentation are based upon what management of the Company believes are reasonable assumptions, there can be no assurance that forward-looking statements will prove to be accurate, as actual results and future events could differ materially from those anticipated in such statements. The Company undertakes no obligation to update forward-looking statements if circumstances or management's estimates or opinions should change except as required by applicable securities laws. The reader is cautioned not to place undue reliance on forward-looking statements.

## **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 risk Vs benefit 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:
  - IH22 Envisaged uplist to Nasdaq Stockholm Main Market
  - 2022 Continue Phase 2b clinical development in RA under IND
  - 2022 Continue development in Nephrotic Syndrome (redesigned study)
  - 2022 Continue development in virus induced hyper inflammation
  - 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

Founded in 2012 Listed on Spotlight Stock Market with p	
Listed on Spotlight Stock Market with p	
uplist to Nasdaq Stockholm Main Marke	
Ticker: (SYNACT:SS)	
Market cap: c. SEK 2.75b/€275m (March	18)
Management holds c. 20% ownership	



## Leadership

## **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 TXP Pharma
- Former CFO and VP BD of Action Pharma



chemometec

TXP pharma

action pharma

#### 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



#### James Knight, MBA – CBO

 >25 years' experience in biotech ranging from R&D through commercial strategy and business development at Biogen, Dura, Elan, Ouestcor and BioTime



 Formerly VP of Portfolio Strategy at Questcor overseeing expansion of Acthar<sup>®</sup>-promoted
 QUESTCOR indications, growing sales from \$110m to \$1b



- >20 years' experience from finance roles in pharma
- Former head of R&D Finance at LEO Pharma
- Experience from divestments, acquisitions and licensing deals



#### 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





SYNACT PHARMA

## **SynAct Pharma – Senior Advisors**

#### Henrik Stage, MSc – Senior Advisor to CEO

santaris

Phizer

pharma

Wyeth

Roche

**Shire** 

- >25 years' experience in biotech and financial industry
- CFO of SynAct Pharma 2016-2021
- Former CEO and CFO at Santaris Pharma, sold to Roche for \$450m
- >\$150m from Big Pharma deals; prepared Santaris for US Nasdaq IPO

#### Thierry Duvachelle, MD – Early Clinical Development Advisor



- MD, Independent consultant with More than 30 years experience with early clinical development- including several hundred Phase 1 studies
- Former CEO Aster Cephac
- Former EVP SGS

#### Andrew Makin, MSc – Preclinical/Toxicology Advisor



- CEO of Andrew Makin, Preclinical Consulting ApS
- A toxicologist with significant experience in preclinical pharmaceutical development.
- Nearly 40 years working for major preclinical Contract Research Organisations in the UK and Europe. 3 years as an independent preclinical consultant, based in Denmark.
- Has provided preclinical toxicology support to SynAct Pharma ever since the company was founded and has supported the AP1189 project from the start.

#### Scientific Advisory Board

#### Mauro Perretti, Professor

- Professor of immunopharmacology and dean of science (Dean of Research) at Barts and London School of Medicine
- Published >300 scientific articles and cited >17,000 times
- Collaboration with SynAct since 2012.



#### Mauro Teixeira, Professor

- Professor of Immunology and Head of the Center for Advanced and Innovative Therapies of the Federal University of Minas Gerais (UFMG) in Brazil.
- Published >680 scientific articles, cited >39,000 times.
- Professor Teixeira has collaborated with SynAct Pharma since 2020.

#### SYNACT PHARMA

## 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**

John Haurum, MD – Board Member

Chairman TXP Pharma, Carelight Ltd

Former CEO of F-star (UK) with deal

flow in excess of €200m

Symphogen

Co-founder and former CSO of

Board member of a number of

European biotech companies



TXP pharma

#### 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

#### 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



TXP pharma

action pharma

and development at Biovitrum AB (now SOBI AB), and has held various positions within Pharmacia AB.

#### 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



#### 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

Pharmaceuticals AstraZeneca 📣 **MEDIVIR** 

symphogen

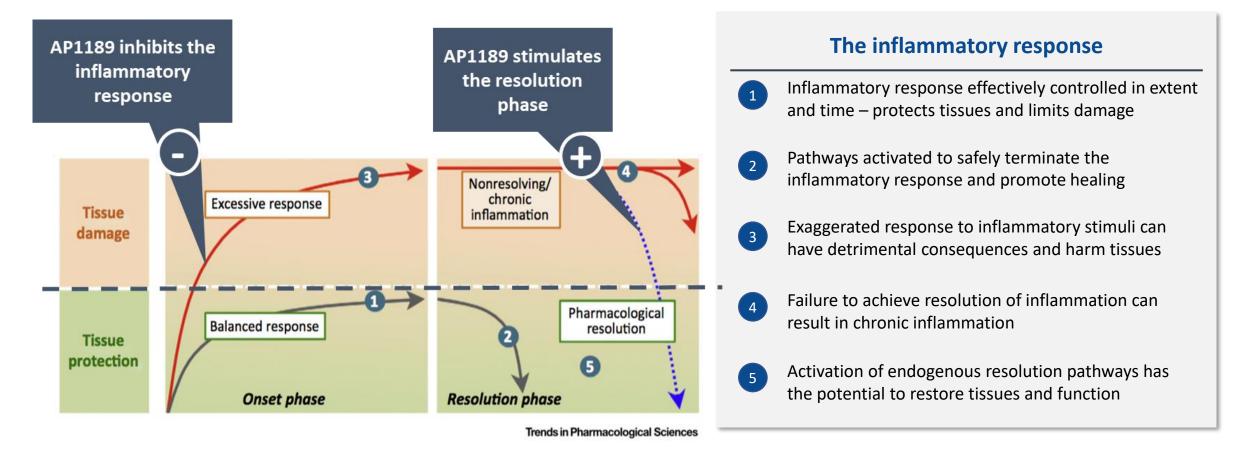


#### SYNACT PHARMA

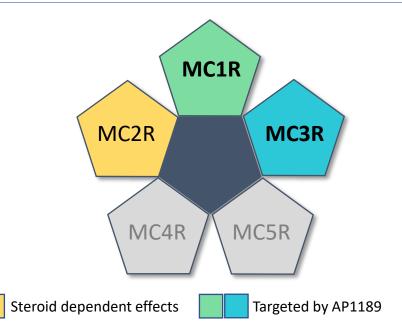
## **SynAct Pharma – Pipeline overview**

Asset	Indication	Preclinical	Phase I	Phase IIa	Phase IIb	Phase III	Next milestone
	Rheumatoid Arthritis – First line treatment						Filing CTA Q2 2022 High level data Q3 2023
	Rheumatoid Arthritis – DMARD-IR						Pre-IND meeting Q2 2022 IND filing PH2b H2 2022
AP1189	Nephrotic syndrome						Redesigned development program Q2 2022
	Virus- induced respiratory insufficiency						Data in non- COVID disease models H2 2022
Next indication							
Next generation of compounds	Inflammatory diseases						

# Inflammation Resolution can correct dysregulated inflammation without inducing immunosuppression



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



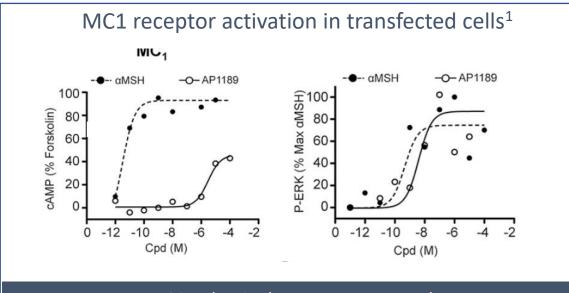
mφ Inflammation **Pro-inflammatory** Resolution t CAMP  $\odot$ Apoptotic Zymosan body o particles mφ &. **↑HO-1** Inflammatory response genes ↑ Efferocytosis œ8° mø ↑Phagocytosis ↓IL-1, IL-6, TNFα

MC3

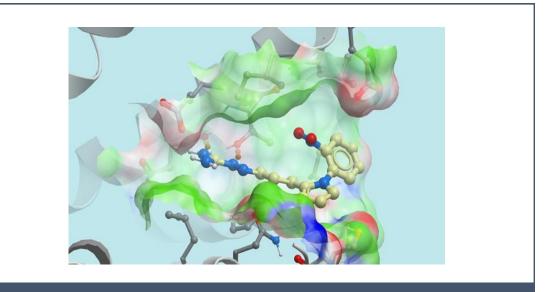
- AP1189 was designed to activate melanocortin receptors 1 and 3 (MC1R and MC3R), which are believed to be responsible for direct immunomodulatory effects
- Importantly, AP1189 does not activate MC2R, which is found on the adrenal glands and is responsible for the release of cortisol and the subsequent steroid side effects and tolerability issues that are associated with ACTH therapies

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

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



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).

SYNACT PHARMA

## Phase 1 Program Supports Once-Daily Oral Dosing

#### AP1189

- SAD and MAD studies have been conducted in healthy Male Volunteers with additional dosing in a cohort of Postmenopausal Women using a Suspension of AP1189/Placebo for oral administration
- SAD (n=56) : Consecutive cohorts of 8 pts (6 active, 2 placebo) dose range 15-800 mg, PMW: 400 mg with the conclusion that safety and tolerability of the compound in tested dose range were good
- MAD: (n=36): Three cohorts of 12 (9 AP1189, 3 Placebo)- dose levels: 50, 100 and 200 mg once daily. Overall conclusion well tolerated, MTD not reached, excellent CV safety (including Telemetric QTc evaluation)
- Well tolerated No SAEs reported. All AE's were with mild to moderate intensity Most common AE was nausea likely attributed to used formulation (suspension)

PK profile following repeat dosing in man<sup>1</sup> 1 200 1 000 •100 mg -200 mg 800 ng/ml 600 400 200 Target level for 0 efficacy 16 18 14 22 hrs

#### PK profile demonstrates once daily potential

1. AP1189-CS001 study MAD part

## Ready for 12 weeks development with once daily dosing with tablets

#### **Toxicology:**

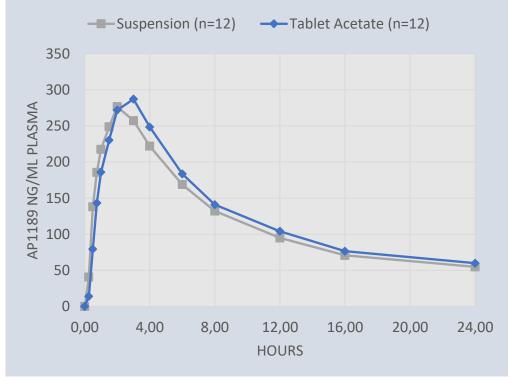
- Three Months Tox studies with recovery groups successfully been completed
- NOAEL rat: 100 mg/kg
- NOAEL pig: 50 mg/kg
- No new findings compared to the 4 weeks studies completed before entering FIM

#### **Tablets humans:**

Crossover study in 12 healthy male volunteers completed

Tablet well tolerated – reports of nausea following dosing with suspension, up to now no reports following dosing with tablets

#### AP1189-CS004 STUDY – ORAL DOSING WITH 100 MG

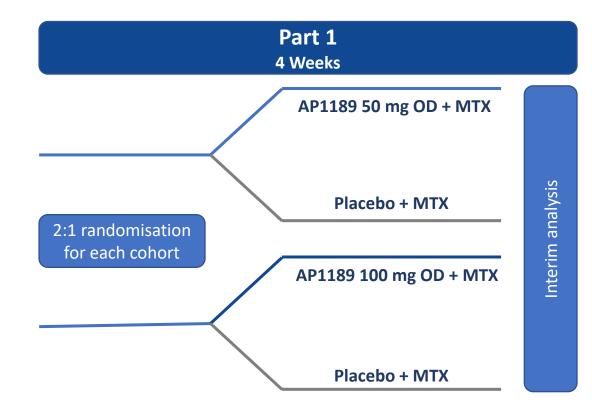


## The **BEGIN** study

A double-blind, multi-centre, two-part, randomized, placebo-controlled study of the safety, tolerability, and efficacy of 4 weeks of treatment with AP1189 in early rheumatoid arthritis patients with active joint disease

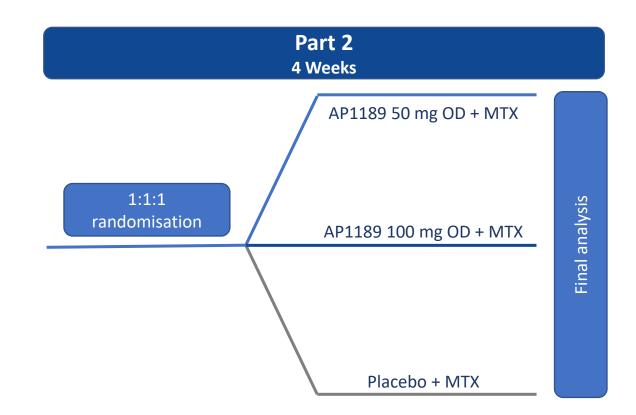
## **BEGIN: P2a POC 4-week study of AP1189 + MTX in severely active early RA**

Study Population	Primary safety endpoint	Primary efficacy endpoint
Adult patients (aged 18 to 85 years) with severe RA defined as CDAI >22, who are about to begin up-titration with MTX	Safety of AP1189 vs placebo (AEs and SAEs)	<ul> <li>Mean change in CDAI or</li> <li>% of patients improving from severe (CDAI &gt;22) to at least moderate (CDAI ≤22)</li> </ul>



SYNACT

PHARMA



## **Baseline characteristics of randomized population**

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

cm, centimetre; kg, kilogram; SD, standard deviation



### **Baseline disease activity in efficacy assessment population**

	Placebo (n=30)*	AP1189 50 mg (n=29)*	AP1189 100 mg (n=33)*
CDAI	36.7±8.7	36.1±9.7	39.5±9.1
SJC	10.4±379	10.2±3.9	12.1±4.9
TJC	13.7±6.1	13.6±6.0	15.2±6.0
DAS-28	5.5±1.0	5.4±0.8	5.7±0.9
Patient Global Assessment (VAS)	6.5±1.8	6.1±2.1	5.8±2.2
Physician Global Assessment (VAS)	6.2±1.1	6.3±1.3	6.4±1.3
CRP (mg/L)	18.7±26.6	14.9±18.9	26.3±41.9

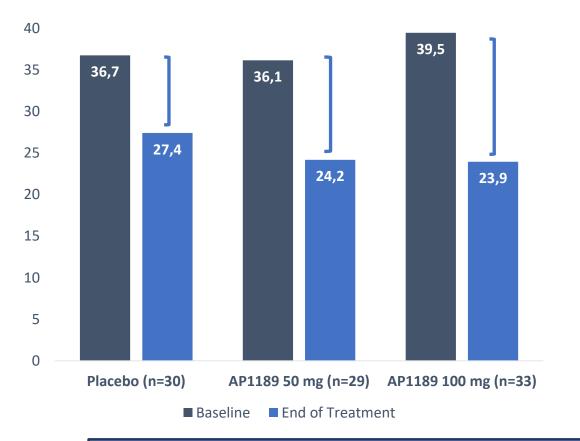
All values are mean±SD. \* mean baseline levels per group in the efficacy analyse set:. 2 randomised pts in each group did not complete dosing. 7 patients were taken out of the efficacy evaluation due to protocol violation. Placebo: n=2; AP1189 50 mg: n=4; AP1189 100 mg: n=1-

CDAI, Clinical Disease Activity Index; CRP, C-reactive protein; DAS-28, Disease Activity Score in 28 joints; SJC, Swollen Joint Count; TJC, Tender Joint Count; VAS, visual analogue scale

## BEGIN P2a POC RA study topline results: AP1189 100mg once-daily oral dose group was efficacious and safe

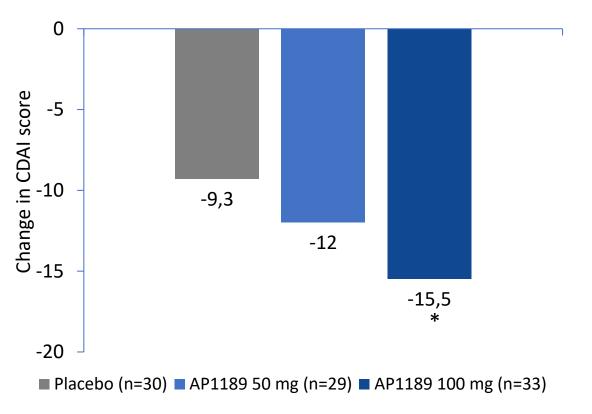
- After 1-mo of treatment, the 100mg once-daily oral AP1189 group had:
  - Significantly better CDAI improvement Vs placebo and that was above the established minimally important clinical difference (MCID) (15.5-point improvement for 100mg and 9-point for placebo)
  - Significantly higher ACR20 response than placebo (61% for 100 mg and 33% for placebo)
  - Good DAS28(CRP) response in severely active patients (68% for 100 mg and 37% for placebo)
  - Mean improvement in FACIT-Fatigue score that was 2x the established minimally important clinical difference (MCID) (8 for 100 mg and 4.8 for placebo)
- The 50mg AP1189 dose was found to be partially effective
- AP1189 was safe and well tolerated with no SAEs, no discontinuations deemed due to study drug, no infections and no discernible impact on wbc count or vital signs

### Mean change in CDAI at 1-mo (primary read out)



#### **CDAI** at Baseline and End of Treatment

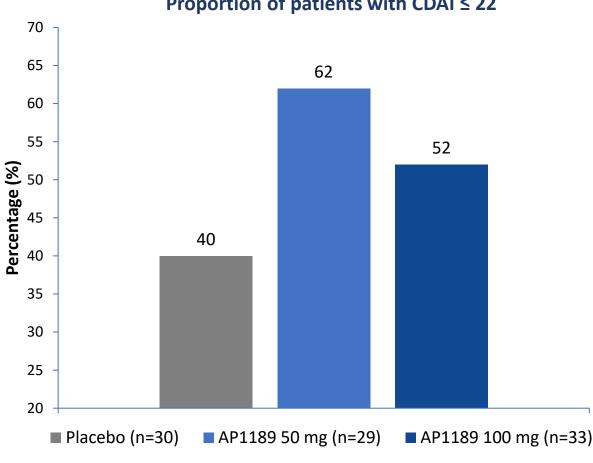
#### Mean change in CDAI from baseline to Week 4



## AP1189 100mg group had a mean improvement in CDAI above the established minimally important clinical difference (MCID)<sup>+</sup> score and was significant Vs placebo

**SYNACT PHARMA** \* = p<0.05 vs placebo, study primary endpoint

#### % of patients improving from severe CDAI to at least moderate disease activity (CDAI $\leq$ 22)

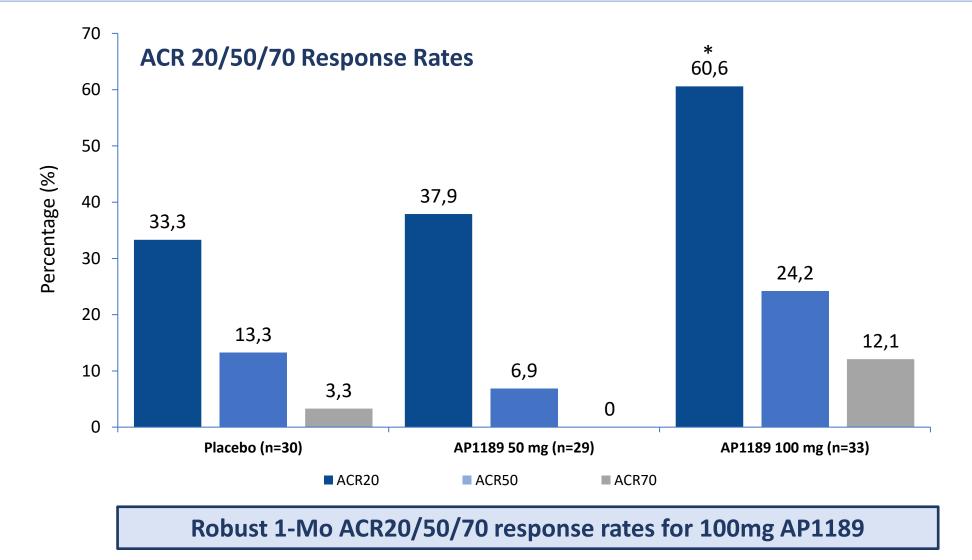


Proportion of patients with CDAI  $\leq$  22

- While the study showed a clear dose dependent reduction in mean change in CDAI (the primary read out) in the AP1189 treated patients, reaching statistically significance at the 100 mg group, the fraction of patients going from high (CDAI >22) to moderate or lower disease activity, even though numerically higher in the AP1189 groups, did not reach statistical significance.
- This lack of a dose response on this read-out most likely is due to:
  - That the response defined as reaching a specific threshold,  $CDAI \leq 22$ , does not take baseline measures into account.
  - Consequently, even with >60% higher reduction in CDAI in the 100 mg group, the threshold was not reached in a proportional higher fraction of pts as the baseline levels was somewhat higher in 100 mg group
  - Block randomization which assigned the higher baseline CDAI patients to the 100mg group

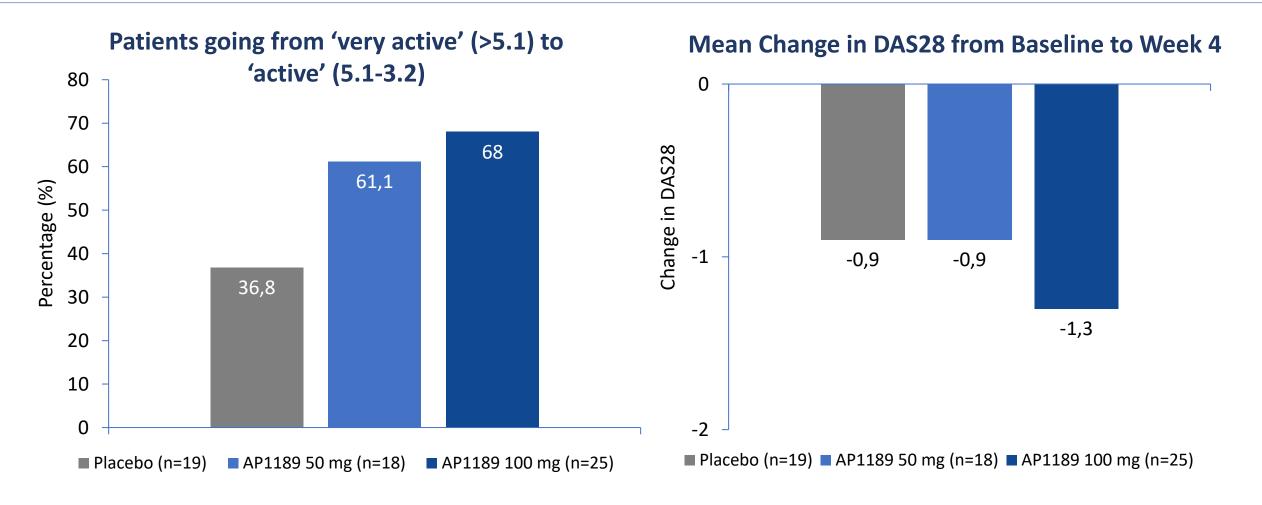
CDAI, Clinical Disease Activity Index

## **Proportion of patients achieving ACR20/50/70 response at 1-mo**



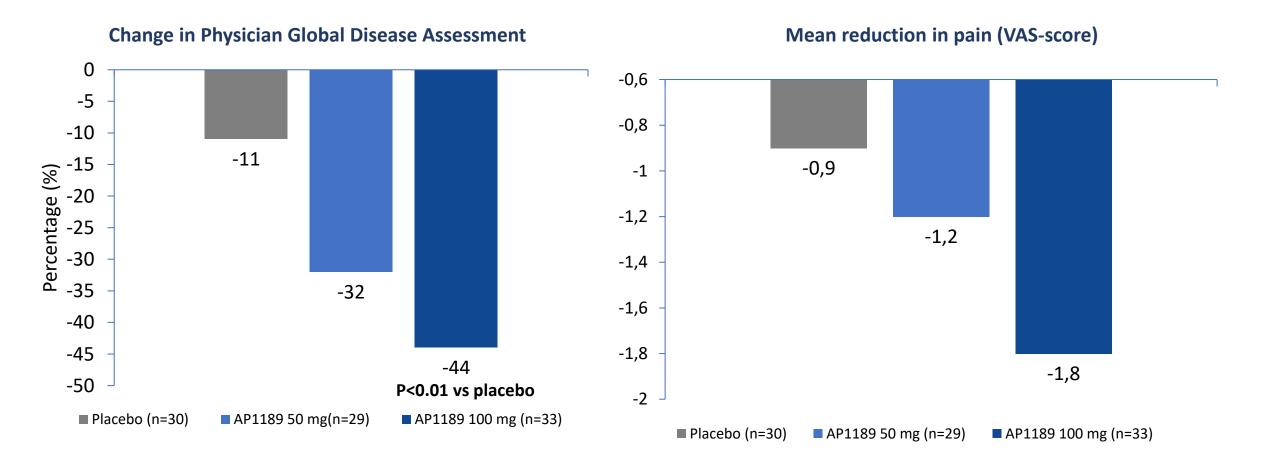
SYNACT PHARMA

### Change in DAS28 (CRP) - subset of 'very active' with >5.1 score at baseline



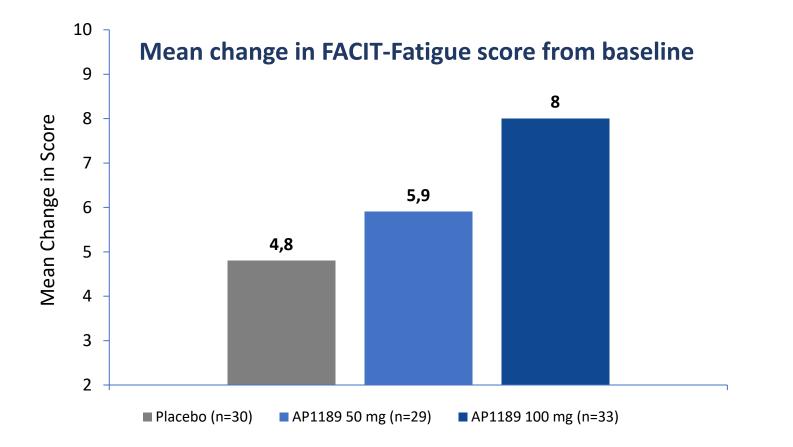
Good effects seen with 100mg in patients with very active DAS28 (>5.1) at baseline

# % improvement in physician global disease assessment (VAS) and and mean change in pain VAS score



VAS, visual analogue scale

### Mean change in FACIT-Fatigue score at 1-mo



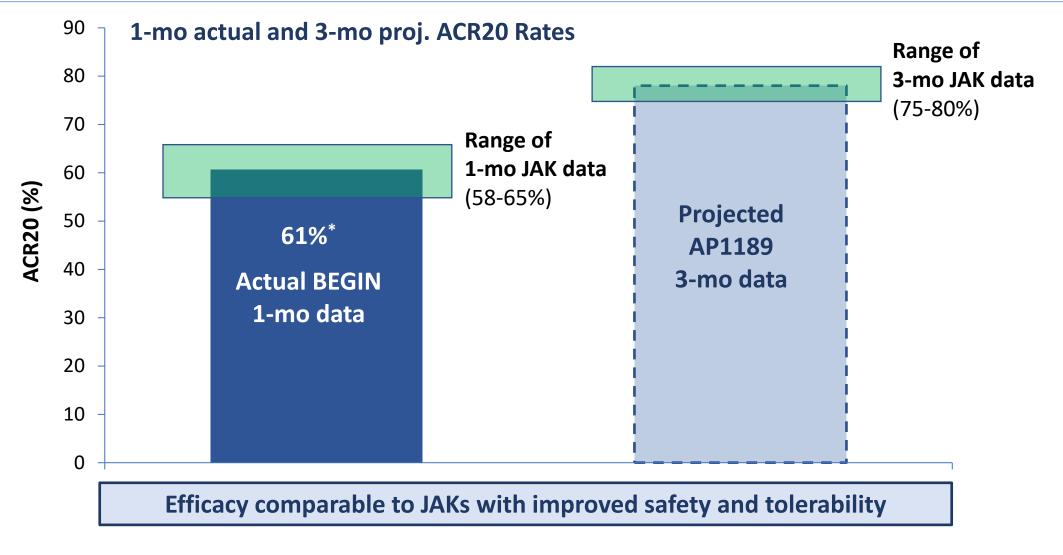
Mean change in 100mg group is 2x the established minimally important clinical difference (MCID)<sup>+</sup>

## **Primary safety endpoint: AEs**

	Placebo (n=32)	AP1189 50 mg (n=31)	AP1189 100 mg (n=35)	Total (n=98)
SAEs, n (%)	0	0	0	0
AEs, n reported from baseline and on	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
Discontinuation due to MTX related AEs, n (%)	1	0	0	1
AEs occurring in >5% patients:				
Nausea , numbers	4	3	4	11
Increase in amino transferases, numbers/clinical significant	3/2	6/2	0/0	9/4
Gastrointestinal AE's other than nausea	2	3	7	12

- Nausea and other transient GI side effects are believed to be attributable to the suspension formulation the new oral tablet under development has not elicited these effects to date
- AP1189 was safe and well tolerated with no SAEs, no discontinuations deemed due to study drug, no infections and no discernible impact on wbc count or vital signs

### AP1189 100mg 1-mo ACR20 scores are comparable to JAKs ACR20 in MTX-Naïve P3 trials -Response rates should increase over time with 3-mo dosing as with JAKs



SYNACT PHARMA

\* = p<0.05 vs placebo

) Lee et. Al., N Engl J Med 2014;370:2377-86.

2) Fleishman et. Al., Arthritis & Rheumatology, Vol. 69, No. 3, March 2017, pp 506–517

3) van Vollenhoven et. Al., Arthritis & Rheumatology, Vol. 72, No. 10, October 2020, pp 1607–1620

4) Westhovens et al. Ann Rheum Dis 2021;80:727–738.

## **BEGIN study summary**

- In this 4-week study, patients treated once-daily with 100 mg AP1189 achieved a significantly greater reduction in mean Clinical Disease Activity Score (CDAI) as compared to placebo
- Change in disease activity from severe to moderate was numerically higher in groups treated with AP1189 as compared to placebo, with the lack of statistical difference likely explained by higher baseline CDAI and inflammation (C-reactive protein, CRP) in the 100 mg group
- While this was a relatively small trial, consistent dose-dependent effects were seen across mean CDAI change and all secondary read-outs including DAS-28, ACR score, investigators global disease assessment (VAS), FACIT-fatigue score and pain (VAS)
- AP1189 was well-tolerated and presented with a favorable safety profile with no serious adverse events were reported in the study
- We believe that the level of efficacy will increase with longer dosing duration and we will be assessing adding a higher dose group(s) in the ongoing P2 program

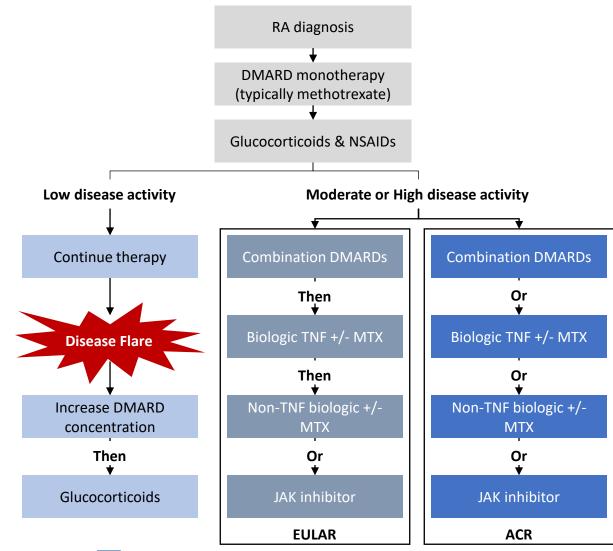
Based on the positive results, SynAct will seek scientific advice and open an IND with the FDA to prepare for Phase 2 trial in DMARD-IR patients to be initiated in 2022



## **AP1189 - Rheumatoid Arthritis**

## Positioning and next development steps

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



SYNACT

PHARMA

#### 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

Treatment paradigm adapted from Global Data RA: Global Drug Forecast and Market Analysis to 2027, 2019; (1) Byerk et al., J Rheumatol 2014;41:227-34

# AP1189 has the potential to be positioned for several potential uses in RA

#### **Emerging AP1189 Clinical profile**

- Once-Daily Oral Dosing new oral solid formulation to be used in next clinical trial
- Quick Onset of Action as early as days
- Efficacy approaching JAKs within 4 weeks
- Safe and Well Tolerated no emerging AEs and No Immunosuppression
- Steroid-Free MoA potential to be steroid sparing
- **Compatible with MTX** no known theoretical DMARD drug interactions

**Multiple RA Positioning Opportunities** 

- The emerging AP1189 clinical profile supports RA development at several treatment inflection points:
  - **DMARD-IR** patients who have had an incomplete response, lost response or are intolerant of DMARDs
  - First line treatment in previous treatment naïve patients Newly diagnosed patients where the compound can be given in combination with DMARDs
  - **Flares** Short-term use to treat for moderate or severe flares in patients who experience multiple flares per year

# Rheumatologists expressed high degree of interest in AP1189 in DMARD-IR

The combination of efficacy, safety, tolerability and oral convenience positions AP1189 well for

DMARD-IR Recent FDA labelling actions with JAKs in RA reduces direct competition in the space

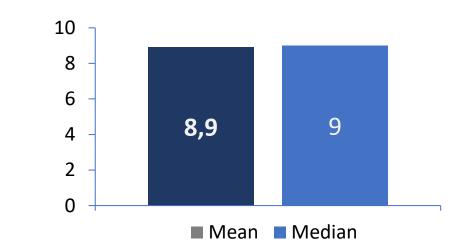
SynAct Pharma has conducted a market research in high subscribing Rheumatologists to evaluate the potential of the drug in DMARD-IR

Rheumatologists support use in DMARD-IR and expressed a willingness to both use it earlier in select patients

PHARMA

SYNACT

#### **Rheum Interest in AP1189 in DMARD-IR**



- Stated intent to use in 45% of DMARD-IR patients
- "Oh man. I'd love to use this up front. I'd love to use it right after methotrexate. I'd love to use it before. I'd love to see this upfront. I mean the non immunosuppressive working kind of endogenously and not doing all the steroid evils, but almost kind of kicking butt like a steroid, uh, yeah, count me in for that one..."

## High Volume US Rheumatologists Reacted Very Favorably to the AP1189 Profile

Respondents were all pleased that so many of their unmet needs were addressed with the AP1189 Profile:

Novel MOA S Oral ROA

## Clean Safety Profile 🔗

## Potential to be combined with other advanced therapies

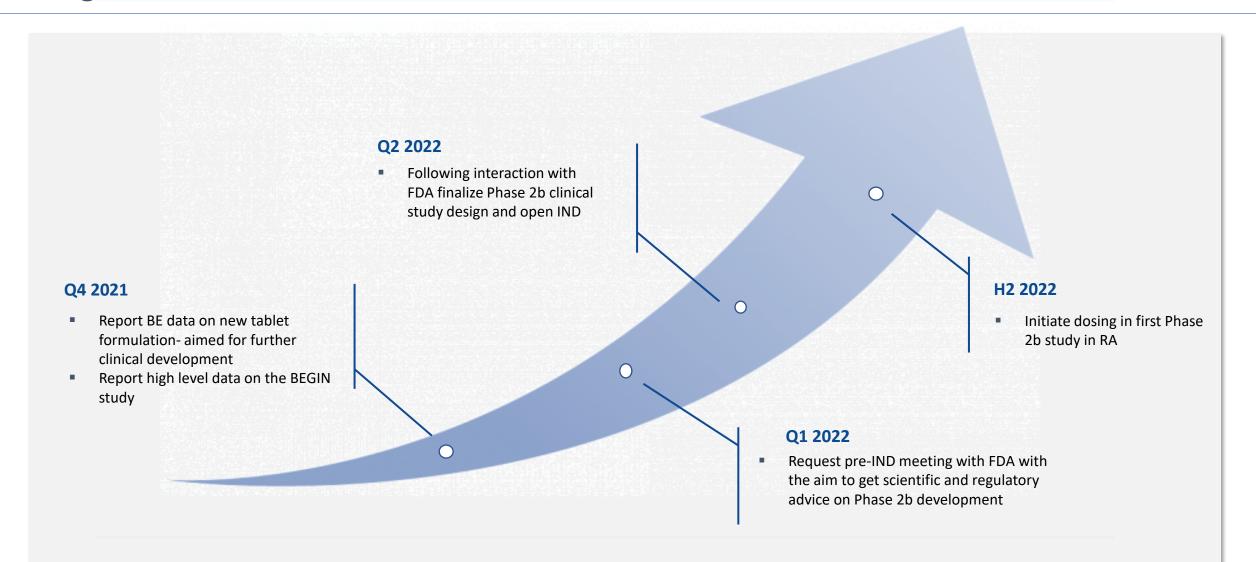
We know from oncology...there's definitely benefit in combining things. And sometimes I get away with triple therapy myself and Plaquenil, MTX, and a TNF inhibitor, you know, there's some cocktail they're on that seems to provide a lot of relief with some patients. This seems very safe so, it'd be nice to swap out one of the oldies and put that in there - US08

Initial impression is very good...they've reallyI'd say rock on. I mean, this is pretty awesome. I like the fact that it's notnarrowed down these specific melanocortin receptorsimmunosuppressive, it's working with the immune system. It's reallyso that's actually very, very exciting.-US02producing some powerful ACR responses...So, I mean, it's very exciting. -US07

Wow. Okay. That's good. Okay. That sounds extremely interesting, very promising. The safety profile looks like a huge plus, that they're not seeing significant or severe adverse events. No opportunistic infection, no cancer, no cardiovascular. That would be a huge plus. Because I think the Jack inhibitors now, are being marketed now as patients need to fail a TNF inhibitor first. Yeah. So, if this drug is an oral drug with comparable efficacy, but better safety, then they should theoretically have a huge market. - US10



### AP1189 as novel compound treatment of Rheumatoid Arthritis-High level milestones for 2022





## 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)

## **Rheumatologists Describe Two Target Patient Segments for AP1189**

Segment	Description	7 MM segment size
Frequently flaring	<ul> <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> <li>~15% of patients<sup>1</sup></li> <li>&gt;2m flares/year<sup>2</sup></li> </ul>
Other moderate-to- severe flares	<ul> <li>Moderate-to-severe systemic flares affecting average daily functions characterized by significant synovitis</li> <li>Excludes 'frequently flaring' patients</li> </ul>	<ul> <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 conditions1
- Acthar<sup>®</sup> users were interested in potential usage in other conditions where they have had success with Acthar<sup>®</sup>