

## SynAct Pharma AB

Treating Inflammation through Resolution Therapy

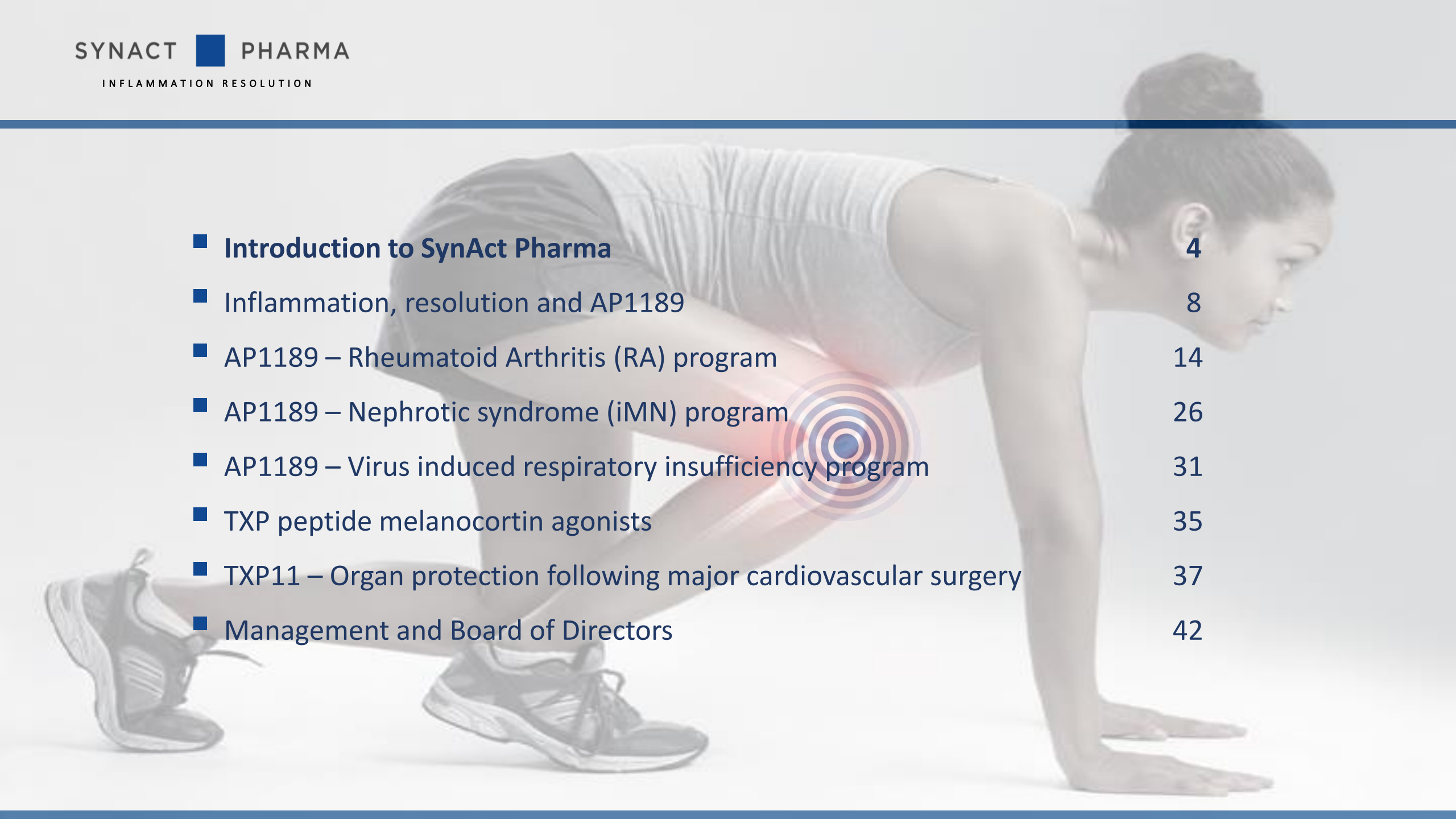


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A woman in athletic wear is shown in a starting crouch for a race. A target icon is overlaid on her back, indicating a focus on the back area. The background is a light blue gradient.

■ Introduction to SynAct Pharma	4
■ Inflammation, resolution and AP1189	8
■ AP1189 – Rheumatoid Arthritis (RA) program	14
■ AP1189 – Nephrotic syndrome (iMN) program	26
■ AP1189 – Virus induced respiratory insufficiency program	31
■ TXP peptide melanocortin agonists	35
■ TXP11 – Organ protection following major cardiovascular surgery	37
■ Management and Board of Directors	42

# SynAct Pharma – In Brief

- SynAct Pharma is a clinical stage biotechnology company focused on resolving inflammation through melanocortin biology to treat inflammatory and autoimmune diseases
- Oral small molecule, AP1189, is currently in active Phase 2 development for rheumatoid arthritis (RA) and nephrotic syndrome (iMN)
- **Achieving communicated milestones:**
  - ✓ 1H22 – Listed on Nasdaq Stockholm Main Market
  - ✓ 2H22 – Resumed amended iMN P2a trial
  - ✓ 2H22 – Filed and opened US IND
  - ✓ 2H22 – Initiated Phase 2b (P2b) in early severe RA
  - ✓ 2H22 – Initiated Phase 2a/b in DMARD-IR RA under FDA IND
  - ✓ 1H23 – Completed acquisition of TXP Pharma
- **Three Phase 2 studies reading out in 2023:**
  - P2b in severe treatment naïve RA patients in combination with methotrexate (MTX)
  - Phase 2a (P2a) in RA patients experiencing an incomplete response to MTX (P2b protocol filed)
  - P2a in patients with nephrotic syndrome (iMN) experiencing severe proteinuria

# SynAct acquired TXP Pharma adding a portfolio of complimentary peptide-based melanocortin assets

## AP1189

Being developed as an

Once daily oral therapy for:

- Early severe RA (P2b)
- DMARD-IR RA (P2a/b)
- Membranous nephropathy (P2a)
- Virus induced respiratory insufficiency

## TXP Peptides

Being developed for:

- **TXP-11:** Intravenous administration for organ protection in major surgery
- Other pre-clinical peptides for inflammatory and orphan diseases

# SynAct Pharma – Pipeline overview

Asset	Indication	Pre-clinical	Phase I	Phase IIa	Phase IIb	Phase III	
AP1189	Rheumatoid Arthritis Severe treatment-naïve with MTX	Completed			Ongoing	Resolve Part B (Approved in IND)	
	Rheumatoid Arthritis DMARD-IR	Completed		Ongoing	Resolve Part B (Approved in IND)		
	Nephrotic syndrome (iMN)	Completed		Ongoing			
	Virus- Induced Respiratory Insufficiency	Completed					
TXP-11	Prevention of organ failures in complicated surgery	Ongoing					
Small Molecules and Peptides	Autoimmune and inflammatory conditions	Ongoing					




Completed



Ongoing



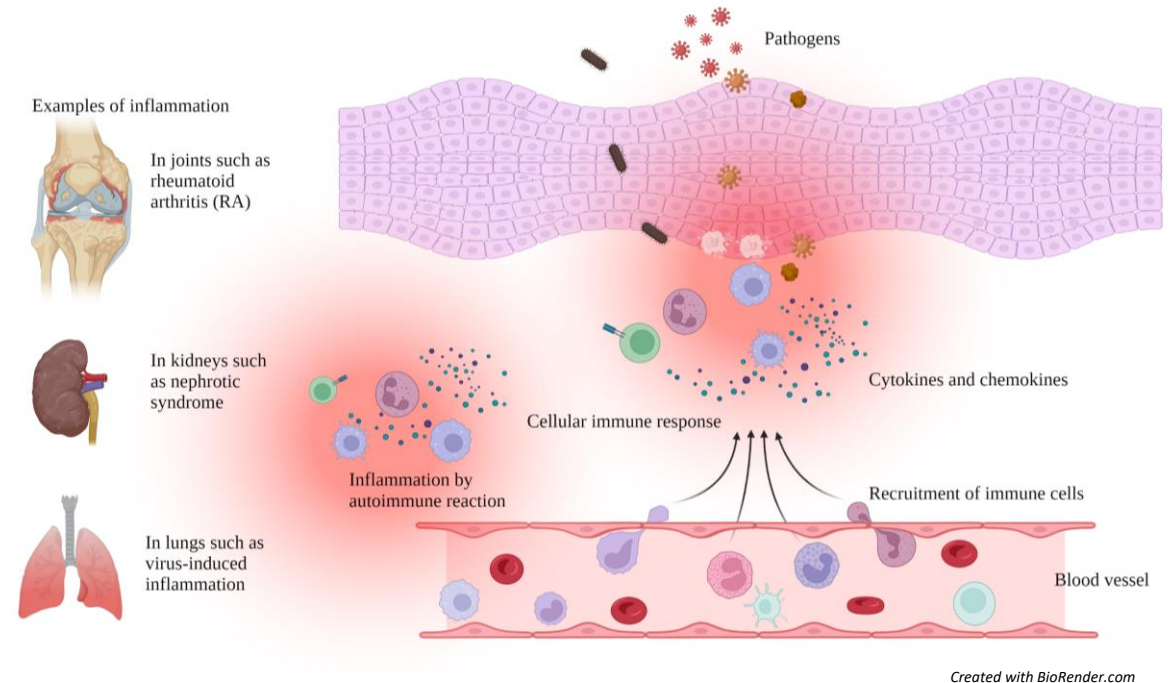
Resolve Part B  
(Approved in IND)



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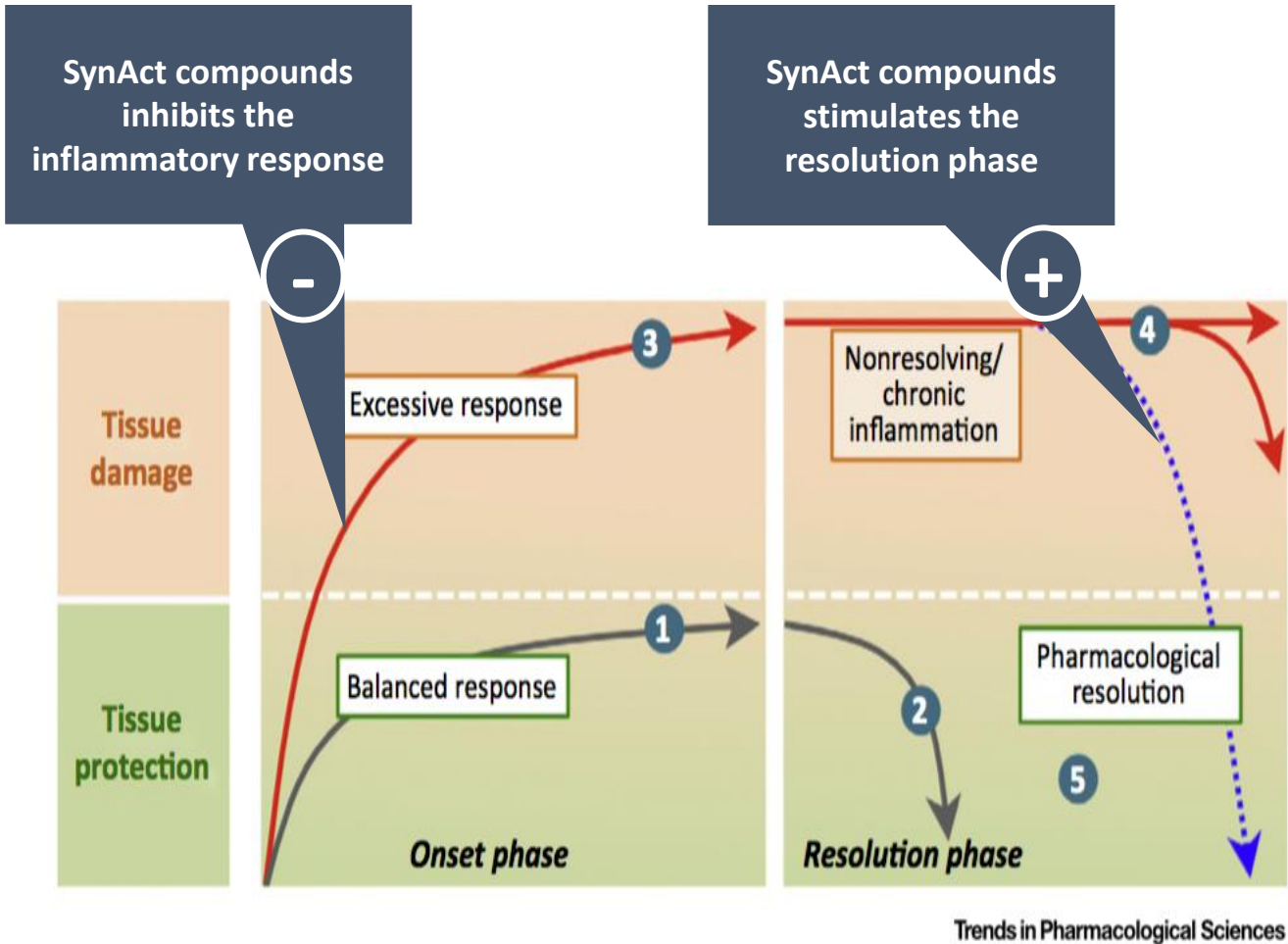
# What is inflammation?

- Inflammation is the immune system's way of responding to infections or injuries. Normally an inflammatory response is self-limiting. The immune system will "deactivate" itself and the inflammation will be resolved after the invading pathogen has been removed or the injury has begun to heal
- **However, in many cases, the inflammation can be excessive or chronic** and it can overwhelm the immune system's ability to resolve the inflammation. This can lead to pain, tissue destruction, and loss of function





# SynAct compounds provides anti-inflammatory and pro-resolving activity



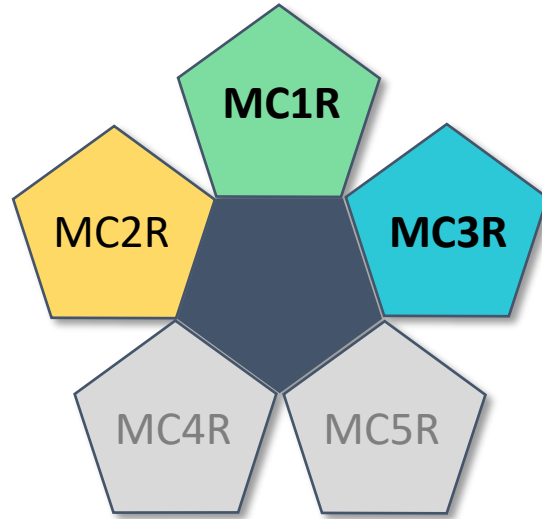
Trends in Pharmacological Sciences

## The inflammatory response

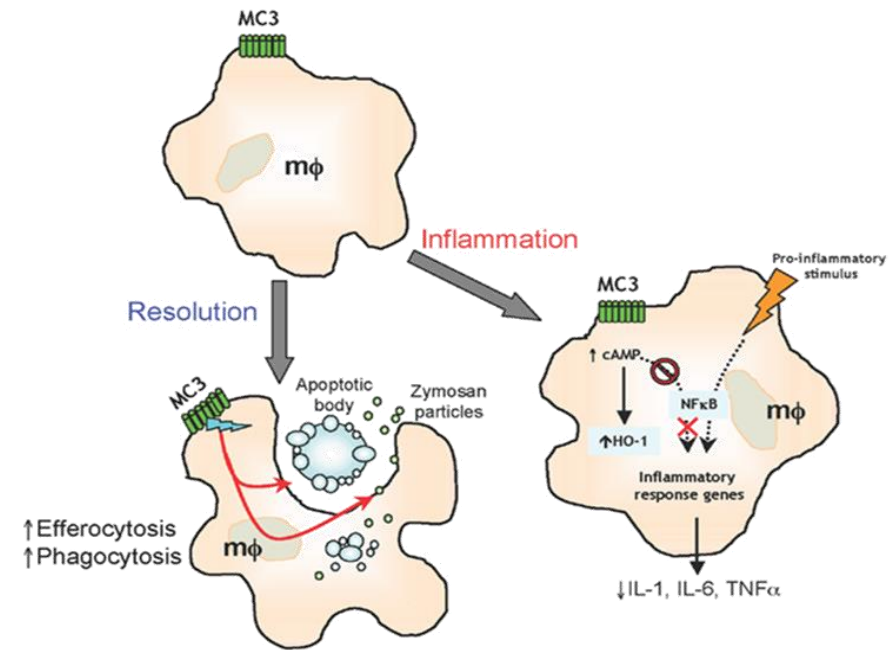
- 1 Inflammatory response effectively controlled in extent and time – protects tissues and limits damage
- 2 Pathways activated to safely terminate the inflammatory response and promote healing
- 3 Exaggerated response to inflammatory stimuli can have detrimental consequences and harm tissues
- 4 Failure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

Cartoon adapted from Perretti *et al. Trends Pharmacol Sci* 2015;36:737–55

# SynAct is developing selective melanocortin agonists with both anti-inflammatory and pro-inflammation resolution activity



Steroid dependent effects
 
 Targeted by AP1189 and TXP-11



- Selective stimulation of **melanocortin receptors 1 and 3 (MC1R and MC3R)** present on immune active cells promotes direct immunomodulatory effects
- **Neither AP1189 nor TXP-11 activates MC2R**, present in the adrenal glands, which causes the release of cortisol when stimulated and results in steroid side effects and tolerability issues

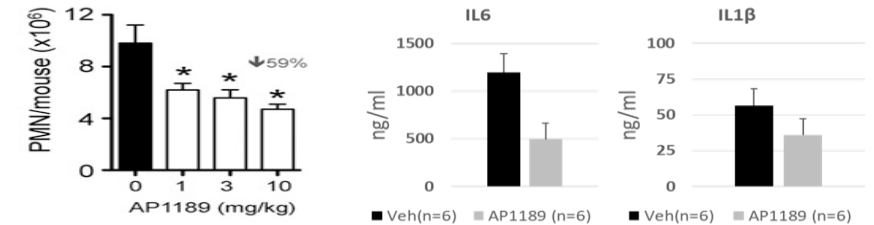
- AP1189 **exhibits anti-inflammatory activity** via MC1R and MC3R stimulation on targets cells – such as lowering the release of pro-inflammatory cytokines
- AP1189 **promotes pro-resolution pathways** following stimulation of MC1R and MC3R on targets cells – such as increasing efferocytosis in macrophages

ACTH: adrenocorticotrophic hormone; MCR: melanocortin receptor

# Lead Program AP1189 – A once-daily oral selective melanocortin agonist

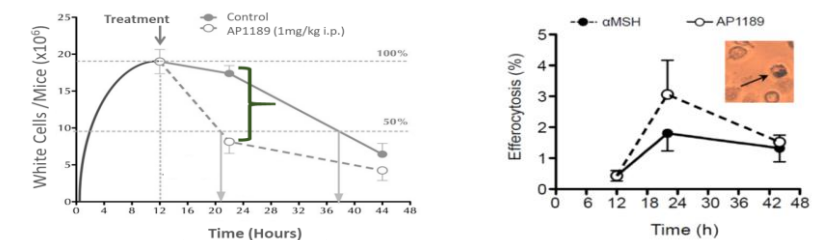
- AP1189 selectively stimulates MC1R and MC3R, the MCRs responsible for direct immunomodulatory effects
- Importantly AP1189 does not stimulate cortisol release that is associated with MC2R activation
  - Avoiding the immunosuppression that is associated with other MC therapies
  - Immunosuppression can be seen with most approved RA therapies
- AP1189 is also a biased agonist that selectively stimulates the ERK phosphorylation pathway and not the classical cAMP pathway that can be associated with hyper skin pigmentation

## Administration at disease induction in peritonitis<sup>1</sup>



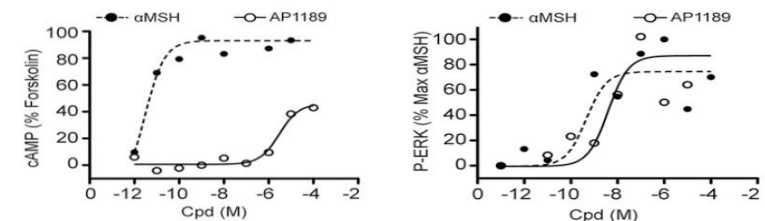
AP1189 inhibits of inflammatory responses

## Therapeutic treatment in peritonitis<sup>1</sup>



AP1189 promotes inflammatory resolution

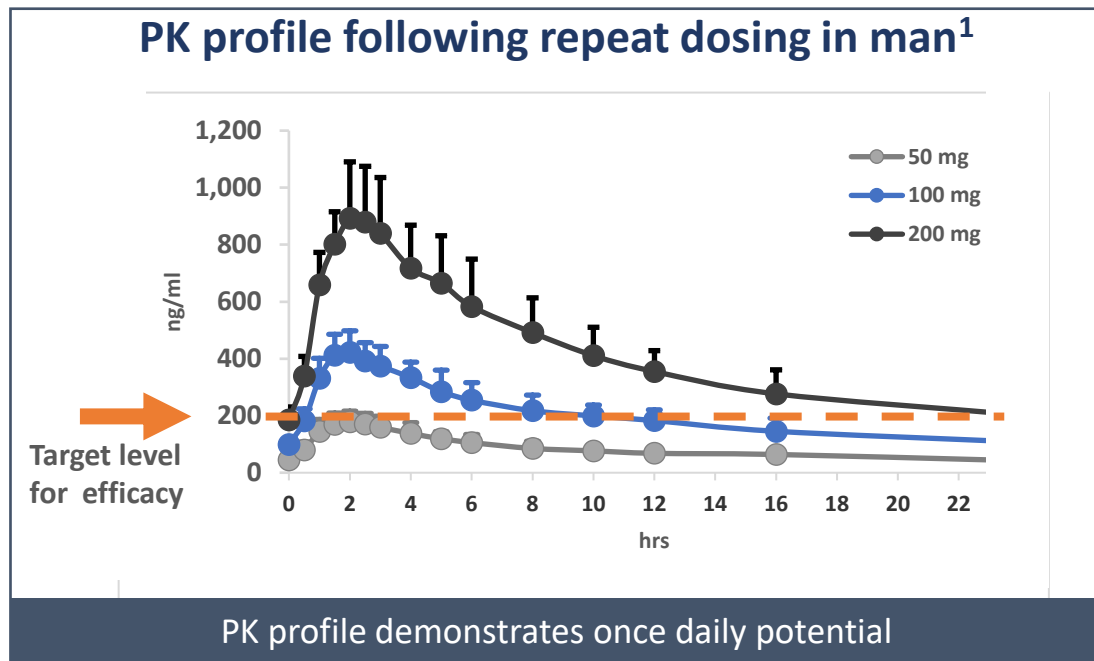
## MC1 receptor activation in transfected cells<sup>1</sup>



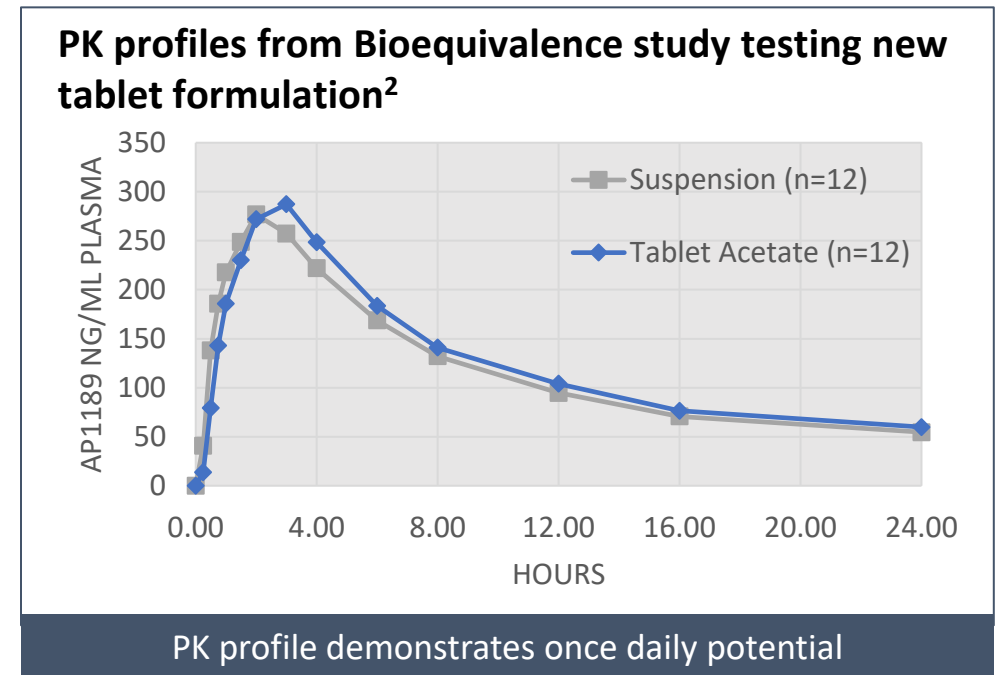
AP1189 selectively stimulates ERK pathway

# AP1189 was well tolerated in Phase 1 and Phase 2a studies with pharmacokinetic profile supporting once daily dosing

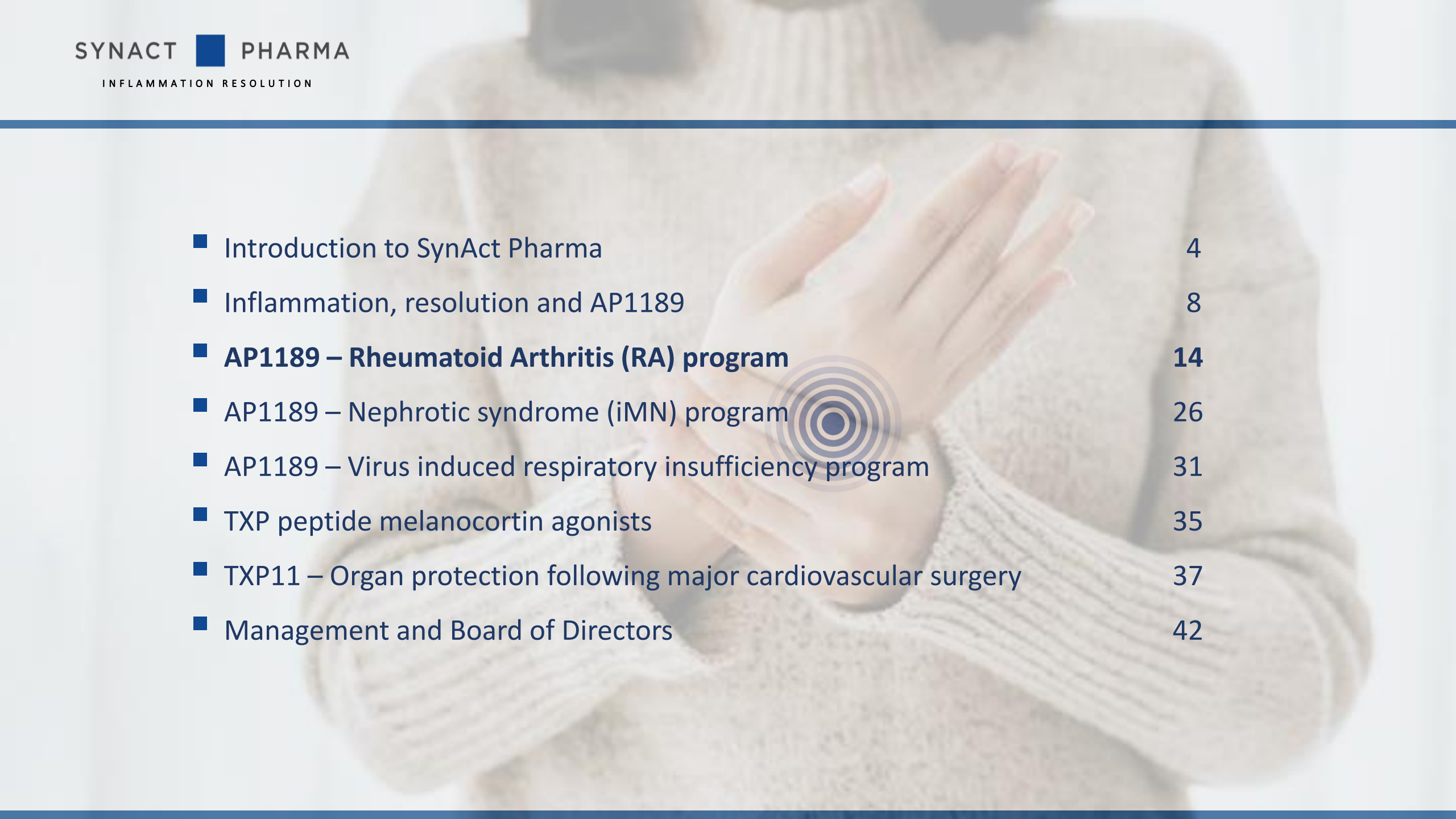
- Initial clinical development, Phase 1 and Phase 2a, performed with suspension for once daily oral administration was overall well tolerated, no signs of immunosuppression or dose limiting Adverse Events
- Novel immediate release tablet with excellent plasma profile developed and is being dosed in 3 ongoing Phase 2 studies



1. AP1189-CS001 study MAD study

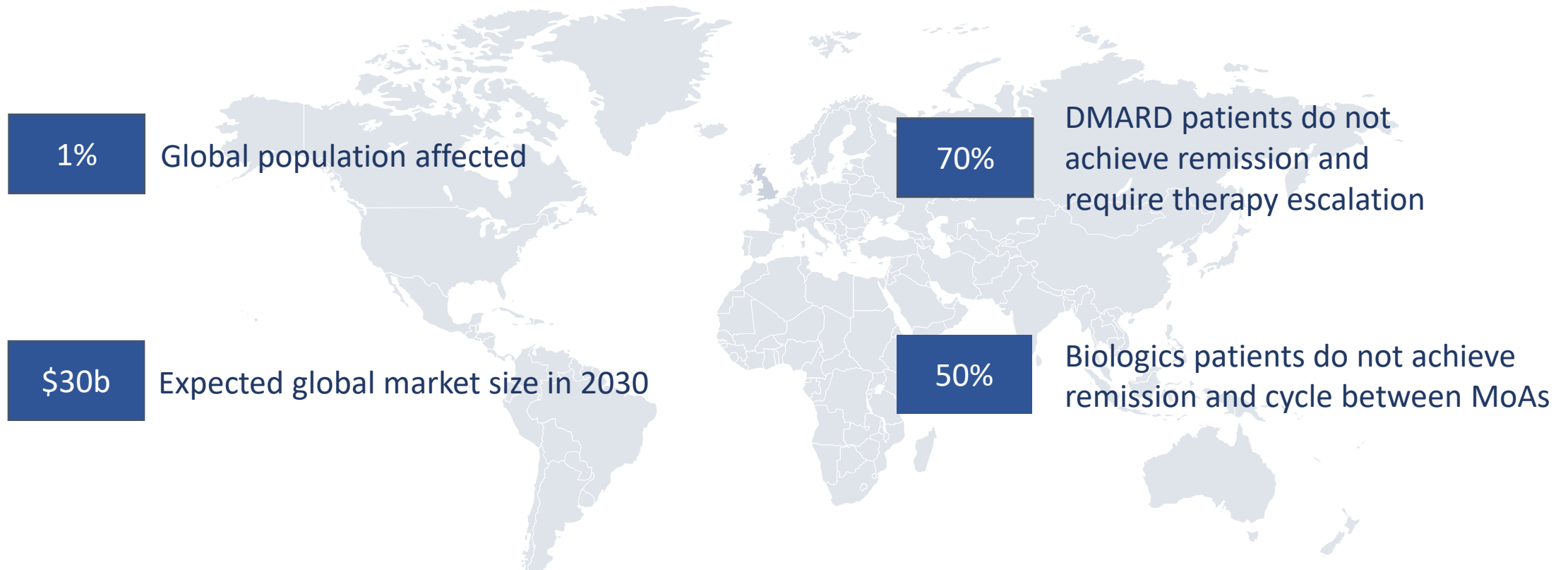


2. AP1189-CS004 bioequivalence study in male volunteers



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# RA affects about 1% of the global population, and while there are several classes of approved therapies remission can remain elusive



AP1189 could be well suited to address the unmet needs in RA

# RA is a large prevalent disease but also has a significant incident population

Figure 14: 8MM, Diagnosed Prevalent Cases of RA, N, Both Sexes, Ages ≥18 Years, 2019

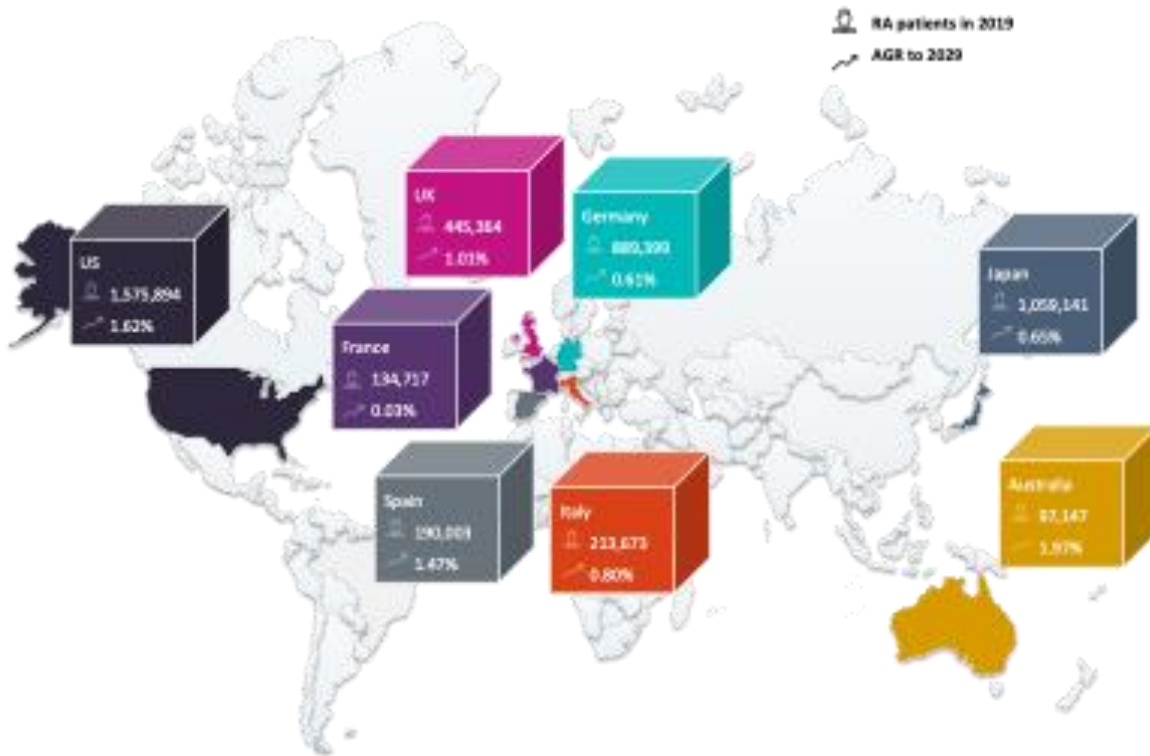
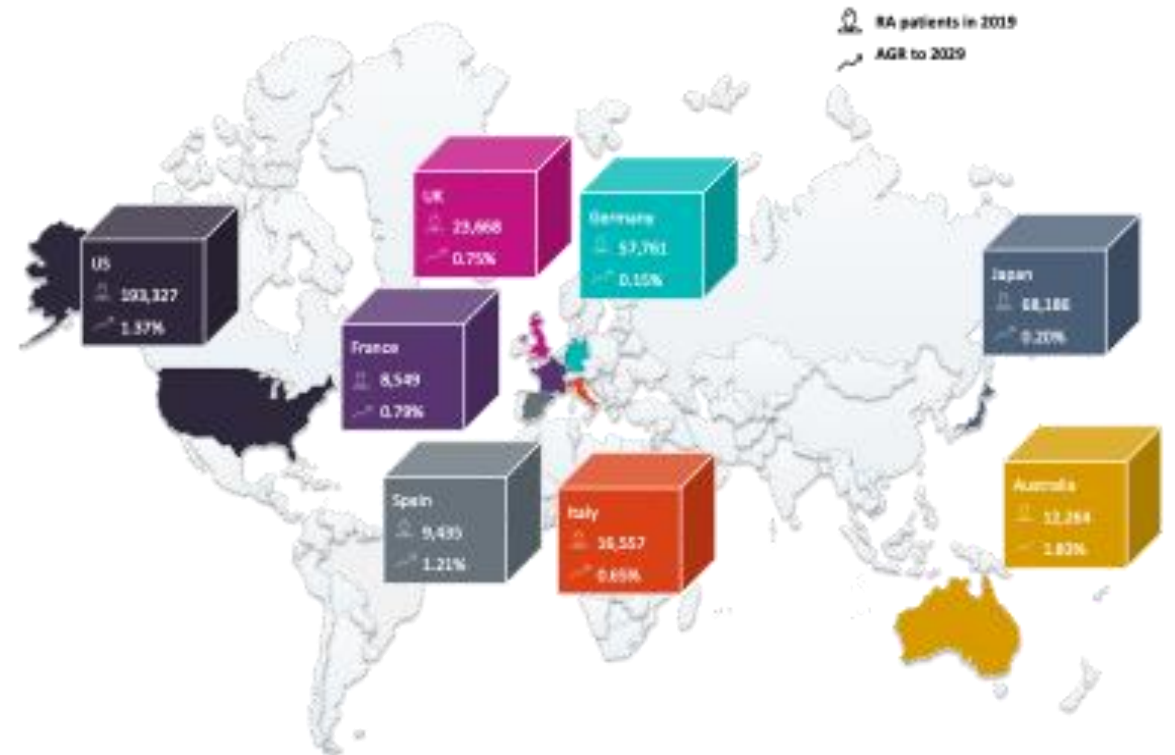


Figure 11: 8MM, Diagnosed Incident Cases of RA, N, Both Sexes, Ages ≥18 Years, 2019

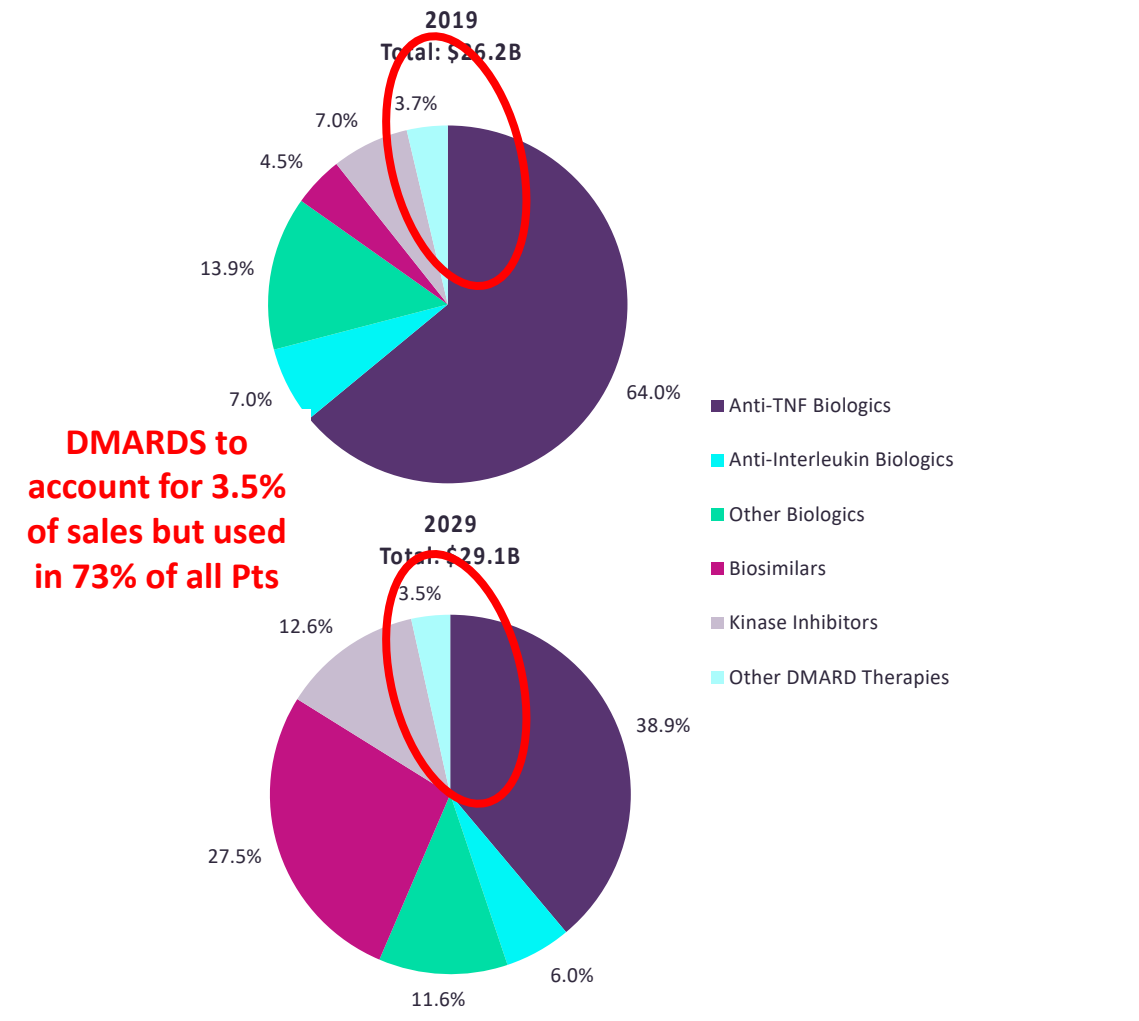


- Commercially, biologic market players are focused on a mix of patient and class share stealing and retention strategies both within and between classes – some biologic usage in naïve patients but limited
- In contrast, MTX and DMARDs are initiated in newly diagnosed Tx naïve patients and are retained for years

GlobalData Rheumatoid Arthritis: Global Drug Forecast and Market Analysis to 2029

# RA market drivers will change product mix amongst advanced therapies

Figure 31: Global (8MM) Sales Forecast for RA, by Class, in 2019 and 2029



- The RA market is expected to reach \$29B by 2029
- While sales are projected to increase, the product mix will likely undergo changes
- Biosimilars are gaining traction even in US with launch of 1<sup>st</sup> Humira biosimilar by February-23
- First Xeljanz generic entrant expected in 2025
- While biosimilars will make a market impact, the US impact may not be felt by consumers as a two-tiered pricing system exists that supports a higher price with steeper discounts
- Important to note that the vast majority of RA sales come from the ~40% of patients who are on an advanced therapy (a biologic or JAK inhibitor)



# RA market drivers will increase pricing pressure for advanced therapies

Table 34: Key Events Impacting Sales for RA in the US, 2019-2029

Year	Event	Level of Impact	Type of Impact
2019	Launch of rituximab biosimilars	Low	□
2019	Launch of AbbVie's Rinvoq	High	□ □ □
2022	Launch of R-Pharm's olokizumab	Low	□
2022	Patent expiry for Roche's Actemra (tocilizumab) and launch of biosimilars	Medium	□ □
2022	Launch of Remsima SC (infliximab biosimilar)	Low	□
2023	Patent/exclusivity expiration for AbbVie's Humira (adalimumab) and launch of biosimilars	High	□ □ □
2023	Launch of GSK's otilimab	Medium	□ □
2024	Patent/exclusivity expiry for UCB's Cimzia (certolizumab pegol) and launch of biosimilars	Low	□
2024	Patent/exclusivity expiry for J&J's Simponi (golimumab) and launch of biosimilars	Low	□
2025	Launch of Roche/Genentech's fenebrutinib	Low	□
2025	Patent/exclusivity expiry for Pfizer's Xeljanz (tofacitinib) and launch of generics	High	□ □ □
2026	Patent/exclusivity expiry for BMS' Orencia (abatacept) and launch of biosimilars	Medium	□ □
2028	Patent/exclusivity expiry for Amgen's Enbrel (etanercept) and launch of biosimilars	High	□ □ □
2029	Patent/exclusivity expiry for Sanofi's Kevzara sarilumab and launch of biosimilars	Low	□

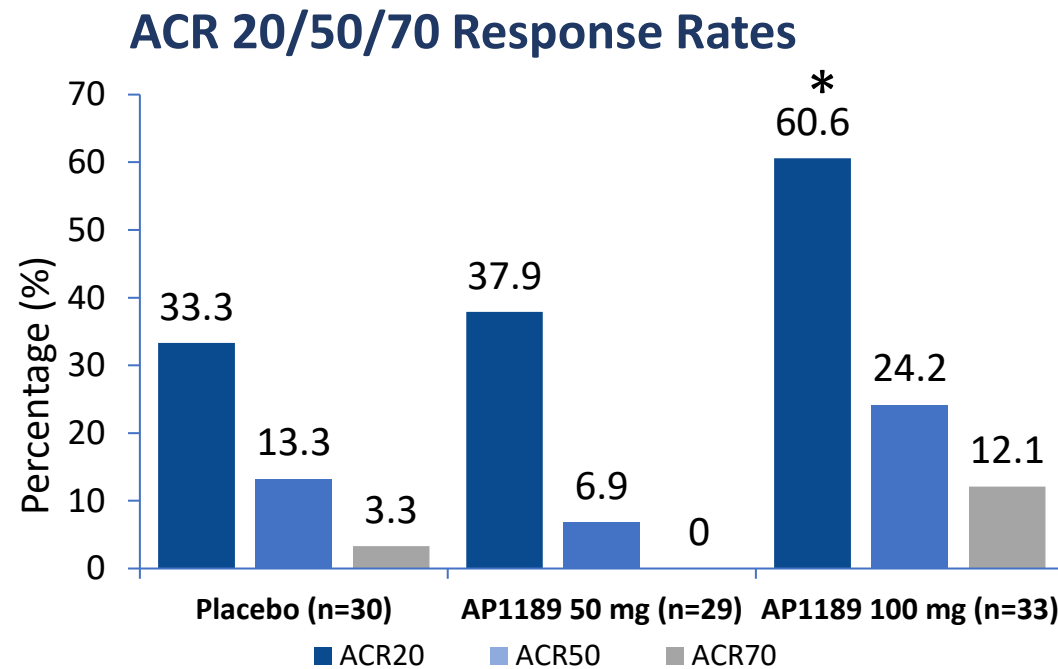
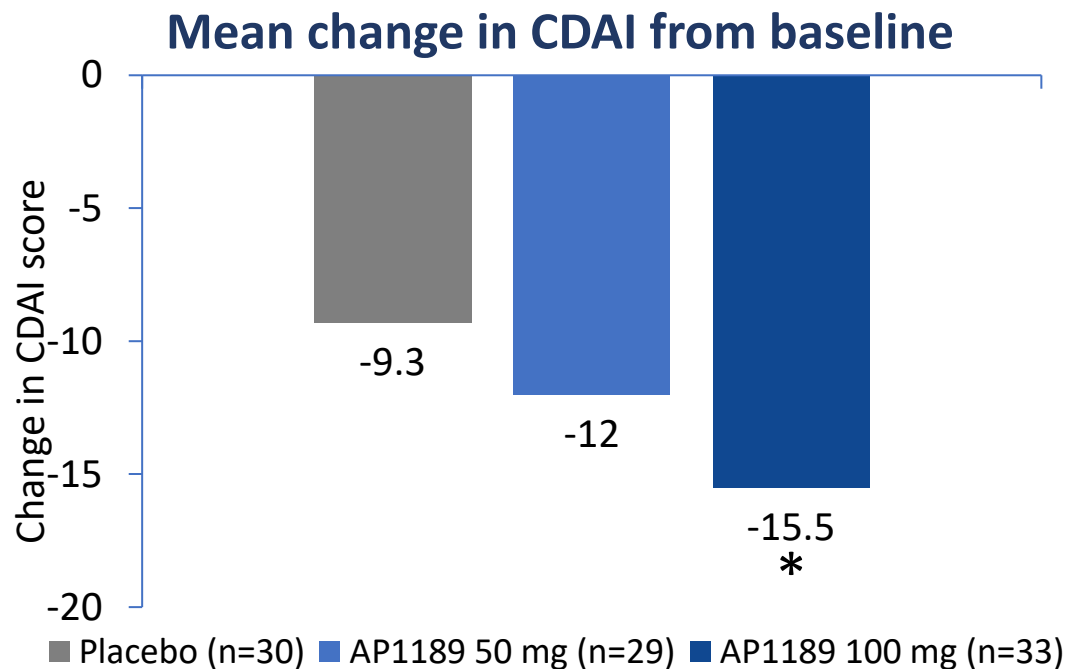
Source: GlobalData

© GlobalData

- The table from GlobalData illustrates the forecasted key events through 2029
- Market pressures from LoE and continued penetration of biosimilars will increase pricing pressure and slow market expansion
- The recent discontinuation of the otilimab program removes a key 'new MoA' therapy
- With biosimilars gaining momentum and generic Xeljanz expected in 2025, pricing pressure will be felt across all lines of therapy
- Differential positioning will be key to securing premium pricing for new treatment options

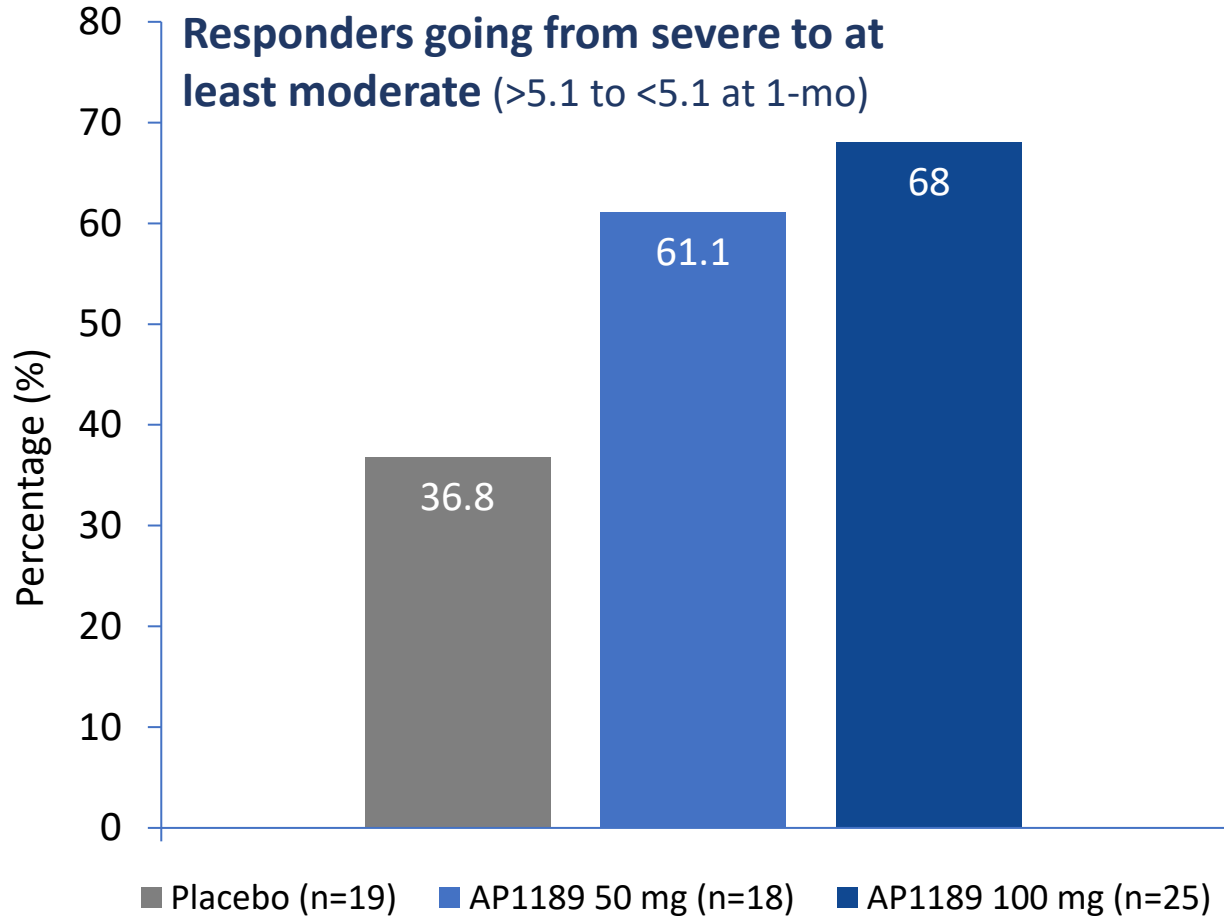
# AP1189 demonstrated significant treatment effects in patients with severe treatment-naïve RA in the 4-week BEGIN P2a clinical trial

Phase 2a study in treatment naïve RA patients with high disease activity (CDAI >22 at randomization) in combination with MTX with 4 weeks treatment

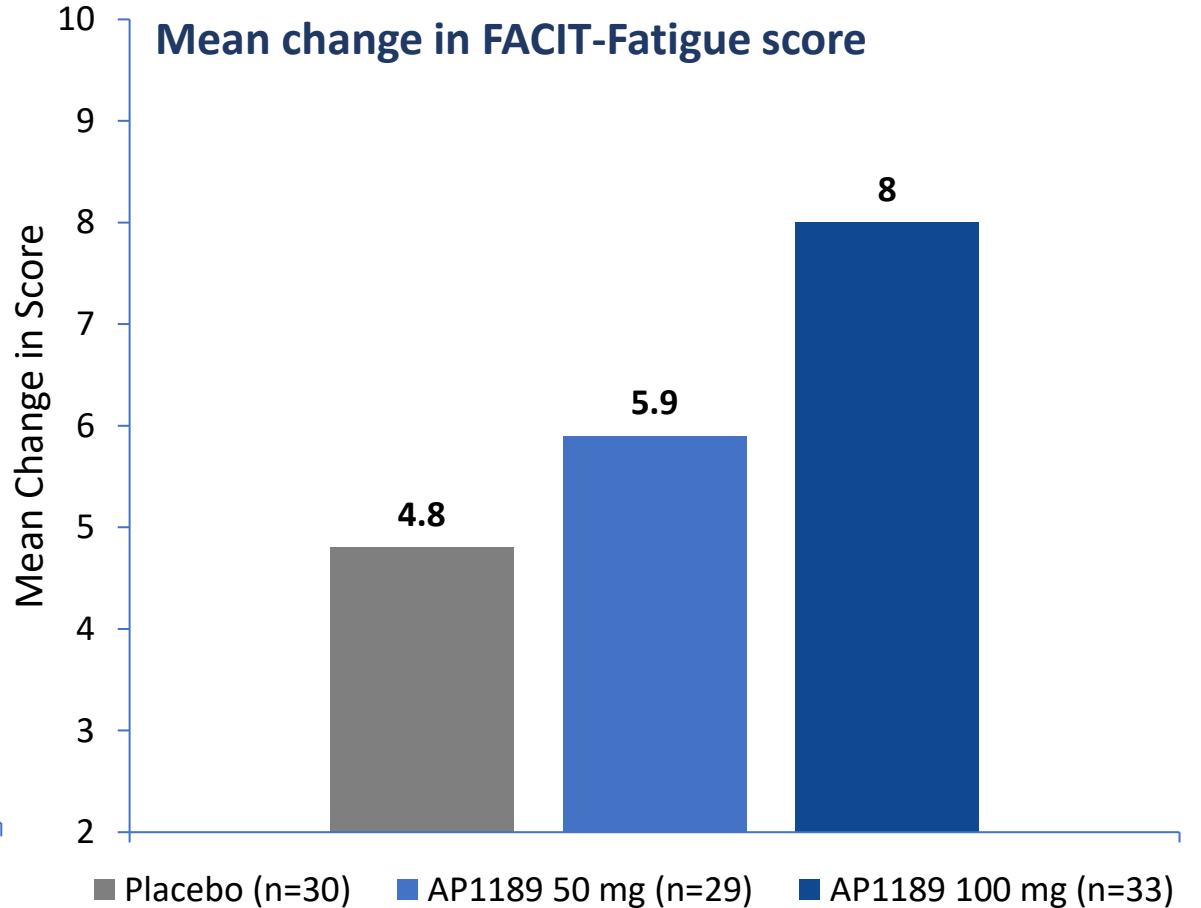


**Mean improvement in CDAI above the minimally important clinical difference (MCID)<sup>+</sup>  
Robust 1-Month ACR20/50/70 response rates for 100mg AP1189**

# Meaningful improvements were also seen in DAS28 (CRP) and FACIT-Fatigue Scores

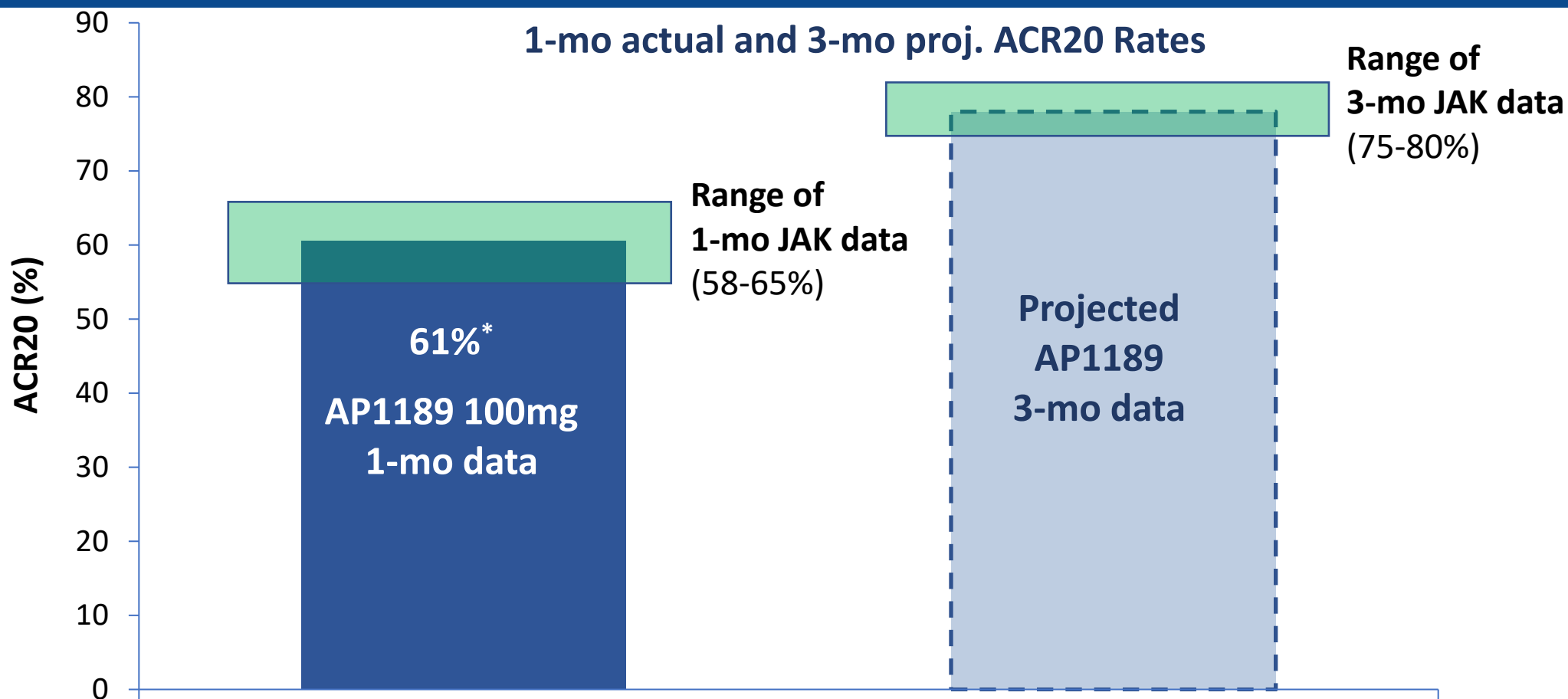


**Good effects seen with 100mg in patients with very active DAS28 (>5.1) at baseline**



**Mean change in 100mg group is 2x the minimal clinically important difference (MCID)<sup>+</sup>**

# 100mg AP1189 ACR20 scores are in the range of the JAK inhibitors in P3 MTX-Naïve trials - Response rates should increase over time with 3-mo dosing as seen with JAKs and biologics



**Efficacy in the range of to JAKs with potential for improved safety and tolerability**

\* = p<0.05 vs placebo

- 1) 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.

# The emerging AP1189 clinical profile supports continued RA development for patients where DMARD therapy is insufficient

## Emerging AP1189 Clinical profile

- **Once-Daily Oral Dosing** – new oral solid formulation ready for clinical use
- **Quick Onset of Action** – as early as days
- **Efficacy similar to JAKs** – at 1-mo
- **Safe and Well Tolerated** - no emerging AEs and no signs of immunosuppression
- **Steroid-Free MoA** – potential to be steroid sparing
- **Compatible with MTX** – no known or theoretical DMARD drug interactions or biologic agents

## DMARD-insufficient RA Positioning

### Severely Active Treatment Naïve:

- Severe or highly active disease activity is the dominating poor prognostic factor in all current treatment recommendations
- From 29% to 54% of treatment-naïve RA patients present with severe disease activity and tend to have a lower response to DMARDs including MTX<sup>2</sup>

### DMARD-IR:

- Up to 50% of 1<sup>st</sup> DMARD Tx will not achieve low disease activity and 70% will fail a 2<sup>nd</sup> DMARD Tx<sup>3</sup>
- Up to 22% of patients experience intolerance even with long-term usage<sup>4</sup>

**With DMARD-insufficient positioning, AP1189 has the potential to become a foundational therapy in RA**

1. Albrecht and Zink Arthritis Research & Therapy (2017) 19:68
2. Shpatz et al. IMAJ (2021) vol 23
3. Baganz et al. Seminars in Arthritis and Rheumatism 48 (2019) 976!982
4. Amaral et al. Advances in Rheumatology (2020) 60:43

# High volume US rheumatologists expressed a high degree of interest in AP1189 for DMARD-IR patients

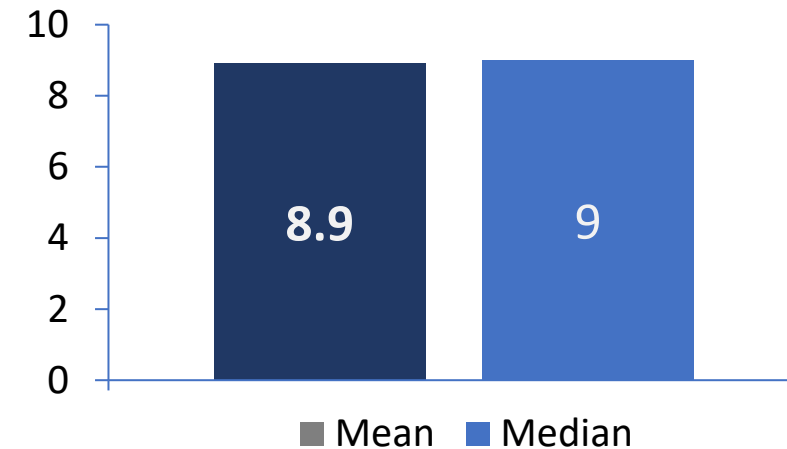
The combination of efficacy, safety, tolerability and oral convenience positions AP1189 well for DMARD-IR

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

SynAct conducted market research with high volume US Rheumatologists to evaluate the potential of AP1189 in DMARD-IR

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

US 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 upfront. 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. . .”*

GlobalData RA Primary Research Project December 2021; 10 1:1 interviews with US high volume rheumatologists in December 2021  
Y-axis is Intent to use of a 1-10 scale

# AP1189 has the potential to become a foundational therapy in and beyond RA

	Product	External or Internal	Black Boxed Warnings	Indications
1	Humira	External	<ul style="list-style-type: none"> <li>• Serious Infections</li> <li>• Malignancy</li> </ul>	9
2	Enbrel	External	<ul style="list-style-type: none"> <li>• Serious Infections</li> <li>• Malignancy</li> </ul>	5
3	Orencia	Internal	<ul style="list-style-type: none"> <li>• None</li> </ul>	4
4	Actemra	External	<ul style="list-style-type: none"> <li>• Serious Infections</li> </ul>	6
5	Simponi	External	<ul style="list-style-type: none"> <li>• Serious Infections</li> <li>• Malignancy</li> </ul>	4
6	Rinvoq	Internal	<ul style="list-style-type: none"> <li>• Serious Infections</li> <li>• Malignancy</li> <li>• MACE</li> <li>• Thrombosis</li> </ul>	6
7	Xeljanz	External	<ul style="list-style-type: none"> <li>• Serious Infections</li> <li>• Malignancy</li> <li>• MACE</li> <li>• Thrombosis</li> </ul>	5
8	Remicade	External	<ul style="list-style-type: none"> <li>• Serious Infections</li> <li>• Malignancy</li> </ul>	8
9	Cimzia	Internal	<ul style="list-style-type: none"> <li>• Serious Infections</li> <li>• Malignancy</li> </ul>	6
10	Olumiant	External	<ul style="list-style-type: none"> <li>• Serious Infections</li> <li>• Malignancy</li> <li>• MACE</li> <li>• Thrombosis</li> </ul>	3

- **7/10 of the top RA brands were originally external programs that were acquired through business development highlighting the importance of external innovation**
- **Despite black boxed safety warnings for 9/10 of these brands each has been approved for multiple indications**
- **AP1189 has the potential with DMARD-insufficient positioning to become a foundational therapy in RA – a multi billion-dollar opportunity**
- **AP1189 also has broad potential to treat numerous inflammatory diseases where an effective safe, and well tolerated therapy can help address the limitations of first-line therapies**
- **Similar DMARD-insufficient positions exist in additional inflammatory conditions like systemic lupus, psoriatic arthritis, ankylosing spondylitis and atopic dermatitis – each with significant revenue potential**

# SynAct is currently conducting 2 additional P2 RA studies with AP1189 with data readouts in 2023

EXPAND – 3-mo P2b trial in severe treatment-naïve RA patients		H2-22	H1-23	H2-23
<b>Patients</b>	<ul style="list-style-type: none"> <li>Severe treatment-naïve (CDAI&gt;22) min 6 s/t joints, RF(+)</li> </ul>			
<b>Groups &amp; Size</b>	<ul style="list-style-type: none"> <li>2 groups of 60: 1) 100mg* AP1189, 2) Placebo</li> </ul>	Q3 Initiation		Data Readout
<b>Dosing</b>	<ul style="list-style-type: none"> <li>12 weeks of once-daily AP1189 or placebo + MTX</li> </ul>			
<b>MRI -Study</b>	<ul style="list-style-type: none"> <li>MRI evaluation of inflammation (n=40)</li> </ul>			

RESOLVE – 1/3-mo P2a/b trial in MTX incomplete responders		H2-22	H1-23	H2-23	2024	2025
<b>Patients</b>	<ul style="list-style-type: none"> <li>Patients experiencing mod/severe disease after &gt;3mo MTX</li> </ul>	Q4 Initiation		Data Readout		
<b>Groups &amp; Size</b>	<ul style="list-style-type: none"> <li>P2a- 60, 80 or 100mg AP1189+ and placebo, n=30/group</li> <li>P2b- Up to 3 AP1189 groups and placebo, n=75/group</li> </ul>		P2a			P2b
<b>Dosing</b>	<ul style="list-style-type: none"> <li>P2a- 4 weeks of once-daily AP1189 or placebo + MTX</li> <li>P2b- 12 weeks of once-daily AP1189 or placebo + MTX</li> </ul>					
<b>MRI Study- 2b</b>	<ul style="list-style-type: none"> <li>MRI evaluation of inflammation (n=20/group)</li> </ul>					

\*Corresponds to 125 mg of suspension formulation used in the BEGIN study

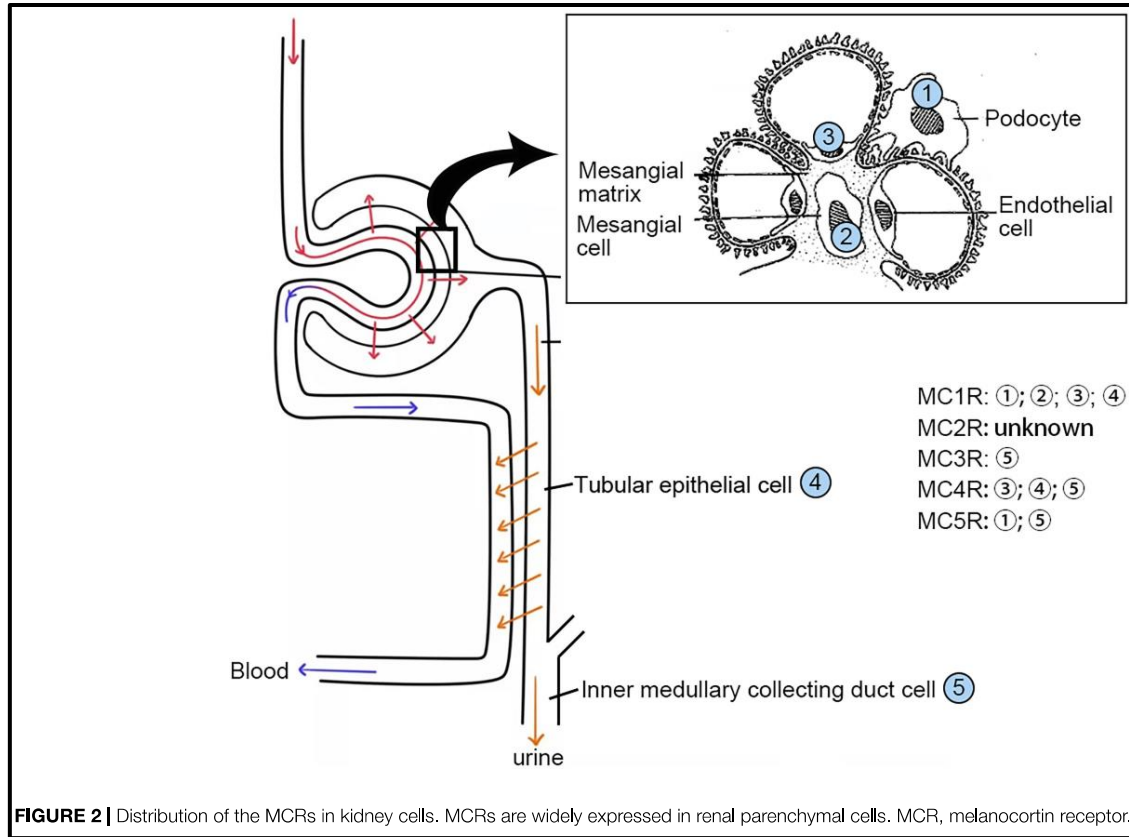
+ Corresponds to 75, 100 and 125 mg of suspension formulation used in the BEGIN study



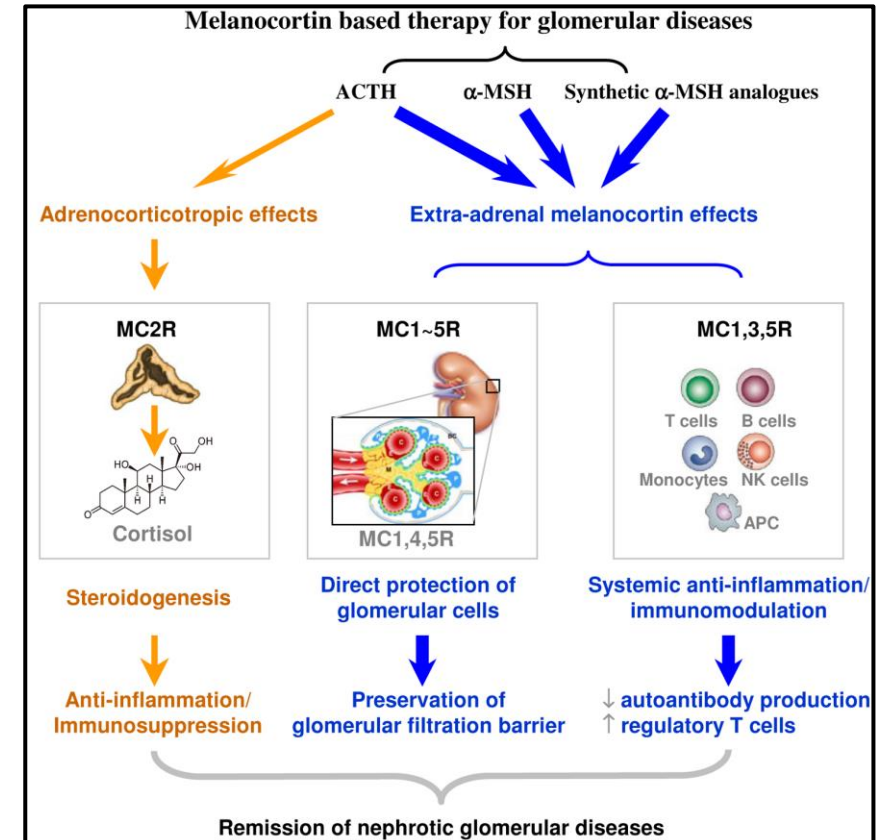
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# MCRs are widely distributed in the kidney and provide both direct protective actions as well as provide immunomodulation and anti-inflammatory benefits

## MCRs are widely expressed in renal parenchymal cells<sup>1</sup>

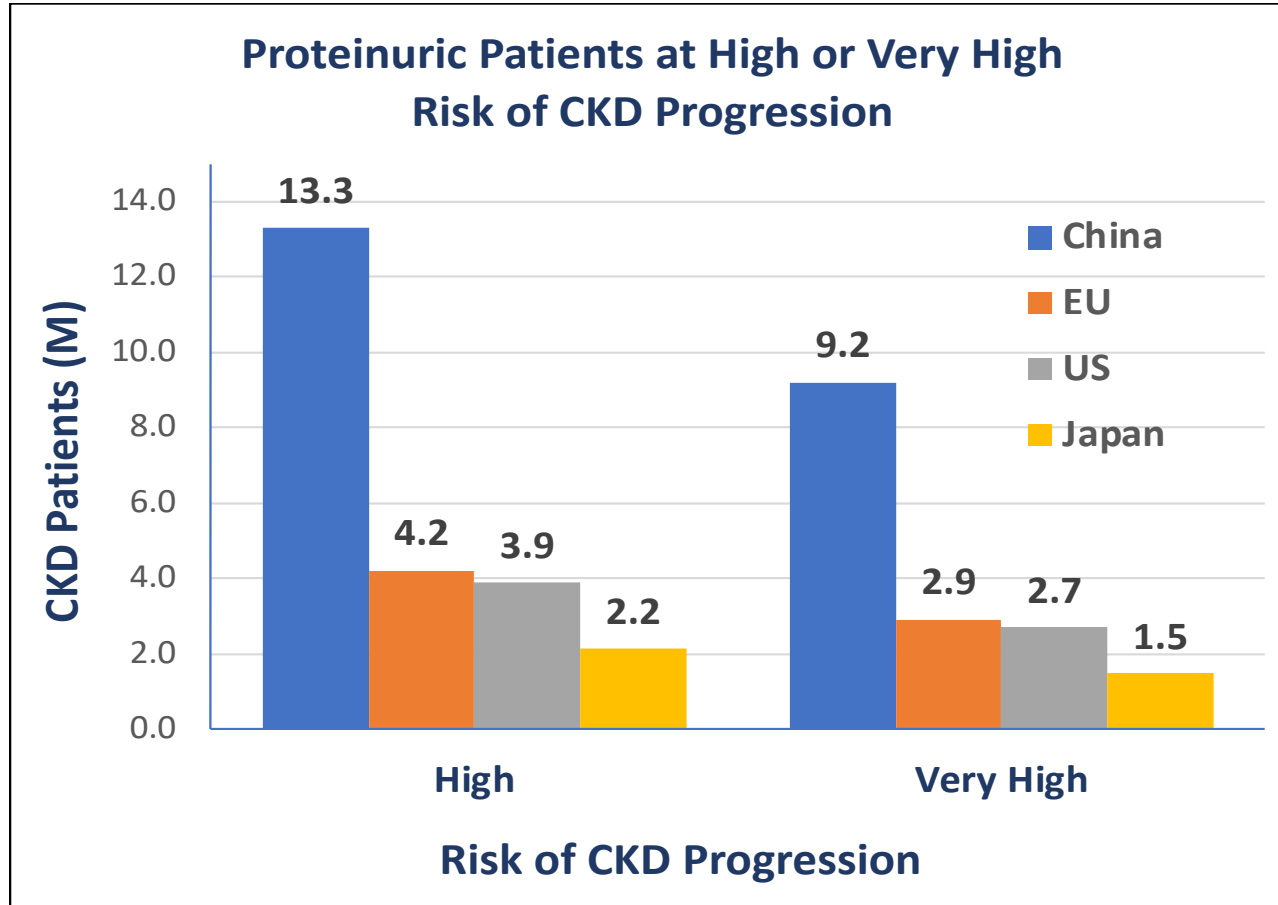


## Melanocortins can both directly protect Glomerular cells and provide immunomodulation<sup>2</sup>



1. Chang et. Al., 2021 Front. Physiol. 12:651236; 2. Gong, Adv Chronic Kidney Dis. 2014 March ; 21(2): 134–151

# Given the impact upon kidney disease progression, proteinuria is a significant global health issue



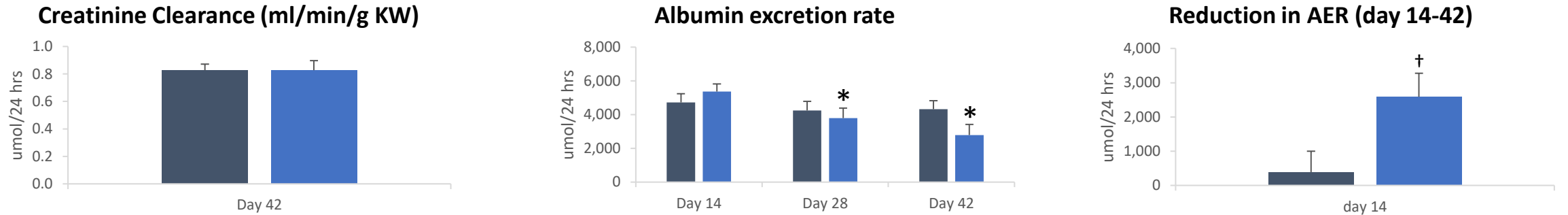
- There are an estimated 40M CKD patients with moderate or severe proteinuria who are at a high or very high risk of disease progression across the US, Western EU, Japan and China
- ~24M of these are at a high risk of progression and 16M are at a very high risk of progression
- In the US, the prevalence of albuminuria is:
  - 28.8% in persons with diabetes,
  - 16.0% in those with hypertension, and
  - 5.1% in those without diabetes, hypertension, or cardiovascular disease

United States Renal Data System. 2020 USRDS Annual Data Report: Epidemiology of kidney disease in the United States. <https://adr.usrds.org/2020>  
GBD CKDC Lancet 2020; 395: 709–33

# AP1189 is effective in pre-clinical nephritis models

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

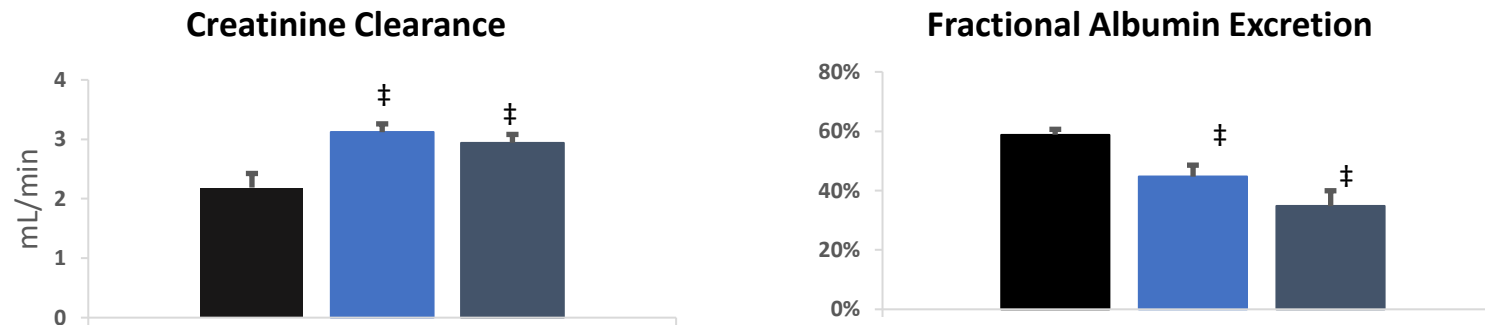
## Membranous nephropathy rat model (passive Heymann Nephritis)



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)

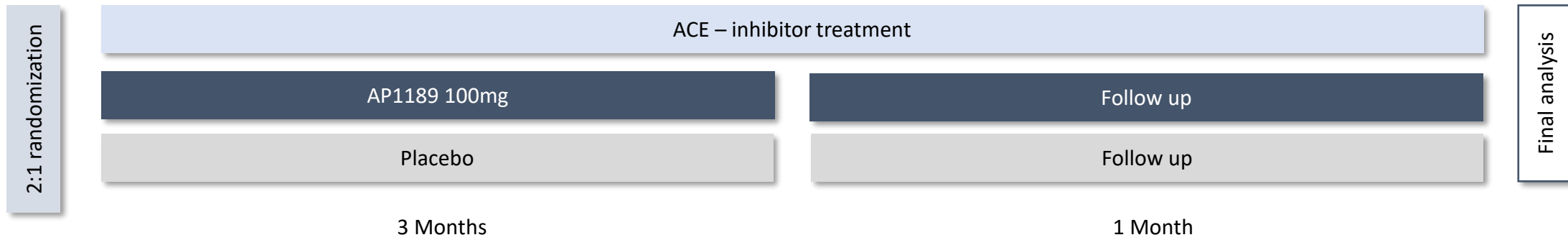
## AP1189 vs ACTH in a model of Nephrotic Syndrome



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

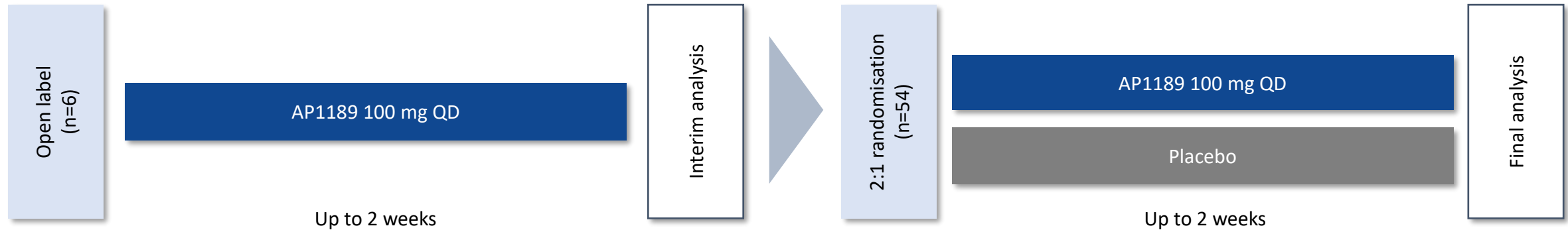
# Ongoing study: CS-003 study – 12 weeks explorative Phase 2a trial in idiopathic membranous nephropathy (iMN) with severe proteinuria



- Dosing is ongoing following approval of major amendment changing from suspension to tablet and dosing extended to 12 weeks.
- The trial resumed in H2 2022 with topline data expected late in 2023

■ Introduction to SynAct Pharma	4
■ Inflammation, resolution and AP1189	8
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■ Management and Board of Directors	42

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



## Key inclusion criteria

- Positive COVID-19 infection
- Need for supplemental oxygen\*

## 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  $\geq 93\%$  determined by pulse oximetry in the patient on ambient air for a minimum of 30 minutes

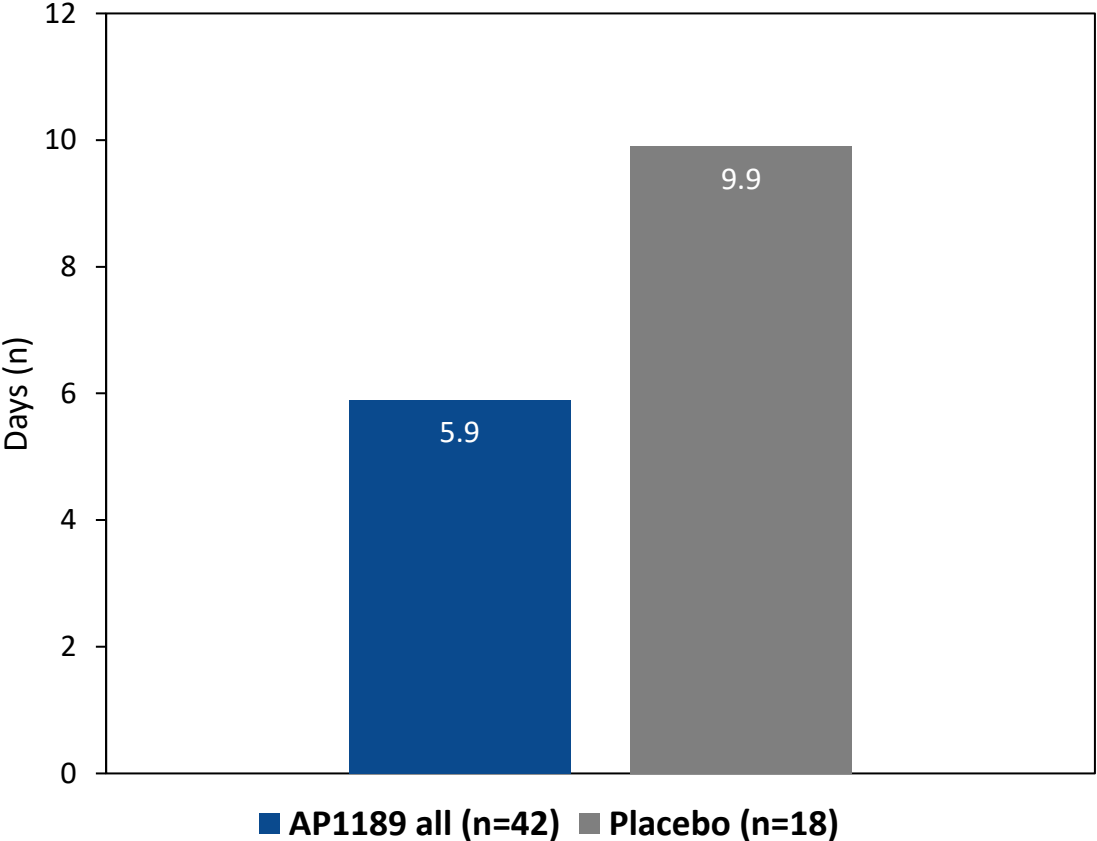
## Key secondary endpoints

- Rate of ICU admission during the treatment period
- Proportion of patients who go to mechanical ventilation at any time during hospitalization
- Proportion 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

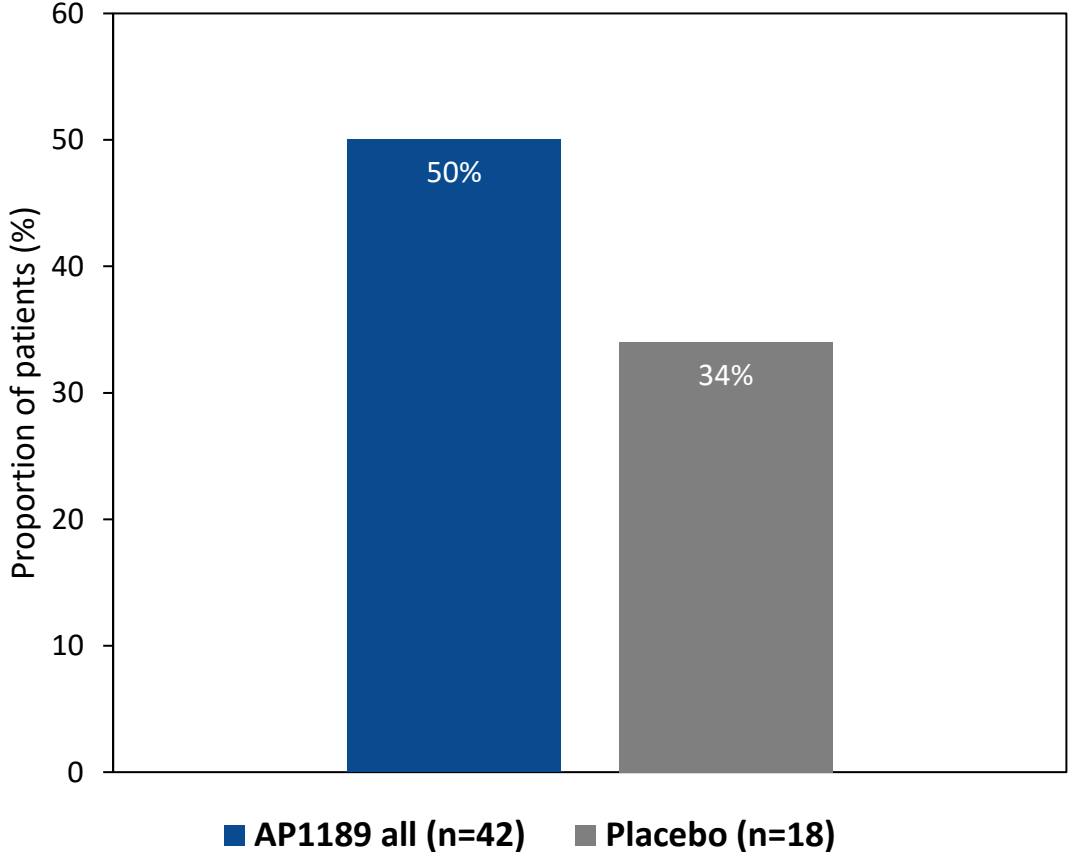
\*Defined as either SpO<sub>2</sub> <93% without supportive oxygen treatment or PaO<sub>2</sub>/FiO<sub>2</sub> <300 mmHg despite supportive oxygen treatment  
COVID-19, coronavirus 2019; FiO<sub>2</sub>, fraction of inspired oxygen; ICU, intensive care unit; PaO<sub>2</sub>, oxygen partial pressure; QD, once daily; SpO<sub>2</sub>, oxygen saturation

# RESOVIR-1: Treatment with AP1189 resulted in a greater proportion of patients achieving respiratory recovery quicker than placebo

### Average respiratory recovery time\*



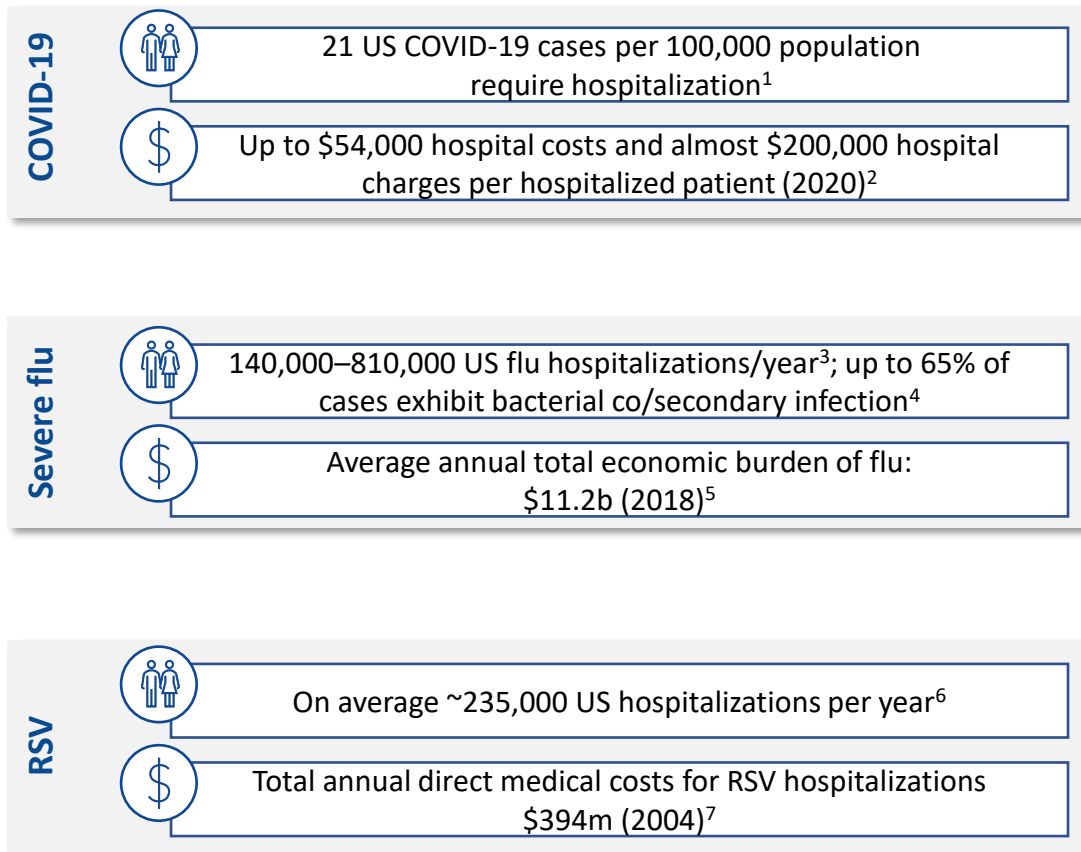
### Cumulative respiratory recovery by Day 4\*



\*Normal saturation without oxygen supplementation. "AP1189 all" includes the 6 open-label safety run-in patients



# AP1189's broad anti-inflammatory and pro-resolution mechanism can target viral induced respiratory insufficiency in and beyond COVID-19



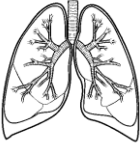


**Respiratory  
insufficiency, potentially  
developing into ARDS**

ARDS, acute respiratory distress syndrome; COVID-19, coronavirus disease 2019; RSV, respiratory syncytial virus  
1. [https://gis.cdc.gov/grasp/COVIDNet/COVID19\\_3.html](https://gis.cdc.gov/grasp/COVIDNet/COVID19_3.html); 2. Fusco *et al. J Med Econ* 2021;24:308–17; 3. <https://www.cdc.gov/flu/about/burden/index.html>; 4. Morris *et al. Front Microbiol* 2017;8:1041;  
5. Putri *et al. Vaccine* 2018;36:3960–6; 6. <https://www.cdc.gov/rsv/research/us-surveillance.html>; 7. Paramore *et al. Pharmacoeconomics* 2004;22:275–84

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# Peptides to Target High Unmet Needs and High Value Opportunities

Therapeutic Area	Evidence for Targeting With Melanocortin agonists	Development Strategy
 <p><b>Critical Care</b></p>	<ul style="list-style-type: none"> <li>▪ <math>\alpha</math>MSH has demonstrated organ protective effects in several models of systemic inflammation</li> <li>▪ An <math>\alpha</math>MSH analogs demonstrated activity in preventing the need for RRT in CABG surgery patients</li> <li>▪ Wealth of animal modelling data on <math>\alpha</math>MSH and analogs</li> </ul>	<ul style="list-style-type: none"> <li>▪ Short-term dosing, IV administration and ability for multiple daily doses provide quick straightforward path to clinic</li> <li>▪ Ability to target multiple organs/systems including pulmonary, cardiac and renal</li> </ul>
 <p><b>Rheumatology</b></p>	<ul style="list-style-type: none"> <li>▪ Complete melanocortin system is expressed in joints</li> <li>▪ Demonstrated Acthar efficacy in RA, PSA, lupus, ankylosing spondylitis and myositis</li> <li>▪ MC1R and particularly MC3R are believed to be the key MC receptors in the osteoarticular system</li> </ul>	<ul style="list-style-type: none"> <li>▪ Numerous large and orphan diseases shown to be responsive to melanocortins are treated by rheumatologists</li> <li>▪ Diseases are addressable with subcutaneous administration</li> </ul>
 <p><b>Ophthalmology</b></p>	<ul style="list-style-type: none"> <li>▪ <math>\alpha</math>MSH is constitutively expressed in eye and has immunomodulating effects on retinal cells</li> <li>▪ Melanocortin agonists demonstrated efficacy in refractory uveitis</li> <li>▪ Positive P2 data form competing technology in dry-eye disease (DED)</li> </ul>	<ul style="list-style-type: none"> <li>▪ Large disease conditions like dry eye disease are accessible via eye drops - quicker path to clinic</li> <li>▪ Both orphan (non-infectious uveitis) and large (AMD) diseases can be targeted with SC</li> </ul>

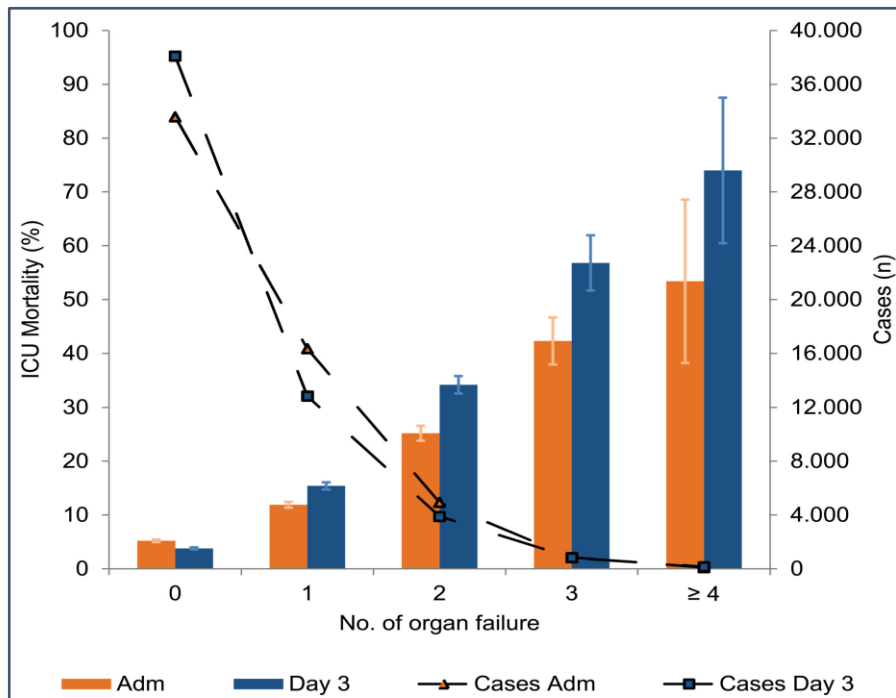
May establish collaborative efforts in additional therapeutic areas like pulmonary and dermatology

■ Introduction to SynAct Pharma	4
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# Postoperative Organ Dysfunction and Failure is a Significant Source of In-Hospital Mortality and Healthcare System Cost

Postoperative Organ Dysfunction/Failure and Associated In-Hospital Mortality From a German National ICU Registry				
Surgery	Status	Pulmonary	Cardiac	Renal
Scheduled	Dysfunction	83%	53%	30%
	Failure	12%	40%	5%
Unscheduled	Dysfunction	85%	56%	36%
	Failure	19%	38%	8%

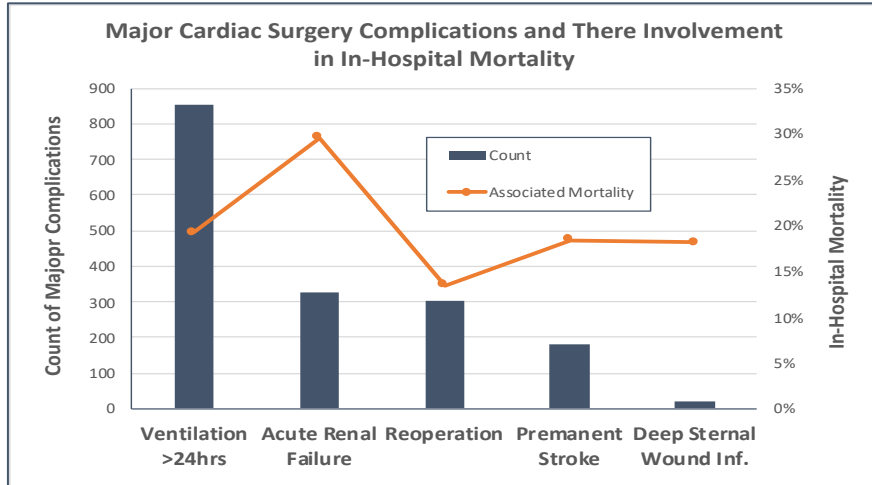


## Postoperative Organ Dysfunction and Failure

- Organ dysfunction and failure are common surgical complications<sup>1</sup>
- The three primary organs/systems involved in perioperative complications include the pulmonary cardiac and renal systems
- In-hospital mortality from surgical-admissions to the ICU was shown to increase substantially with the number of impaired organs (SOFA Score)
- For postsurgical patients the risk of in-hospital mortality was highest for liver, renal and pulmonary with odds ratios of ~3.1, 2.7 and 2.3 respectively in patients with an ICU LoS > 5 days

<sup>1</sup> Bingold, et al. (2015) Individual Organ Failure and Concomitant Risk of Mortality Differs According to the Type of Admission to ICU. PLoS ONE 10(8); <sup>2</sup>Figure from and data table adapted from same

# TXP-11: Cardiac Surgery in particular is associated with Major Postoperative Complications and High Rates of Organ Failure



## Major Surgical Complications Associated With Cardiac Surgery<sup>1</sup>

- Cardiac surgery is associated with 5 major surgical complications as described by the Society of Thoracic Surgeons
- In a recent review published in 2020 the rate of major complications was seen to be 17% at a major US surgical center
- In-hospital mortality highly associated with multiple complications and ranged from 8% for a single complication to 52% for 3+ complications
- Any incidence of renal failure in combination with any other complication was associated with the highest level of associated mortality of 30%

## Postoperative Organ Failure After Cardiac Surgery<sup>2,3,4,5</sup>

Organ Complication	Postoperative Rate
AKI	Up to 50%
AF	20-80%
ARDS	Up to 20%
Stroke	Up to 5%

<sup>1</sup> Seese, et al., Ann Thorac Surg 2020;110:128-35; <sup>2</sup> Hobson et al., Crit Care Clin 31 (2015) 705-723; <sup>3</sup> Bessissow et al., J Thromb Haemost 2015; 13 (Suppl. 1): S304-S12; <sup>4</sup> Su et al., Medicine (2019) 98:29; <sup>5</sup> Sultan et al., Ann Thorac Surg 2020;110:448-56

# TXP-11: Use in On-Pump Cardiac Surgery Presents a Significant Opportunity With Room For Expansion into Transplant and Major Abdominal Surgery

Estimated 2021 On-Pump Procedures <sup>1</sup>		
	CABG	Valve
US	364,499	462,378
EU5M	186,530	81,885
APAC	98,430	49,509
<b>Total</b>	<b>649,459</b>	<b>593,772</b>

## On-Pump cardiac Surgeries are Growing in US and EU<sup>1</sup>

- There were more than 350K and 450K on-pump CABG and cardiac valve replacement (CVR) surgeries respectively in the US in 2021
- In the US and EU, on-pump CABG procedures are forecasted to grow at 3+% and CVR procedures at 8+% in the US and 1% in the EU
- Despite the possibility to conduct off-pump procedures and endovascular procedures the number of on-pump interventions will remain high

## Attractive Commercial Opportunity

- Even at relatively low penetration rates, on-pump cardiac surgery represents a commercially viable opportunity with significant expected pharmacoeconomic savings
- Market research indicated a high intent to use such a MC agonist in 3 out of 4 high-risk patients
- Additional organ preservation opportunities exist within transplant (on-pump surgeries - heart, lung, heart-lung, liver) and major abdominal surgery

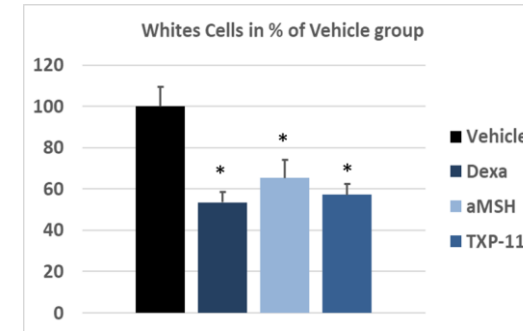
<sup>1</sup> Global Data "Cardiac Surgery Procedures Outlook Outlook to 2025" ; <sup>2</sup> Assessment and Data on file

# TXP-11 is advancing to Phase 1 clinical development in H1 2024 – Targeting organ dysfunction following major CV Surgery

## TXP-11

- Lead candidate in novel class of melanocortin receptor agonists with increased stability and efficacy compared to native melanocortins
- Peptide designed by use of IP-protected BAP (Branched Amino-acid Probe) technology
- Anti-inflammatory and pro-resolving effects in relevant experimental models including in vivo models of systemic inflammation
- TXP-11 is being developed as an intravenous solution for the treatment of organ dysfunction as seen in major surgery and in critical care patients
- Preclinical development including IND enabling tox and GMP production of study medicine has been completed
- Continued supportive pharmacology program including an extensive program conducted in collaboration with WHRI, QMUL, London UK is ongoing
- The is to file CTA for first in man study in H2 2023

## Treatment effect in model of acute peritonitis




- Compounds given iv
- n=18 per group
- Mean ±SE.
- \*: p<0,01 vs vehicle
- Data on file

TXP-11 treatment effect comparable to dexamethasone

## Development status

- Pharmacology program in additional disease models ongoing
- In vivo phase of IND-enabling toxicology and safety pharmacological studies completed – NOAEL: rat: 25 mg/kg given once daily for 2 weeks
- minipig: 10 mg/kg given as 30 infusion once daily for 2 weeks.
- CMC development for Phase 1 and 2a studies completed including release of GMP produced drug substance and release of drug product to be used in the clinical development
- Setup of phase 1 clinical development with filing of CTA in preparation-
- Aim to file CTA in H2 2023





■ Introduction to SynAct Pharma	4
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# SynAct Pharma – Experienced Management Team

## Jeppé Øvli Øvlesen, MBA – CEO



- Over 20 years of experience as CEO of various companies
- Founding Board Member of more than 10 biotech and MedTech companies
- Co-founder of TXP Pharma
- Former CFO and VP of Business Development at Action Pharma



## Patrik Renblad, MSc – CFO



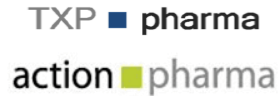
- Over 20 years of experience within various financial roles in the pharmaceutical industry
- Former Head of R&D Finance at LEO Pharma
- Experience in acquisitions, divestments and licensing deals



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



- Associate Professor at Cardiovascular Pharmacology, University of Copenhagen
- Visiting Professor at WHRI, Barts and London School of Medicine
- Co-founder of TXP Pharma and ResoTher Pharma
- Co-founder and former CSO of Action Pharma



## Thomas Boesen, PhD – COO



- Over 20 years of experience in the biotech and pharmaceutical industry
- Inventor on 35 granted patents
- Co-founder of MedChem and TXP Pharma
- Former VP of Discovery at Action Pharma



## James Knight, MBA – CBO



- Over 25 years of experience in the biotech industry, ranging from R&D to Commercial Strategy and Business Development
- Former VP of Portfolio Strategy at Questcor Pharmaceuticals



# SynAct Pharma – Board of Directors

## Torbjørn Bjerke, MD PhD – Chairman



- Over 25 years of experience within private and public pharmaceutical companies as Executive VP, R&D and as CEO
- Co-founder of Action Pharma, Arctic Aurora LifeSciences Fund and Biotech Select
- Chairman and co-founder of TXP Pharma and Carelight Ltd



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



- Over 30 years of investment banking and other healthcare industry experience
- President and CEO of Biothea Pharma
- Strategic Advisor to William Blair & Co
- Board member of AcelRx Pharmaceuticals, Neuro Networks Fund, and Advisory Board Member of Arctic Aurora Life Sciences Fund



## Uli Hacksell, PhD – Board Member



- Over 25 years of experience in senior positions at pharmaceutical and biotech companies
- Former CEO of Medivir and Acadia Pharma, growing it from a startup to a multibillion USD public company
- Board Member of various other life sciences companies



## Kerstin Hasselgren, MSc – Board Member



- CFO of Xspray Pharma
- Former VP Corporate Business Control at SSAB
- Former CFO of Alstom Transport Nordic
- Former VP at Global Finance Operations and VP of Finance Global R&D at AstraZeneca



## Thomas Jonassen, MD – Board Member, Co-founder



- Associate Professor at cardiovascular pharmacology, University of Copenhagen
- Visiting Professor at WHRI, Barts and London School of Medicine
- Co-founder of TXP Pharma and ResoTher Pharma
- Co-founder and former CSO of Action Pharma



## Terje Kelland, MD, PhD – Board Member



- Over 30 years of experience in various management positions within the life sciences industry
- Former Senior VP at Novo Nordisk A/S
- Former Head of R&D at Biovitrum (SOBI AB)
- Held various positions at Pharmacia AB



# SynAct Pharma – In Summary

- SynAct Pharma is a clinical stage biotechnology company focused on resolving inflammation through melanocortin biology to treat inflammatory and autoimmune diseases
- Oral small molecule, AP1189, is currently in active Phase 2 development for rheumatoid arthritis and nephrotic syndrome (iMN)
- **Achieving communicated milestones:**
  - ✓ 1H22 – Listed on Nasdaq Stockholm Main Market
  - ✓ 2H22 – Resumed amended iMN P2a trial
  - ✓ 2H22 – Filed and opened US IND
  - ✓ 2H22 – Initiated P2b in early severe RA
  - ✓ 2H22 – Initiated P2a/b in DMARD-IR RA under FDA IND
  - ✓ 1H23 – Completed acquisition of TXP Pharma
- **Three Phase 2 studies reading out in 2023:**
  - P2b in severe treatment naïve RA patients in combination with methotrexate (MTX)
  - P2a in RA patients experiencing an incomplete response to MTX (P2b protocol filed)
  - P2a in patients with nephrotic syndrome (iMN) experiencing severe proteinuria

**Thank you**

