

# 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**

*Presentation from the investor web cast held by the company on November 30, 2021.  
This version is updated with additional data on ACR score results as per press release issued December 2, 2021.*

December 2021



# Forward Looking Statements - Disclaimer

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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
- Our lead drug candidate AP1189 is a once-daily oral selective melanocortin receptor type 1 and 3 agonist that both elicits anti-inflammatory effects and stimulates the immune system's resolution mechanisms without undesired immunosuppressive side effects. This mode of action can be attractive in several diseases associated with hyper-inflammation.
- 2021 is a pivotal year for SynAct: we will advance our three AP1189 Phase 2a POC studies:
  - **2Q21: COVID-19-induced ARDS**
  - **End Nov'21: Rheumatoid Arthritis**
  - **2022: – idiopathic membranous nephropathy (iMN)**
- Moreover, we will prepare for the next phase of development of AP1189 with a goal of study initiation in H1-2022

## Facts and Figures

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**Founded in 2013**

**Listed on Spotlight stock exchange since 2016**

**Ticker: (SYNACT:SS)**

**Market cap: EUR 350 m**

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

**Management holds app. 20% ownership**

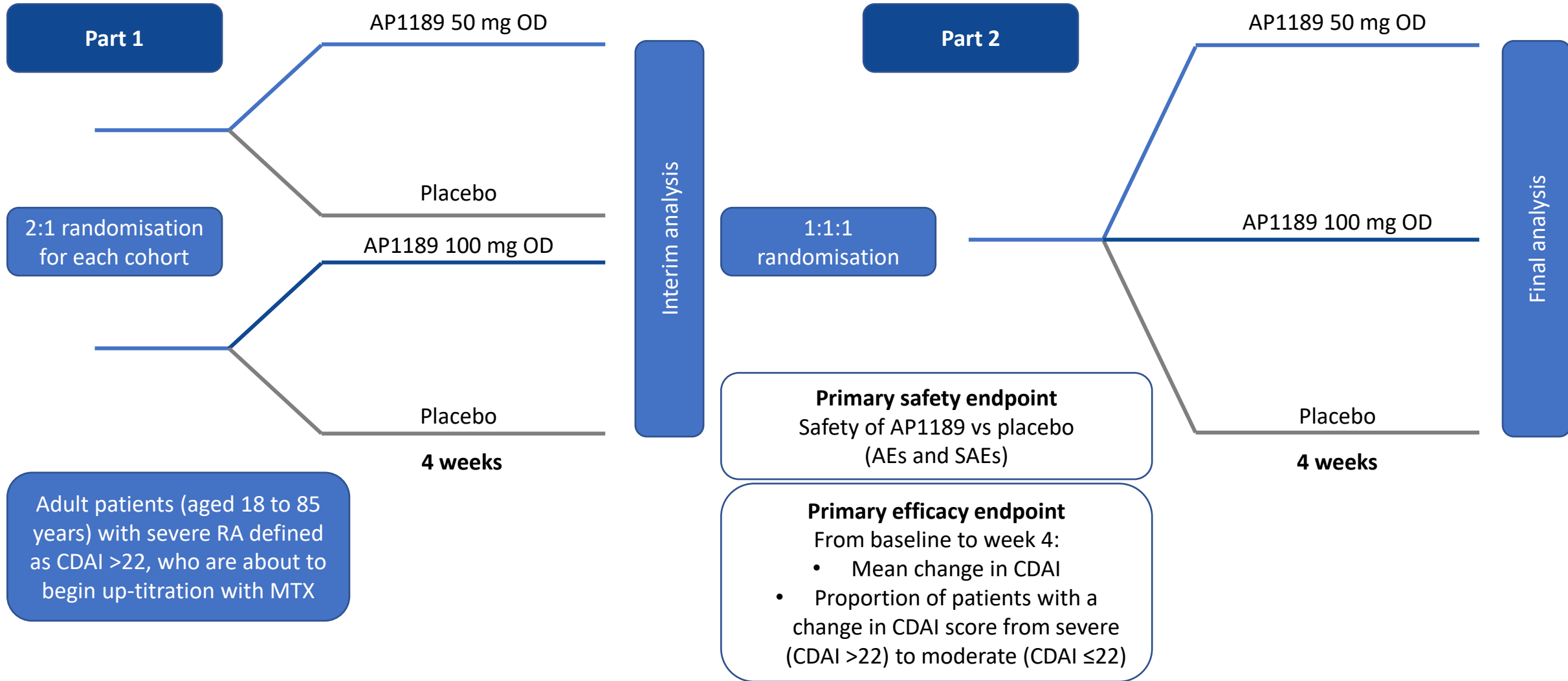
**More than 11.000 shareholders**

# AP1189 for treatment of Rheumatoid Arthritis

- Rheumatoid arthritis (RA) is chronic autoimmune disease with marked joint affection as well as systemic affection.
- Between 0.5 and 1% of adults in the developed world have RA
- Onset is most frequent during middle age and women are affected 2.5 times as frequently as men.
- Despite continued development of new treatment options for RA there is an unmet medical need for oral available agents with the ability to control disease activity without inducing immune suppression and other potential dose limiting side effects
  
- AP1189 is novel compound developed for once daily oral dosing
- AP1189 is a biased melanocortin receptor type 1 and 3 agonist with anti-inflammatory and pro-resolving effects
- Importantly mode of action is not associated with suppression of the immune system and development of immunosuppression is therefore an unlikely adverse event
- The compound is currently in Phase 2 clinical development in RA, Idiopathic Membranous Nephropathy (Nephrotic Syndrome) and for treatment of viral-induced respiratory insufficiency (incl COVID-19 infection)

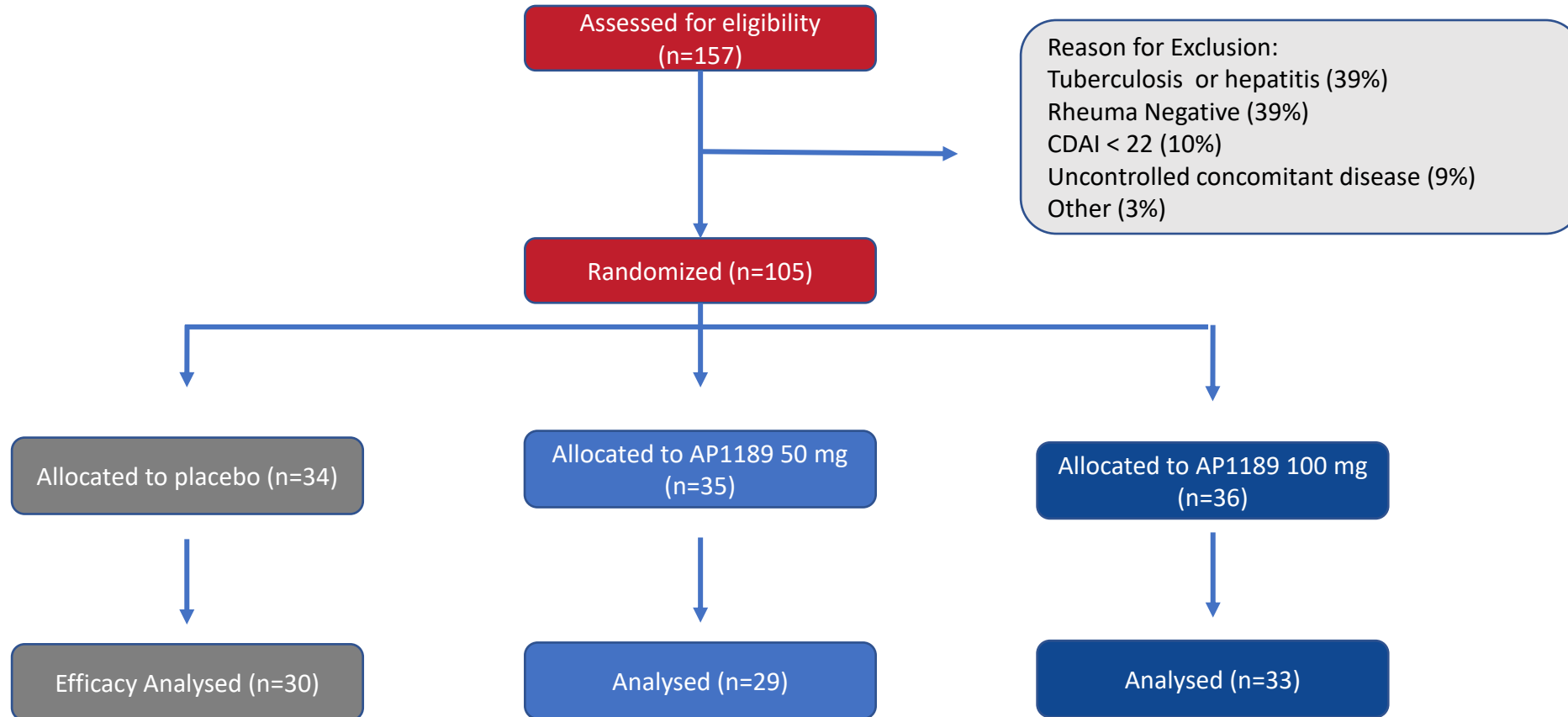
**Aim of the BEGIN Phase 2a study:  
to compare the efficacy and safety of AP1189 vs placebo in patients with severe rheumatoid arthritis**

# Study design



AE, adverse events; CDAI, Clinical Disease Activity Index; MTX, methotrexate; OD, once daily; RA, rheumatoid arthritis; SAE, serious adverse events

# Results: Patient disposition



# Results: 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	116.3±8.4
Median (range)	167 (155–185)	167 (157–183)	165.5 (151–183)

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

# Results: baseline characteristics

	Placebo (n=32)*	AP1189 50 mg (n=31)*	AP1189 100 mg (n=35)*
CDAI	36.3±8.6	36.1±11.0	39.0±9.0
TJC	10.0±3.9	10.3±4.4	11.8±5.0
SJC	13.9±5.6	13.7±6.4	15.0±5.8
DAS-28	5.5±1.0	5.4±0.9	5.7±0.9
Patient Global Assessment (VAS)	6.2±1.2	6.3±1.3	6.4±1.3
Physician Global Assessment (VAS)	6.6±1.8	5.9±2.3	5.8±2.1
CRP (mg/L)	19.1±26.5	14.9±18.4	26.1±40.7

All values are mean±SD. \* 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

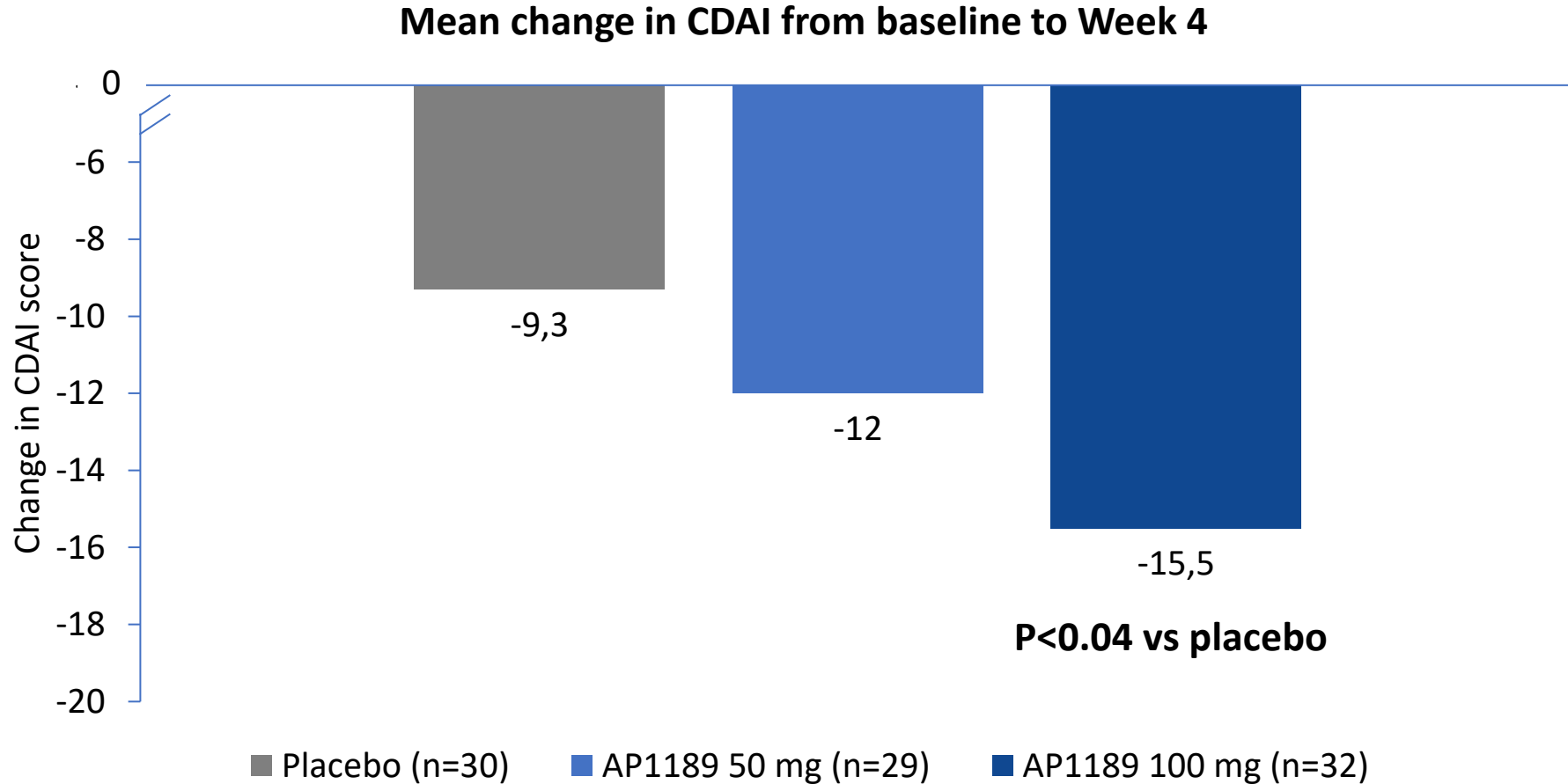
CDAI, Clinical Disease Activity Index; CRP, C-reactive protein; DAS-28, Disease Activity Score in 28 joints; SJC, Swollen Joint Count; TJC, Tender Joint Count; VAS, visual analogue scale



# Primary safety endpoint: AEs

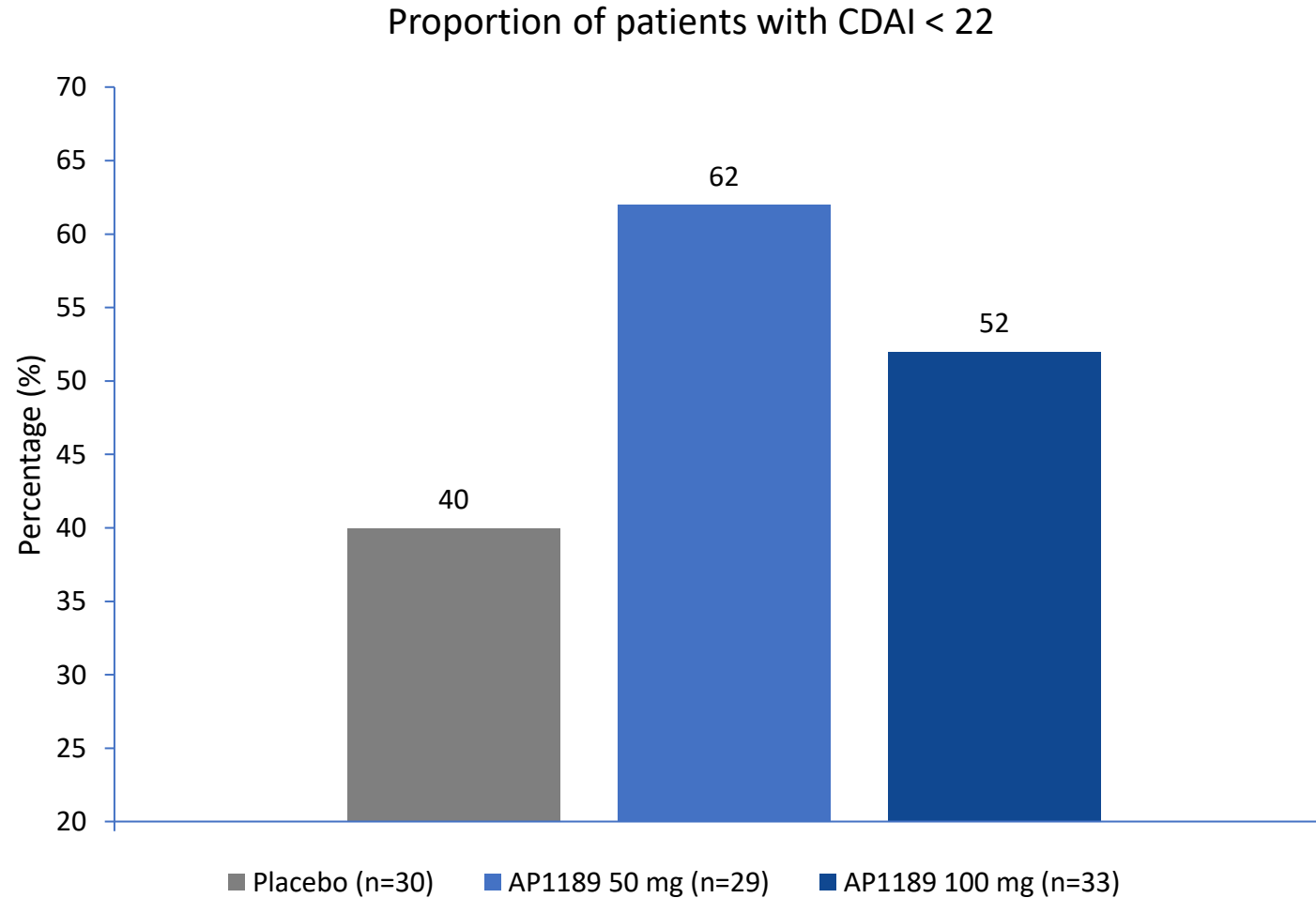
	Placebo (n=32)	AP1189 50 mg (n=31)	AP1189 100 mg (n=35)	Total (n=98)
SAEs, n (%)	0	0	0	0
AEs, n reported from baseline and on	21	38	27	86
AE severity (mild/moderate/severe)	18/2/1	26/12/0	22/5/0	66/19/1
Discontinuation due to IMP related AEs, n (%)	0	0	0	0
Discontinuation due to MTX related AEs, n (%)	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

# Change in Clinical Disease Activity Index (CDAI)



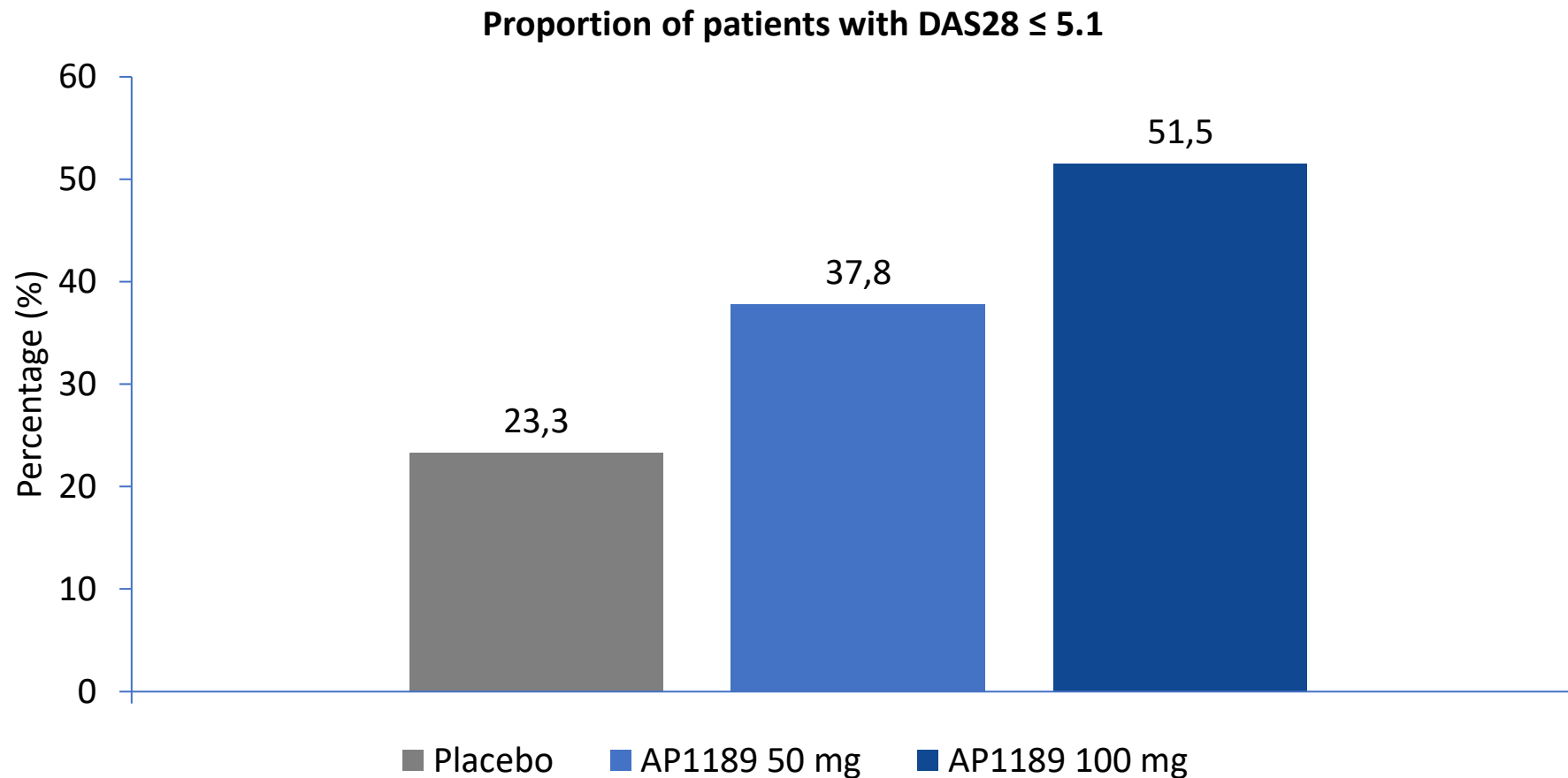
CDAI, Clinical Disease Activity Index

# Treatment effects evaluated by CDAI - proportion of patients with moderate disease activity end of treatment



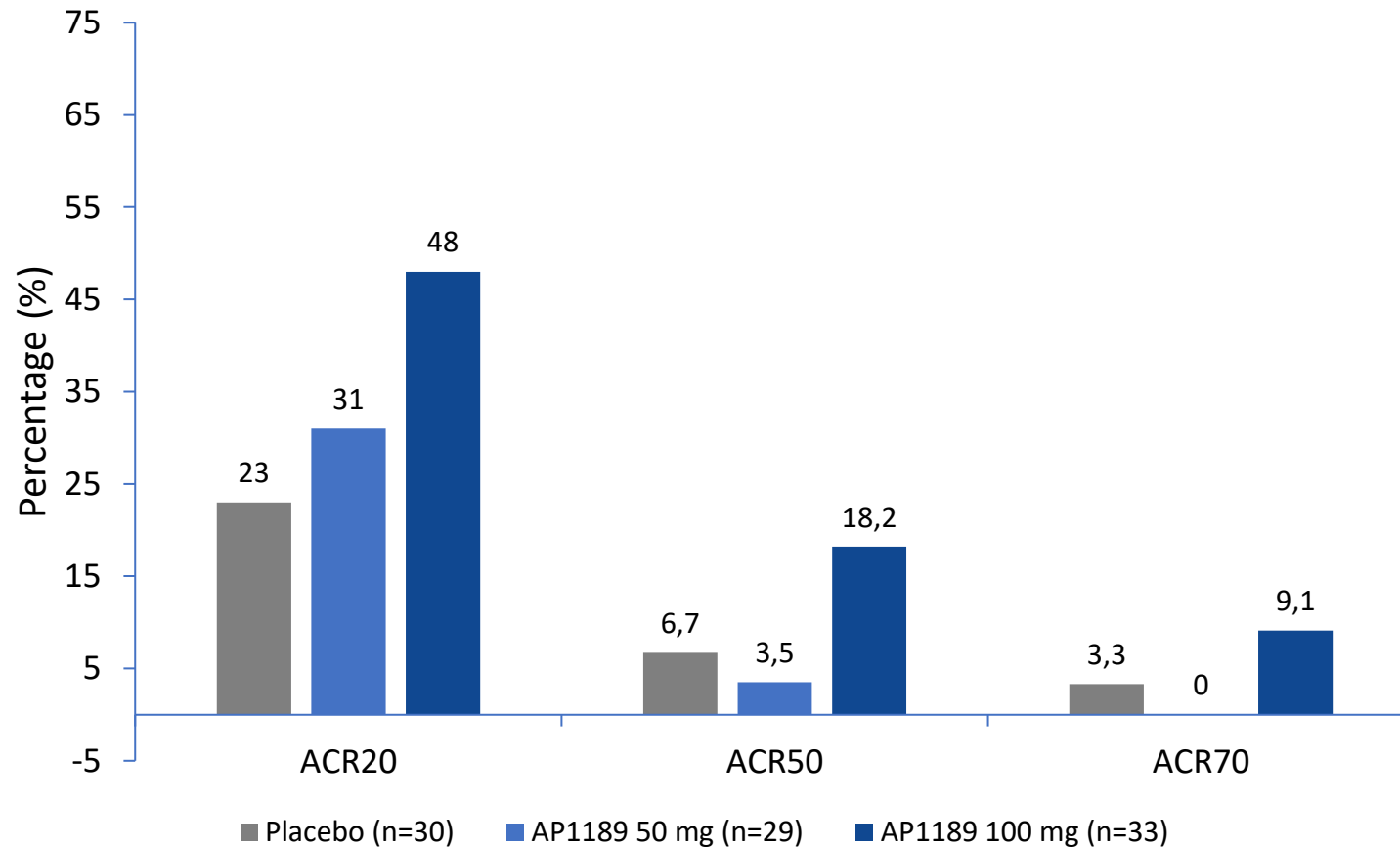
CDAI, Clinical Disease Activity Index

# Treatment effects evaluated by DAS28 - proportion of patients with at least moderate disease activity at 1-mo



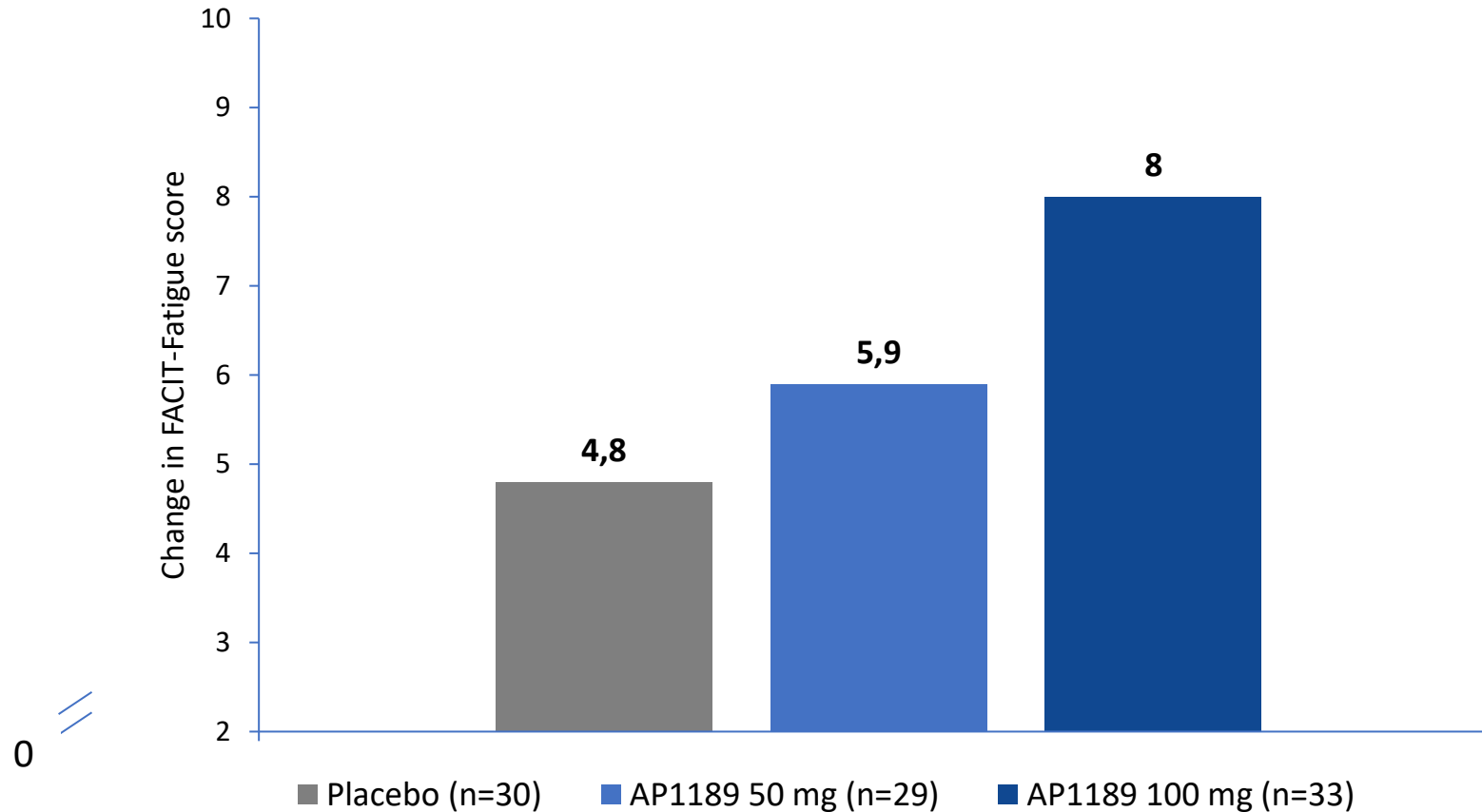
DAS-28, Disease Activity Score in 28 joints

# Treatment effects evaluated by ACR scoring – Proportion of patients with minimum 20/50/70% improvement in disease activity



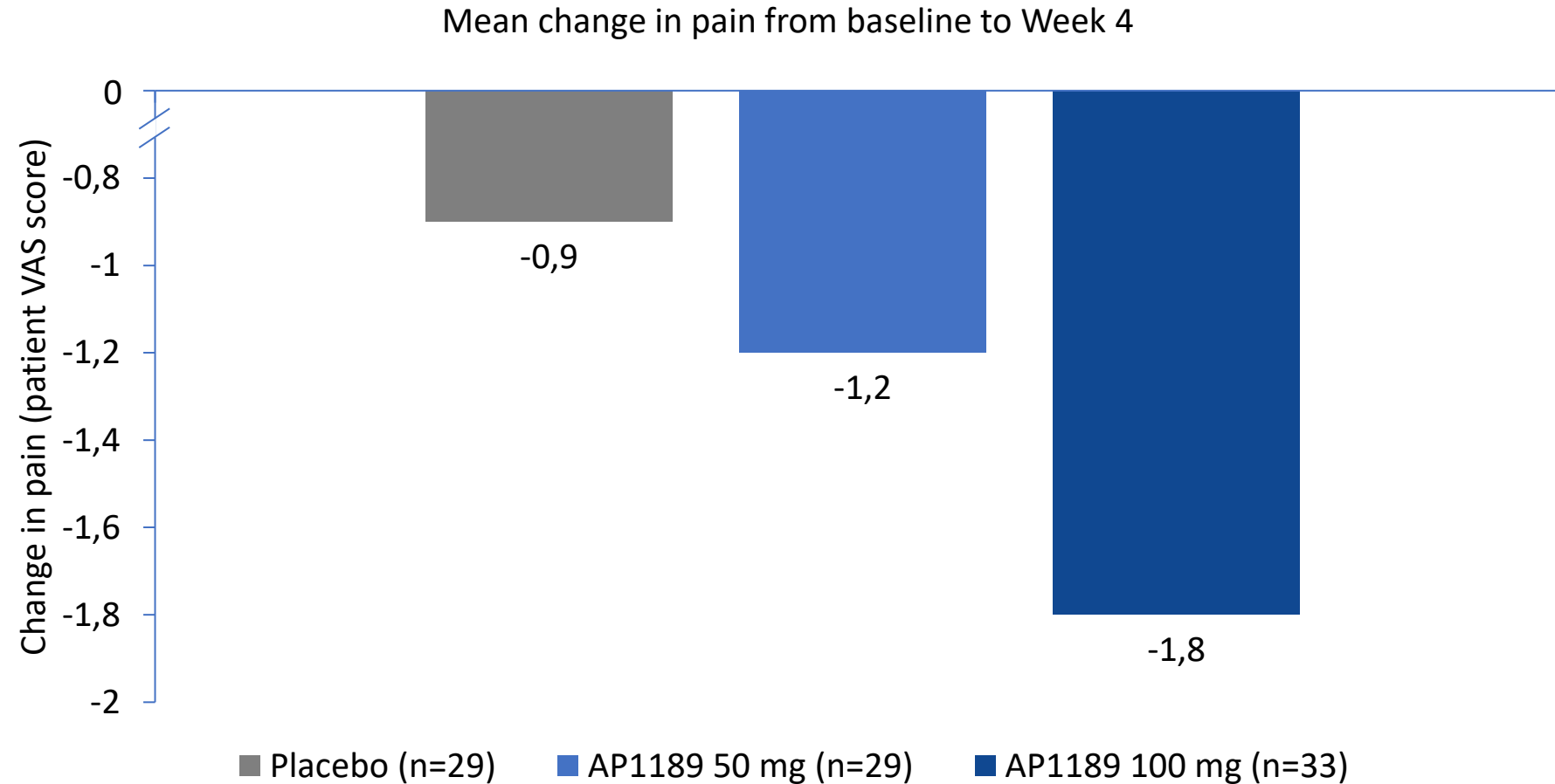
ACR20,  $\geq 20\%$ ; ACR50,  $\geq 50\%$ ; ACR70,  $\geq 70\%$  improvement in American College of Rheumatology criteria

# Treatment effects on patient fatigue evaluated by the FACIT-fatigue score at 1-mo



FACIT, Functional Assessment of Chronic Illness Therapy;

# Treatment effects on patient pain evaluated by VAS



VAS, visual analogue scale

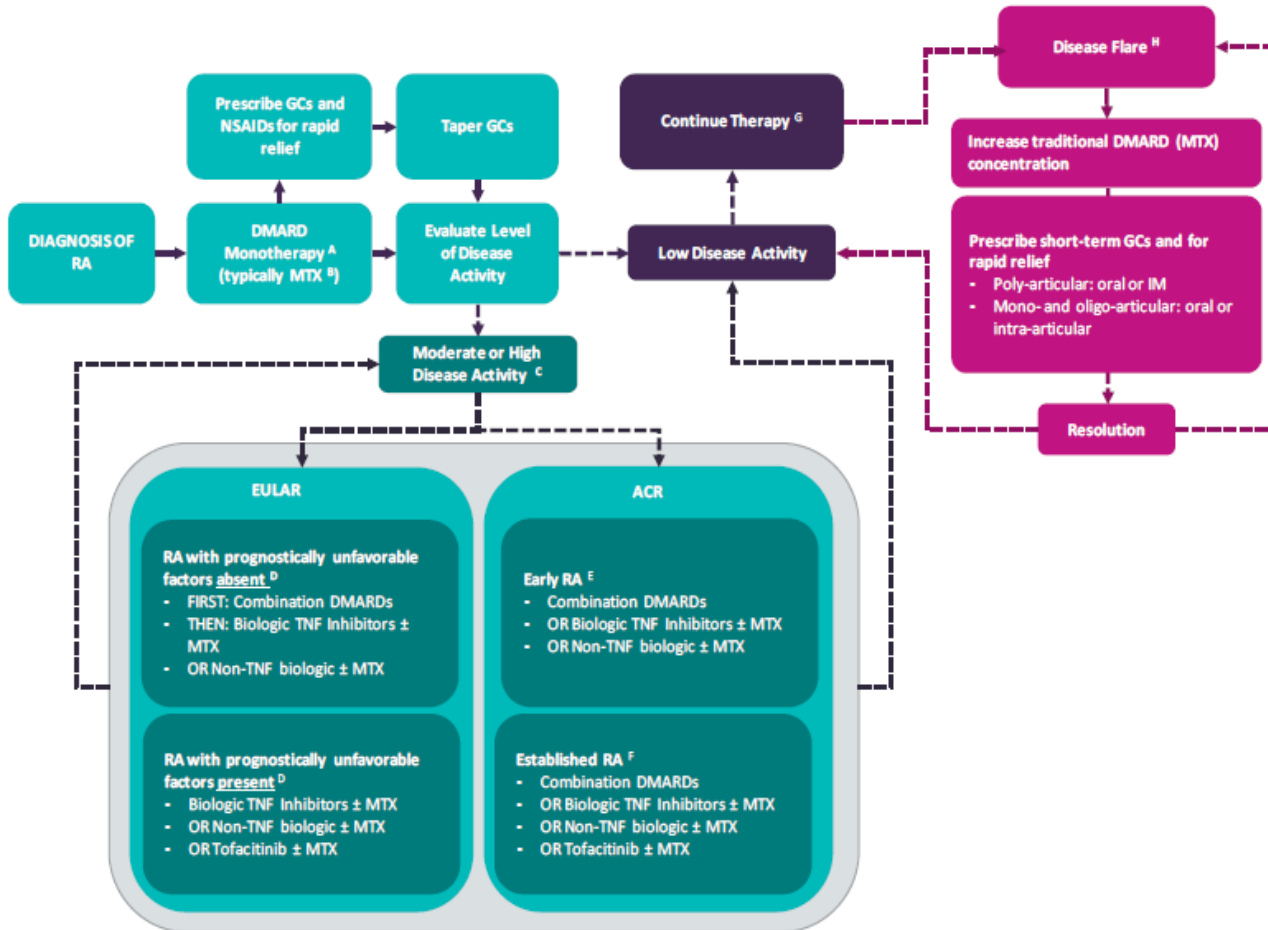
# Summary

- **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.**
- **Consistent dose-dependent effects were also seen across secondary read outs including Disease Activity Score DAS-28, ACR-20 score and FACIT-fatigue score.**
- **AP1189 was well-tolerated and presented with a favorable safety profile. No serious adverse events were reported in the study.**

**Based on the positive results, SynAct will seek scientific advice and open an IND with the FDA to prepare for Phase 2b.**



# AP1189: Multiple Opportunities in the Management of RA



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

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

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