SYNACT PHARMA

INFLAMMATION RESOLUTION

# SynAct Pharma AB

## Treating Inflammation through Resolution Therapy

## September 2023

# Forward Looking Statements

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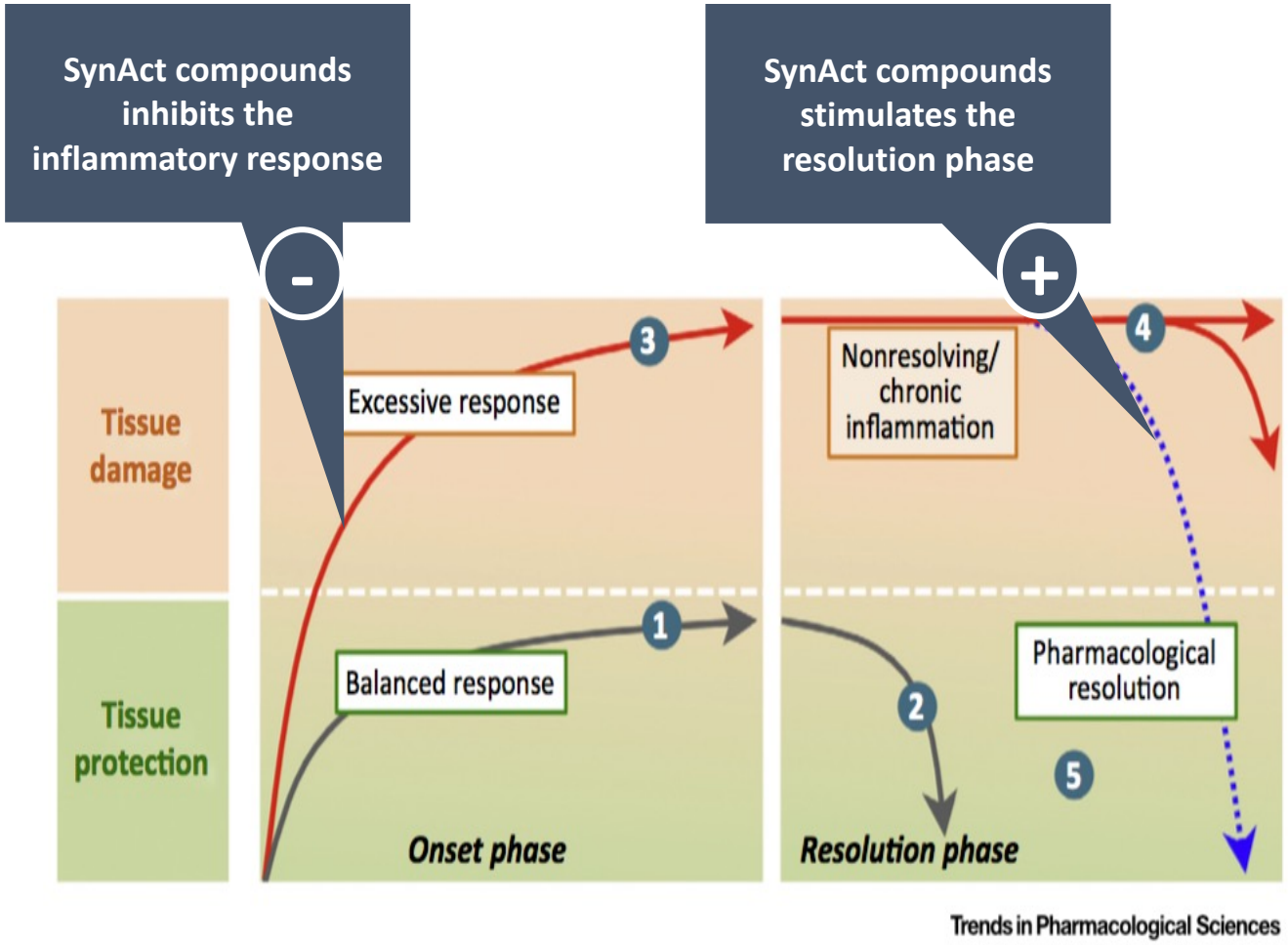
# SynAct Pharma – A leader in Inflammation Resolution

- SynAct Pharma is a clinical stage biotechnology company focused on resolving inflammation through melanocortin biology to treat inflammatory and autoimmune diseases
- Lead molecule resomelagon is a small molecule, once daily tablet, internally developed, wholly owned and with blockbuster potential
- Resomelagon (AP1189) has shown great data in two clinical conditions; i) COVID-19 induced severe lung inflammation and ii) in a 4 weeks Phase II trial in newly diagnosed severe rheumatoid arthritis (RA) patients
- Topline data ACR20 after 12 weeks negative in the Expand study. Awaiting more data in September.
- The Resolve study part A will have read-out in October 2023.
- World class management and board
- Listed on Stockholm Nasdaq

# SynAct Pharma – Pipeline overview

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

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

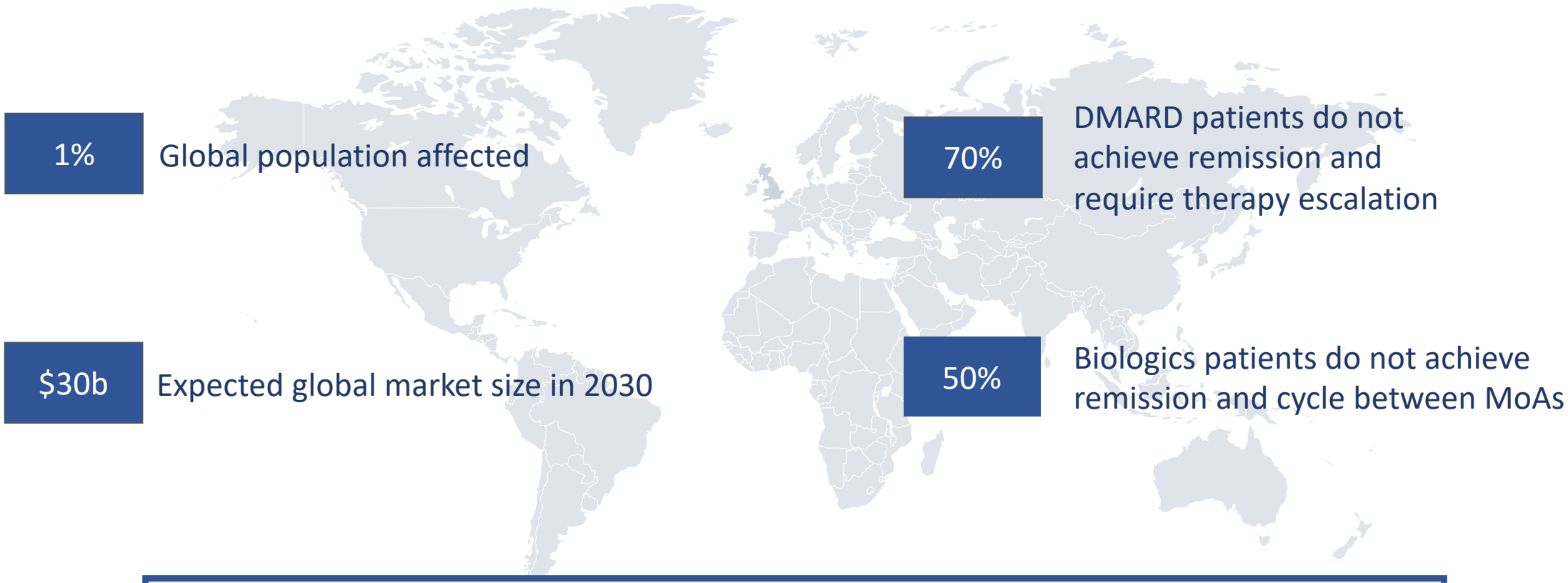



Cartoon adapted from Perretti *et al. Trends Pharmacol Sci* 2015;36:737–55

## 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

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



**1%** Global population affected

**$30b** Expected global market size in 2030

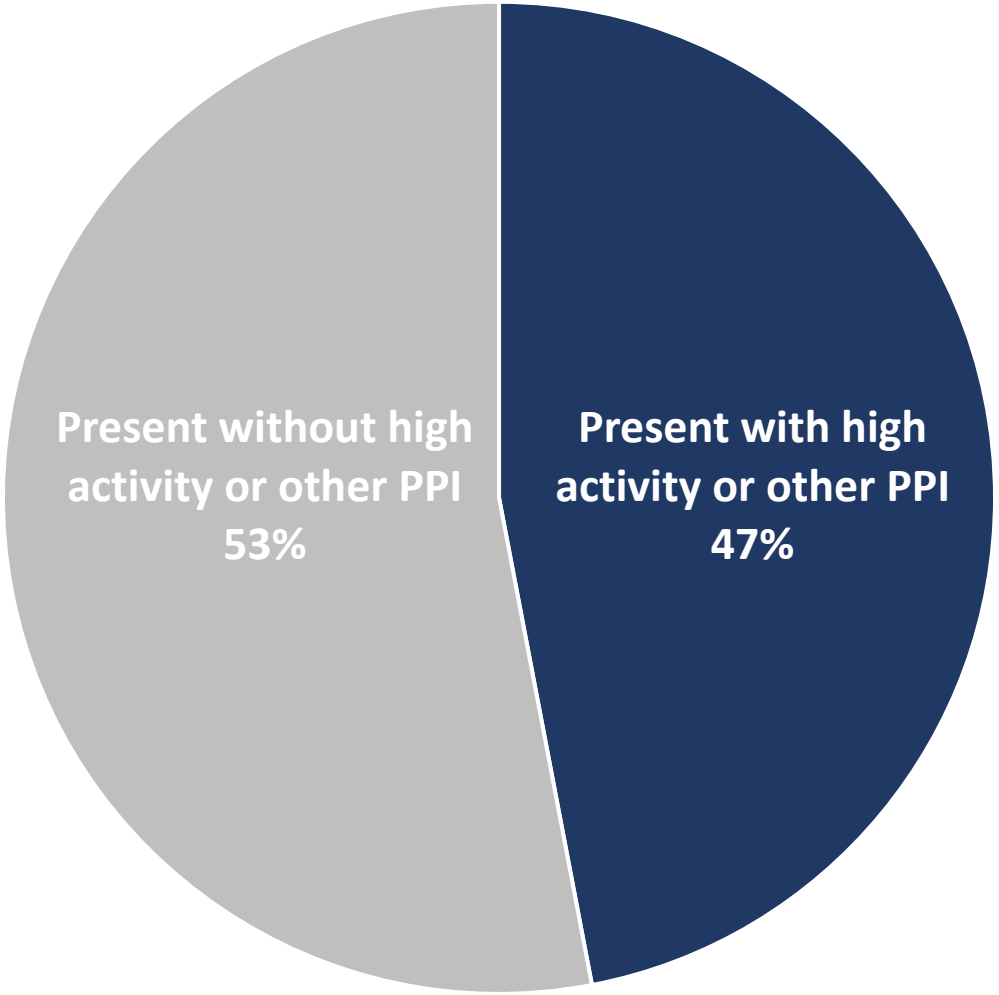
**70%** DMARD patients do not achieve remission and require therapy escalation

**50%** Biologics patients do not achieve remission and cycle between MoAs

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

Rheumatoid Arthritis: Global Drug Forecast and Market Analysis to 2029, Reference Code: GDHC209PID

# Treatment naïve RA patients present with high activity and other poor prognostic indicators almost 50% of the time




**Highly-Active Naïve:**

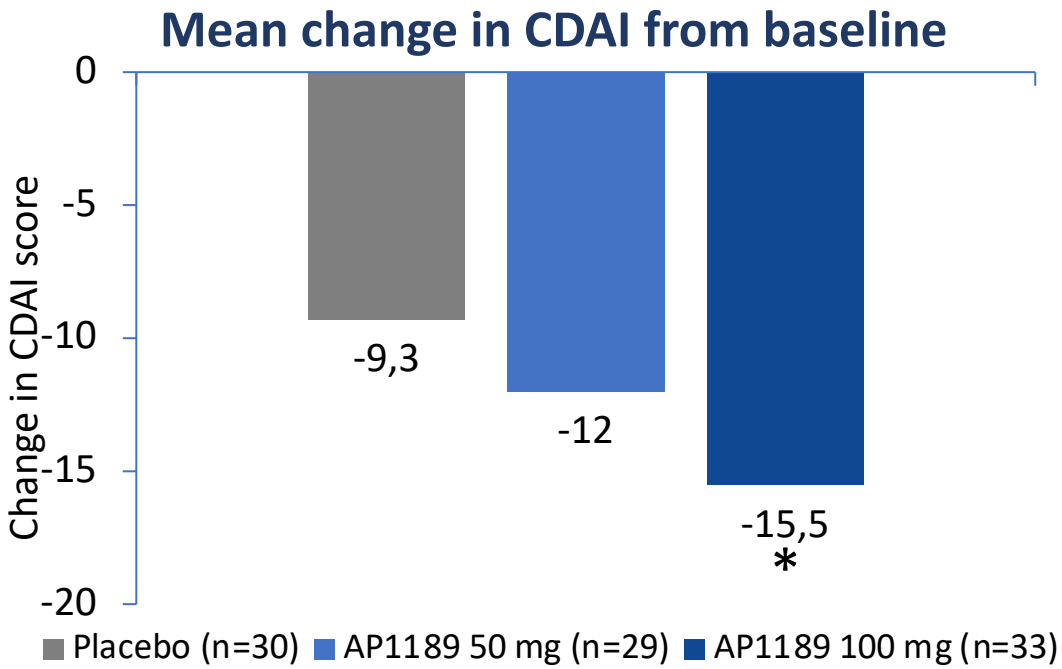
- Studied in BEGIN and EXPAND studies
- Highly active disease is the dominating poor prognostic indicator (PPI) in ACR and EULAR recommendations[1]
- Up to 47% of treatment-naïve RA patients can present with highly active disease and these patients tend to have a lower response to DMARDs including MTX[2,3]

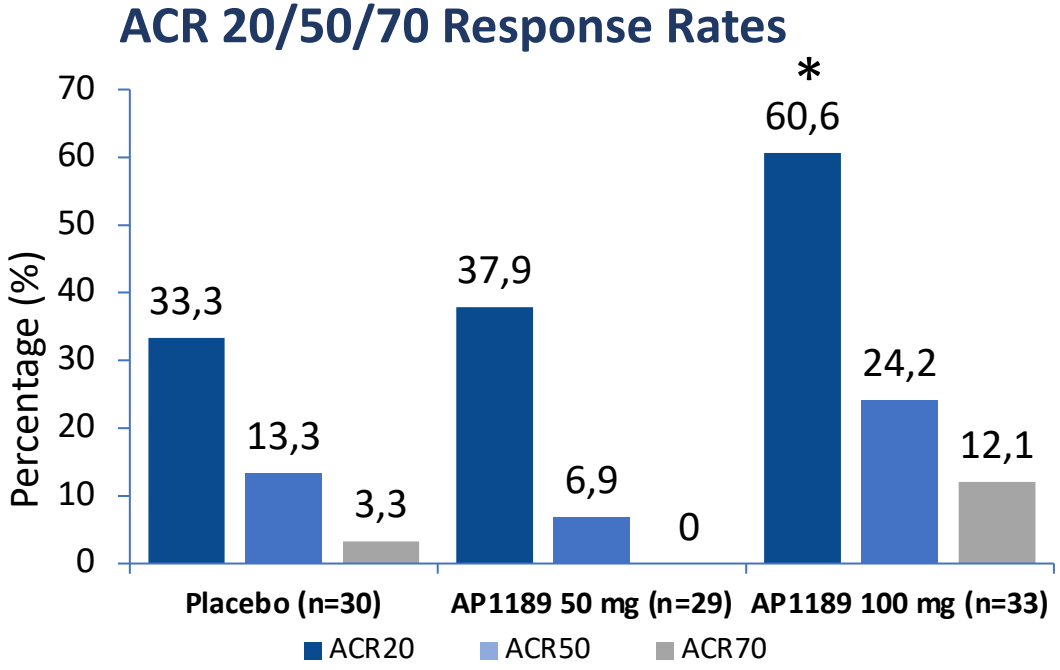


1. Albrecht and Zink Arthritis Research & Therapy (2017) 19:68 2. GlobalData RA custom primary market research studies 2021-2023, on file; 3. Baganz et al. Seminars in Arthritis and Rheumatism 48 (2019)

# Resomelagon (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 naive RA patients with high disease activity (CDAI >22 at randomization) in combination with MTX with 4 weeks treatment



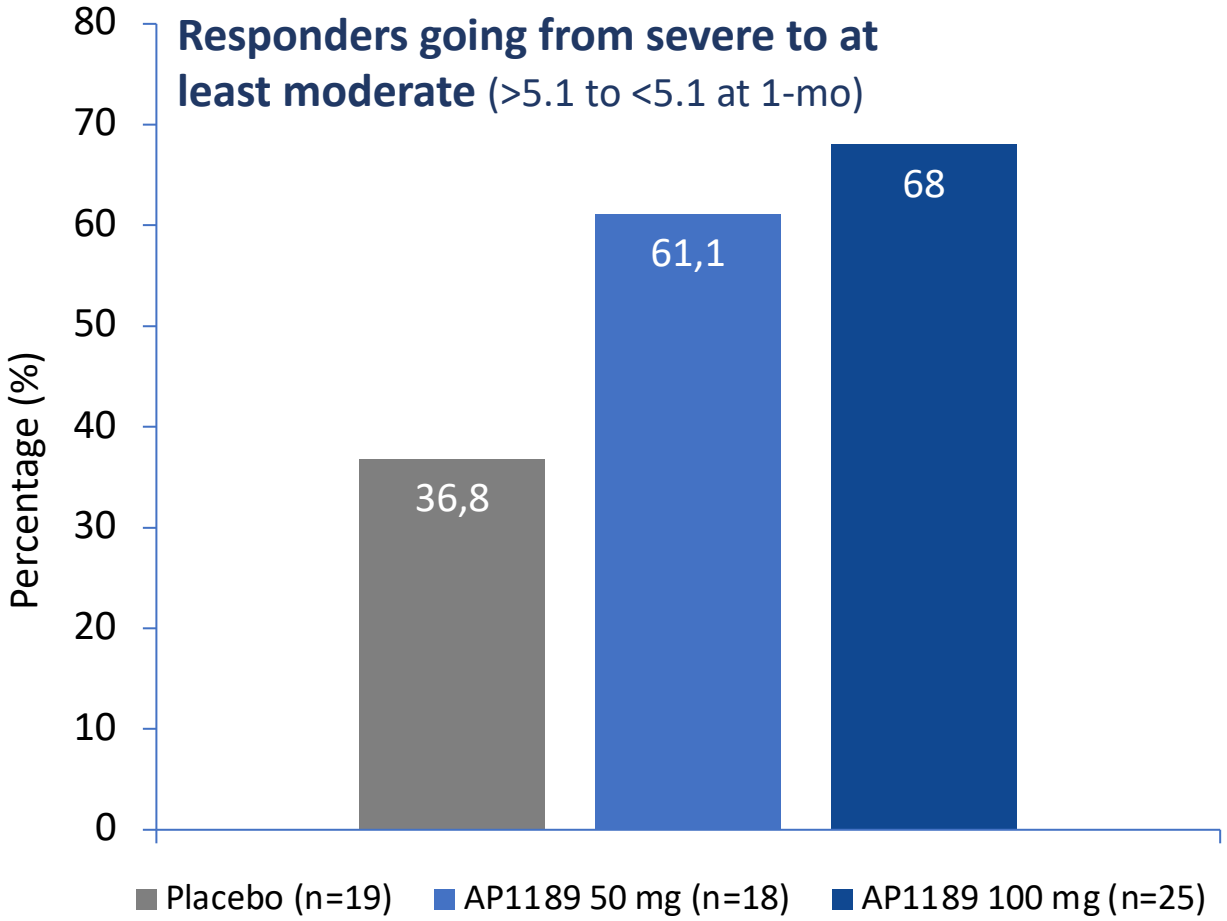



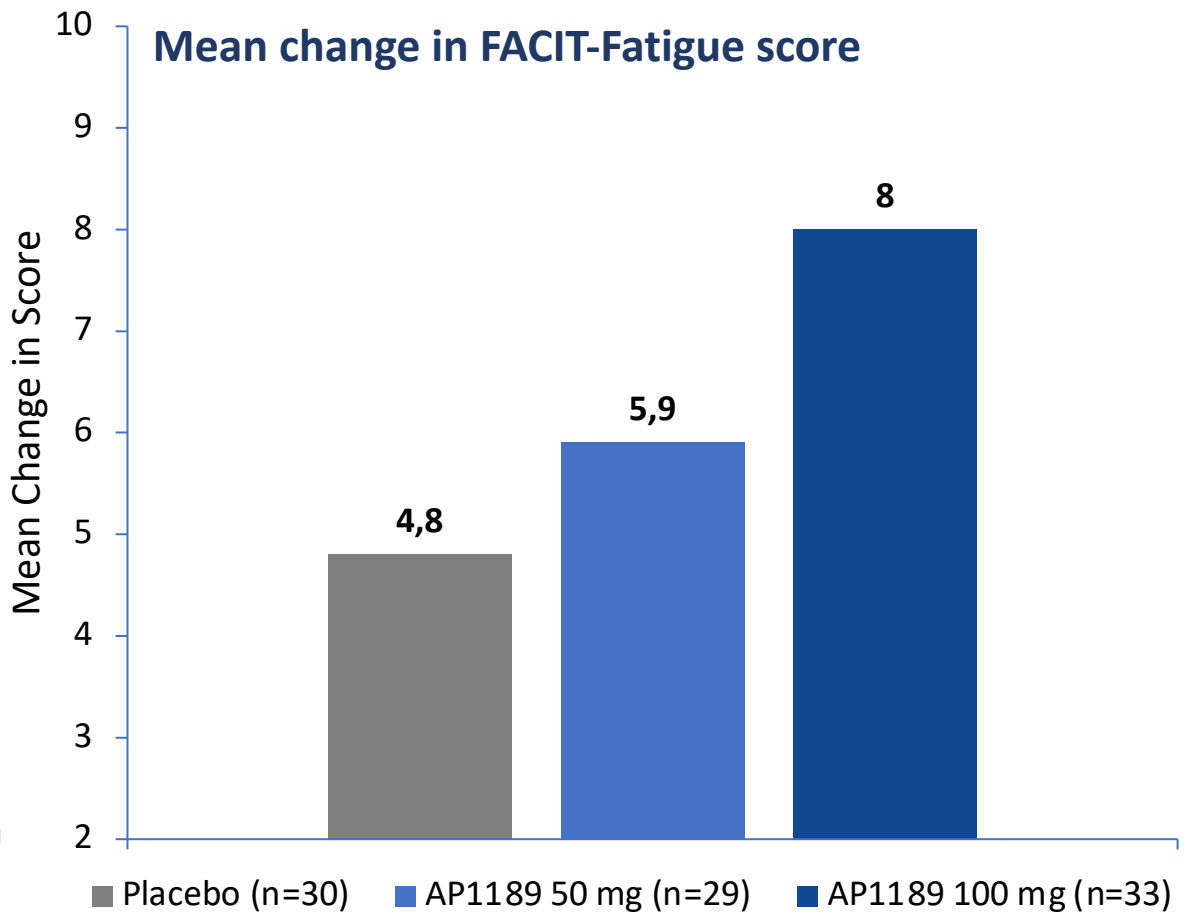

**Mean improvement in CDAI above the minimally important clinical difference (MCID)⁺**
**Robust 1-Month ACR20/50/70 response rates for 100mg AP1189**

* = p<0.05 vs placebo

(+) Curtis et. Al *Arthritis Care Res (Hoboken)*. 2015 October; 67(10 )

# 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)⁺**

(+) Cella et. Al *The Journal of Rheumatology 2005; 32:5*

# 4-Week daily AP1189 dosing was safe and well tolerated in the BEGIN study

## Adverse Events[1]

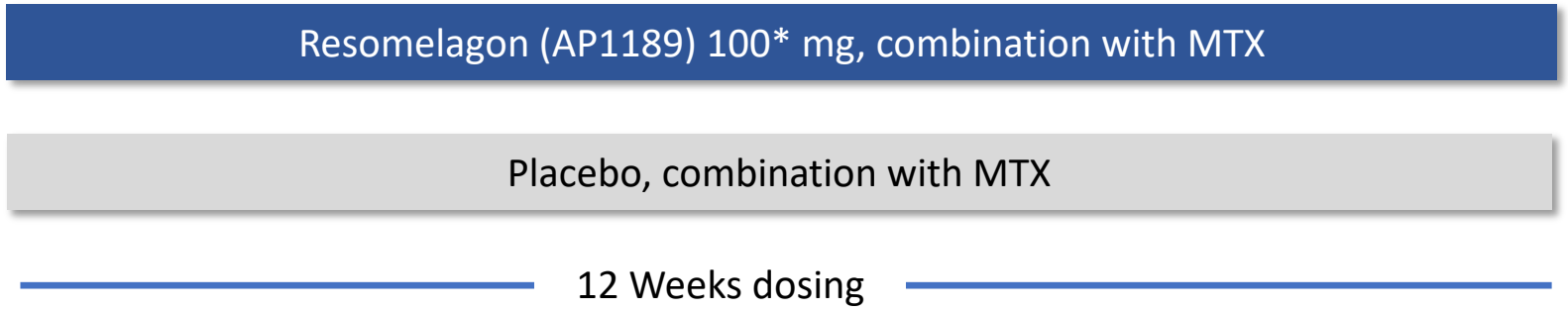
| Group (n) | Placebo + MTX (34) | AP1189 + MTX | | Total (105) |
|---|---|---|---|---|
| | | 50 mg (35) | 100 mg (36) | |
| **SAEs n** | 0 | 0 | 0 | 0 |
| **AEs n** | 34 | 65 | 53 | 152 |
| Mild/Mod/Severe | 28/4/2 | 45/20/0 | 43/10/0 | 116/34/2 |
| % Mild | 82% | 69% | 81% | 76% |
| Pts with ≥ 1 AE n (%) | 17 (50) | 20 (57) | 20 (56) | 57 (54) |
| Discontinuation n (%) | 1[2] (3) | 0 (0) | 1[3] (3) | 2 (2) |
| **AEs >10% of Pts, n** | | | | |
| Nausea[4] | 7 | 5 | 7 | 19 |
| ALT increase[5] | 3 | 6 | 0 | 9 |
| Headache[4] | 0 | 2 | 5 | 7 |

(1) All study AEs; As per protocol safety assessments were conducted at level of all AEs not only treatment-emergent AEs
(2) Baseline ALT>3x upper normal level; patient discontinued from study when levels were read
(3) Onset of herpes zoster; Investigator decided to DC MTX which necessitated study discontinuation
(4) Headache and nausea were transient and occurred more frequently early in dosing period
(5) Laboratory value AEs determined by investigator; 8/10 ALT increases were mild and 3 occurred outside of dosing period

# EXPAND STUDY P2b study in previous treatment naive RA patients. Recruitment completed in April 2023 -

**Patient Population:**

- Previous treatment naïve, eligible for initiation of DMARD treatment (MTX)
- CDAI >22 at baseline – min of 6 swollen and tender joints
- Glucocorticoids only allowed as rescue medicine




| Key Study Parameters | |
|---|---|
| **Dosing and Duration** | ▪ 12 weeks of once-daily dosing of solid tablet AP1189 or placebo- conducted at site in Eastern Europe- Successful completion of recruitment ahead of schedule |
| **Study Size and Sites** | ▪ Designed to recruit 60 patients per group – actual number randomized is 127 |
| **Primary Endpoints** | ▪ ACR20 response rate at 12 weeks as compared to placebo |
| **Secondary Endpoints** | ▪ CDAI score; DAS28 score; FACIT-Fatigue; HAQ/RAQol |
| **MRI- SubStudy** | ▪ Evaluation of Synovial inflammation using Dynamic Contrast Enhanced MRI Quantification (DEMRIQ) |

*:Free base – correspond to 125 mg acetate salt used in the BEGIN study

# Baseline characteristics in the Expand study

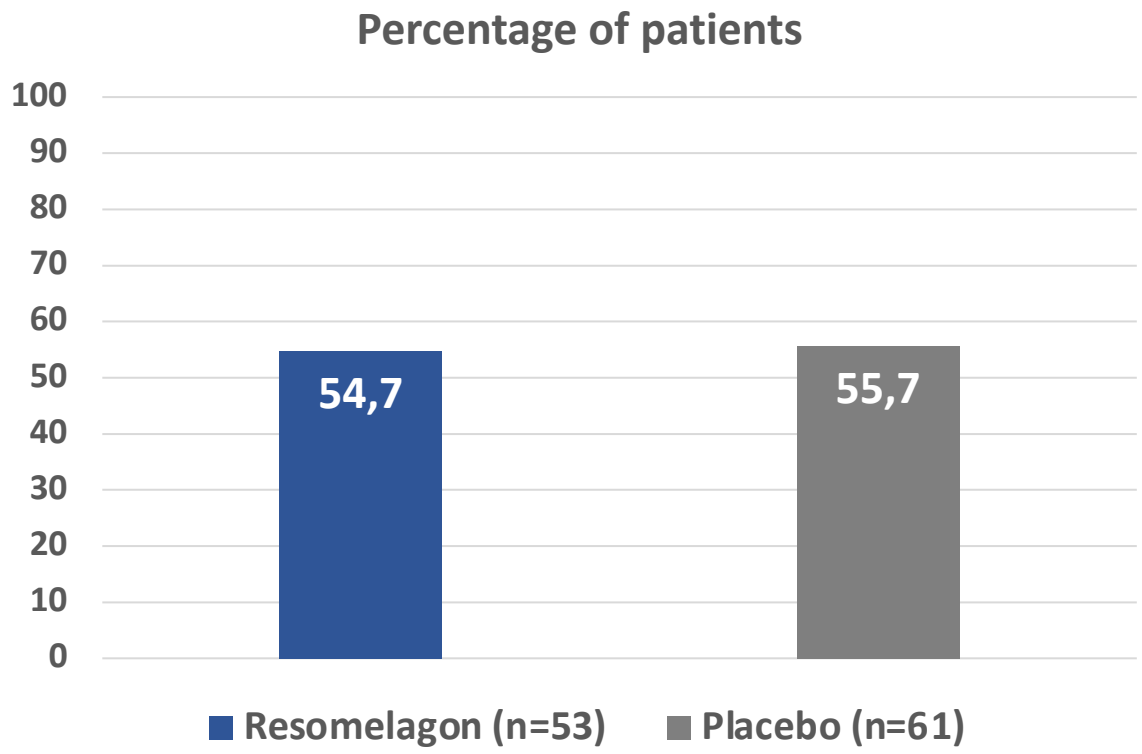
| | Resomelagon (n=63) | Placebo (n=64) |
|---|---|---|
| Age mean | 58.0 | 55.2 |
| Gender<br>% Females | 85.7 | 87.5 |
| RA- history Weeks (Mean) | 42 | 19 |
| RA % Sero Negative | 25.3 | 17.2 |
| CRP % above normal range | 39.6 | 35.9 |
| CDAI | 42.0 | 40.3 |
| ARC class (I/II/III in %) | 3.2/77.8/19.0 | 7.8/71.9/20.3 |
| Corticosteriod treatment % | 0 | 0 |

# Resomelagon was safe and well tolerated in the Expand study

**Treatment Emergent Adverse Events (TEAE)**

| Group (n) | Placebo+ MTX (64) | AP1189 100mg + MTX (63) | Overall (127) |
|---|---|---|---|
| **Serious Treatment Emergent AEs** | | | |
| Patients with ≥ 1 Serious AE n (%) | 1 (1.6) | 1 (1.6) | 2 (1.6) |
| **Non-Serious Treatment Emergent AEs** | | | |
| **TEAEs n (%)** | 43 | 45 | 88 |
| Mild/Mod/Severe | 24/19/0 | 25/20/0 | 49/39/0 |
| Patients with ≥ 1 TEAE | 28 (44.4) | 27 (42.2) | 55 (43.3) |
| Patients with ≥ 1 TEAE leading to study discontinuation | 1 (1.6) | 5 (7.9) | 6 (4.7) |
| Patients with 1 or more TEAE leading to death | 0 | 0 | 0 |
| **TEAEs in ≥ 5% of patients n (%)** | | | |
| Overall infections | 10 (15.6) | 7 (11.1) | 17 (13.4) |
| Elevated liver enzymes | 6 (9.4) | 3 (4.8) | 9 (7.1) |
| Headache | 6 (9.4) | 0 | 6 (9.4) |
| Abdominal pain | 2 (3.1) | 4 (6.3) | 6 (4.7) |
| Nausea | 2 (3.1) | 4 (6.3) | 6 (4.7) |
| Vomiting | 2 (3.1) | 4 (6.3) | 6 (4.7) |

# ACR Scores following 12 weeks treatment in the Expand study




The study could not identify treatment related effects of resomelagon relative to placebo on the primary endpoint

# ACR scoring system – both subjective and objective read-outs

## Subjective read-outs

- **Investigator assessment of disease activity (VAS)**
- **Patient assessment of disease activity (VAS)**
- **Patients Pain assessment (VAS)**
- **Health Assessment Q. (HAQ) of physical functioning**

## Objective read-outs

- **Tender Joint Swollen Joints CRP**

**To qualify for improvement in ACR score reduction in tender and in swollen joints has to be present – and in addition, improvement 3 out of 5 of the other readouts, 4 of which are subjective.**

# EXPAND Study – observations

- In the EXPAND study reduction in tender and swollen joints in the resomelagon group seems to have been reduced to a degree we could expect from the BEGIN study
- The patient and investigator assessment of disease activity in the EXPAND study did not reflect the reduction seen in tender and swollen joint counts
- This is surprising as the reduction in joint counts is in favor of resomelagon rather than placebo – and that nothing in the adverse event profile indicates that the compound is less well tolerated
- Between sites variability in clinical scores was high, which most likely contributed to the ability to discriminate between resomelagon and placebo treatment. This variability seems to be driven mainly by the subjective measures.

# AP1189- Adaptive P2 trial design in DMARD-IR patients
# Data on part A in October 2023

Part A – 4 weeks dosing

3 dose levels of Resomelagon (AP1189) cont. MTX

Placebo, cont. MTX

Part B – 12 weeks dosing

Up to 3 dose levels of Resomelagon (AP1189), cont. MTX

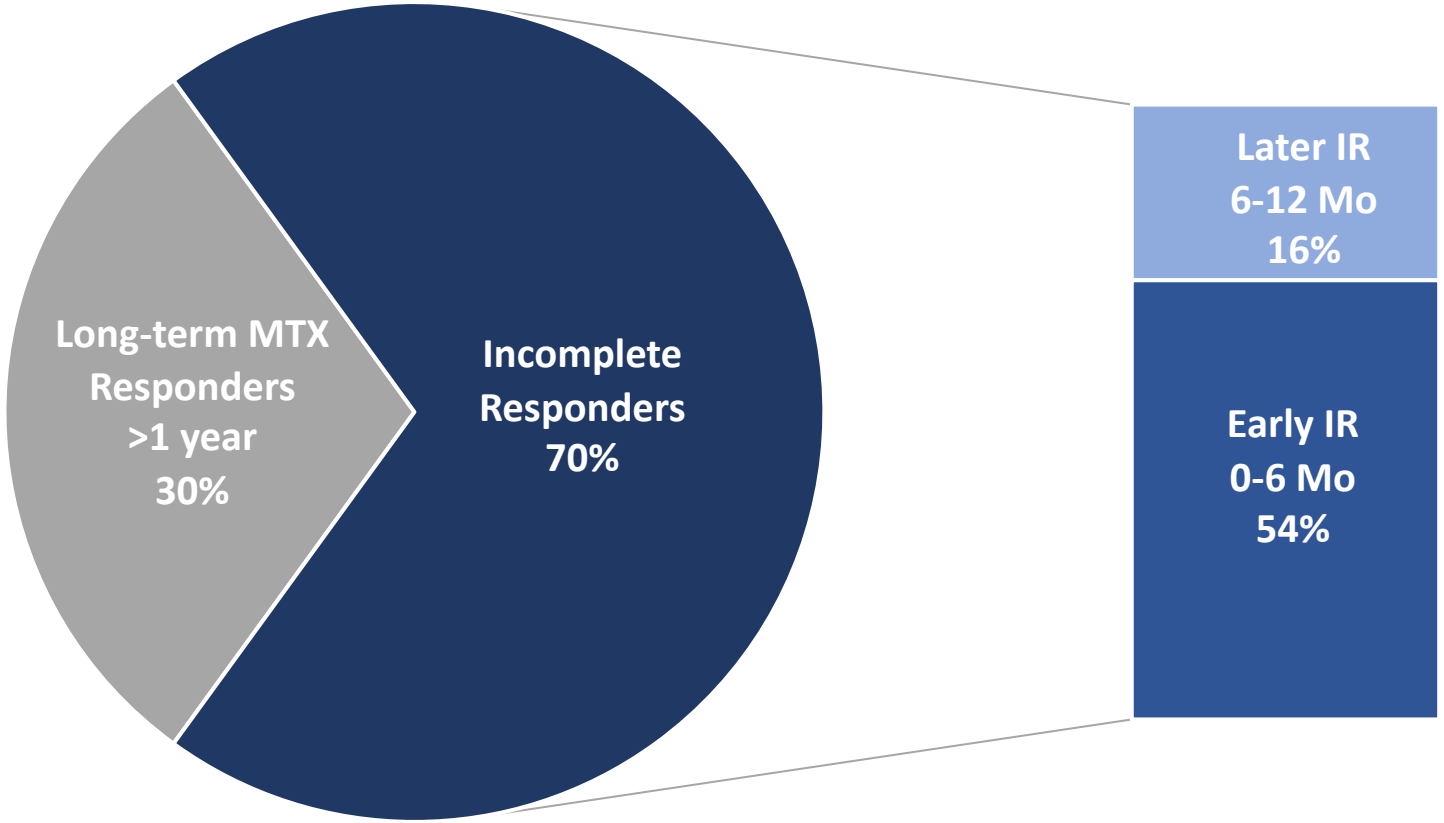
Placebo, cont. MTX

**Patient Population:**

- >3 mo MTX treatment
- Documented incomplete response or loss of response
- Min of 6 swollen and 6 tender joints and/or increased CRP

| Key Study Parameters | |
|---|---|
| **Dosing** | ▪ Once-daily dosing of solid tablet AP1189 or placebo |
| **Study Size and Sites** | ▪ Part A: 30 pts per group<br>▪ Part B: 75 patients per group |
| **Primary Efficacy Endpoints** | ▪ ACR20 response rate at 4 Weeks (part A) and 12 weeks as compared to placebo |
| **Secondary Endpoints** | ▪ CDAI score; DAS28 score; FACIT-Fatigue; HAQ/RAQol |
| **MRI- substudy (part B only)** | ▪ Evaluation of Synovial inflammation and potential effects on joint destruction using Dynamic Contrast Enhanced MRI Quantification (DEMRIQ) |

# DMARDs are time-tested 1st-line RA therapies but the majority of treated patients will not achieve a durable response on DMARD monotherapy




**DMARD-IR:**

- This is the patient population being studied in RESOLVE
- Up to 50% of 1st DMARD Tx will not achieve low disease activity and 70% will fail a 2nd DMARD Tx[1]
- Up to 54% of MTX-Tx patients will be DMARD-IR at 3mo[2]
- ~20% of patients who initially respond to MTX will loose responsiveness[2]
- Up to 22% of patients experience intolerance even with long-term MTX usage[3]



1. Baganz et al. Seminars in Arthritis and Rheumatism 48 (2019) 976!982; 2. GlobalData RA custom primary market research studies 2021-2023, on file; 3. Amaral et al. Advances in Rheumatology (2020) 60:4

# Key differences between RESOLVE and EXPAND studies

- **Disease duration:**
  - **Tx naïve** - <1yr since diagnosis
  - **DMARD-IR** – years since diagnosis
- **Previous methotrexate use:**
  - **Tx naïve** – no previous methotrexate use
  - **DMARD-IR** – patients have a documented incomplete response to MTX after an adequate course of therapy of at least 3mo (many have 1+ year of exposure) at a dosage higher than was used in EXPAND
- **Concurrent steroid use:**
  - **Tx naïve** – No use of steroids at study entry, steroids only used for rescue therapy
  - **DMARD-IR** – Steady doses of steroids below 10mg allowed
- **RESOLVE is approved under new US IND with US sites recruiting approximately 25%**

# DMARD-IR: High unmet need and significant commercial opportunity

- **Currently, DMARD-IR patients are not well served by existing therapies**
  - Advanced therapies like biologics and JAK inhibitors come with serious safety concerns
  - Payors and insurers can deny and delay access to these very expensive therapies
  - In the US, JAK inhibitors have been restricted due to safety concerns by the FDA to use only after a TNF blocker meaning the next therapy after DMARDs is likely an injectable or an infused product

- **Approximately 40% of global RA patients (~8M) are managed on DMARD therapy alone and can have long-lasting side effects even after years of continued use**

- **With the global RA market expected to reach up to $30B dollars by 2030, a successful, convenient and safe oral medication could be established in a market position with multi-billion-dollar potential**

# Upcoming news flow


✓ September: Topline results from Expand

October: Topline results from Part A Resolve

More results from Expand

More results from Part A Resolve

Initiation of Resolve Part B

Initiation of Phase I TXP-11

More pipeline updates

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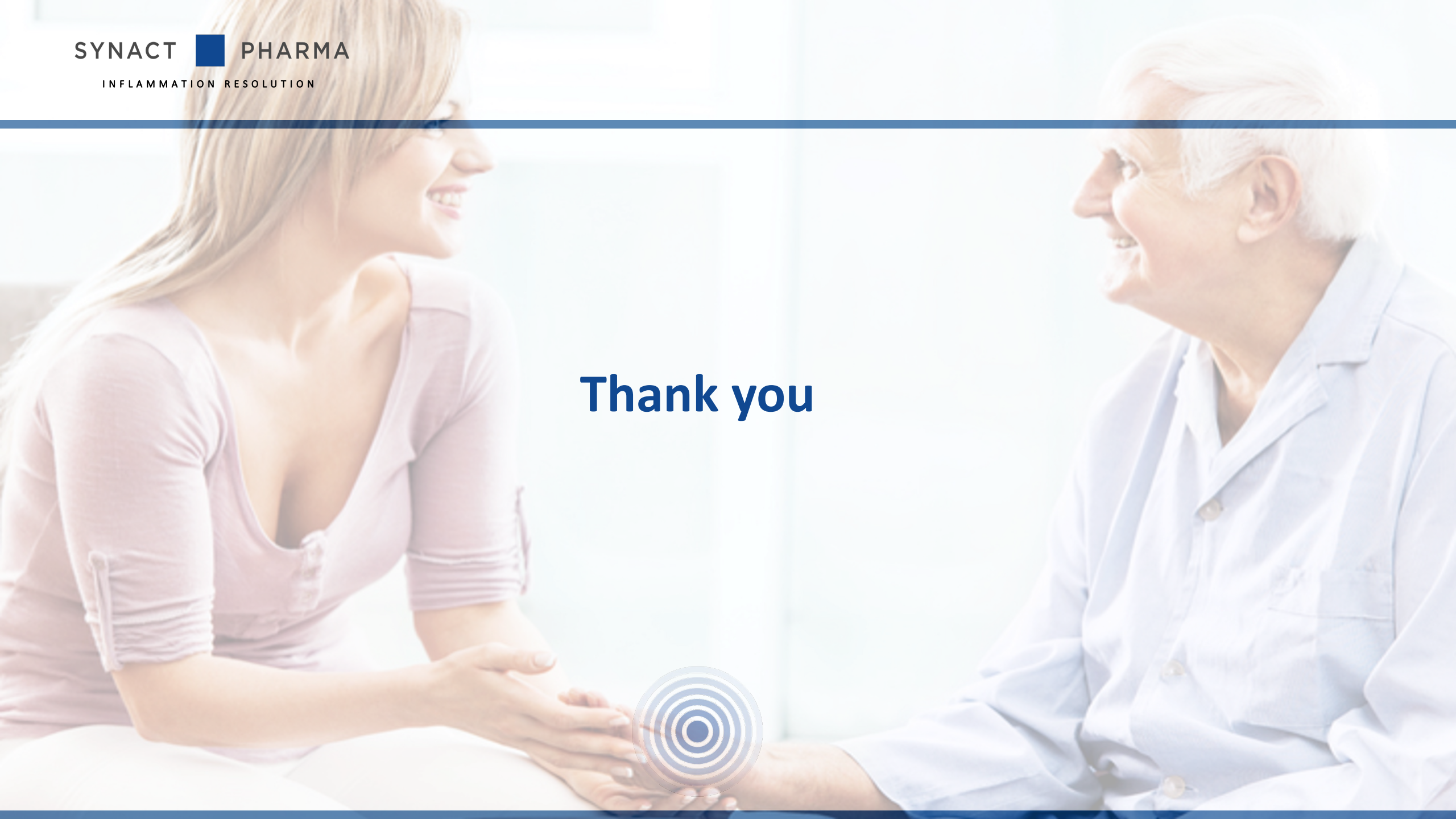

# Thank you