



Every Second Counts!™

Corporate Presentation
October 2020

Forward Looking Statements

This presentation (together with any other statements or information that we may make in connection herewith) contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 with respect to Kiniksa Pharmaceuticals, Ltd. (and its consolidated subsidiaries, collectively, unless context otherwise requires, “Kiniksa,” “we,” “us” or “our”). In some cases, you can identify forward looking statements by terms such as “may,” “will,” “should,” “expect,” “plan,” “anticipate,” “could,” “intend,” “goal,” “design,” “target,” “project,” “contemplate,” “believe,” “estimate,” “predict,” “potential” or “continue” or the negative of these terms or other similar expressions, although not all forward-looking statements contain these identifying words. All statements contained in this presentation that do not relate to matters of historical fact should be considered forward-looking statements, including without limitation, statements regarding our strategy; potential acquisitions and collaborations; potential value drivers; potential indications; potential market opportunities and competitive position; on going, planned and potential clinical trials and other studies; timing and potential impact of clinical data; regulatory and other submissions, applications and approvals; commercial strategy and pre-commercial activities; expected run rate for our cash, cash equivalents and short-term investments; expected funding of our operating plan; and capital allocation.

These statements involve known and unknown risks, uncertainties, and other important factors that may cause our actual results, performance or achievements to be materially different from those expressed or implied by the forward-looking statements, including without limitation potential delays or difficulties with our clinical trials; potential inability to demonstrate safety or efficacy or otherwise producing negative, inconclusive or uncompetitive results; potential for changes in final data from preliminary or interim data; potential inability to replicate in later clinical trials positive results from earlier trials and studies; our reliance on third parties for manufacturing and conducting clinical trials, research and other studies; potential changes in our strategy, operating plan and funding requirements; drug substance and/or drug product shortages; substantial new or existing competition; potential impact of the COVID-19 pandemic, and measures taken in response to the pandemic, on our business and operations as well as the business and operations of our manufacturers, CROs upon whom we rely to conduct our clinical trials, and other third parties with whom we conduct business or otherwise engage, including the FDA and other regulatory authorities; and our ability to attract and retain qualified personnel. These and the other important factors are discussed under the caption “Risk Factors” in our Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (the “SEC”) on August 4, 2020 and other filings subsequently filed with the SEC. These forward-looking statements reflect various assumptions of Kiniksa's management that may or may not prove to be correct. No forward-looking statement is a guarantee of future results, performance, or achievements, and one should avoid placing undue reliance on such statements. Except as otherwise indicated, this presentation speaks as of the date of this presentation. We undertake no obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise.

This presentation also contains estimates, projections, and/or other information regarding our industry, our business and the markets for certain of our product candidates, including data regarding the estimated size of those markets, and the incidence and prevalence of certain medical conditions. Unless otherwise expressly stated, we obtained this industry, business, market and other data from reports, research surveys, clinical trials, studies and similar data prepared by market research firms and other third parties, from industry, medical and general publications, and from government data and similar sources. Information that is based on estimates, forecasts, projections, market research, or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information.

A Clinical-Stage Pipeline of Immune-Modulating Product Candidates



Every Second Counts!™

Focused on modulating different parts of the innate and adaptive immune system

Product candidates based on validated mechanisms and/or strong biologic rationale

Target underserved conditions and offer potential differentiation

Allocate capital across portfolio relative to opportunity

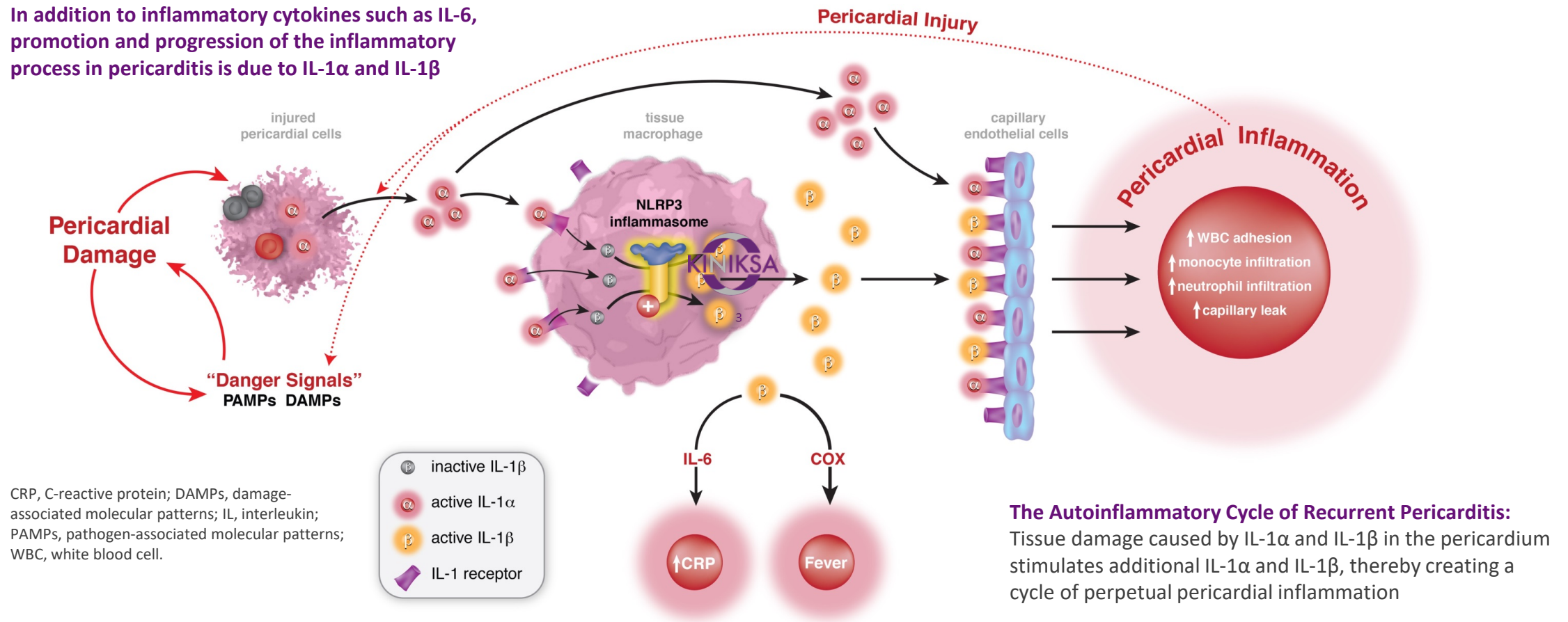
Product Candidates and Clinical Status

Disease Area	Program & Target	Preclinical	Phase 1	Phase 2	Phase 3	Status
Recurrent Pericarditis ¹	Rilonacept² IL-1α & IL-1β					Phase 3 Data Reported in Q3 2020
Giant Cell Arteritis	Mavrilimumab GM-CSFRα					Phase 2 Data Reported in Q4 2020
COVID-19 Pneumonia & Hyperinflammation	Mavrilimumab GM-CSFRα					Adaptive Design Phase 2/3 Initiated in Q3 2020
Prurigo Nodularis	Vixarelimab OSMRβ					Phase 2b Initiation Expected in Q4 2020
Severe Autoimmune Diseases	KPL-404 CD40					Phase 1 Data Expected in Q4 2020

Indication¹	Recurrent Pericarditis: Painful and debilitating autoinflammatory cardiovascular disease
Mechanism of Action²	IL-1 α and IL-1 β cytokine trap
Scientific Rationale²	IL-1 α and IL-1 β are cytokines shown to play key role in inflammatory diseases
Prevalence³	~40k prevalent in U.S.; initially-addressable opportunity of ~14k in U.S.
Competition⁴	No FDA-approved therapies for recurrent pericarditis
Regulatory	U.S. Orphan Drug designation in pericarditis and Breakthrough Therapy designation in recurrent pericarditis
Status	sBLA being submitted to the FDA in recurrent pericarditis in 2020
Economics	50/50 profit split on the approved indications in the U.S.
Rights	BLA in CAPS transferring to Kiniksa; upon approval Kiniksa has the rights to recurrent pericarditis worldwide (excluding MENA)

Role of IL-1 α and IL-1 β in the Autoinflammatory Cycle of Recurrent Pericarditis

In addition to inflammatory cytokines such as IL-6, promotion and progression of the inflammatory process in pericarditis is due to IL-1 α and IL-1 β



Brucato A, et al. Int Emerg Med 2018 <https://doi.org/10.1007/s11739-018-1907-x>
Dinarello CA, et al. Nat Rev Drug Discov 2012;11:633-652

Recurrent Pericarditis Patients Currently Have Limited Treatment Options

Patients with pericarditis are deemed recurrent after symptom-free period of 4-6 weeks

Recurrent Pericarditis

1st Line

NSAID +/- Colchicine

2nd Line

Systemic Corticosteroids

Steroid-Sparing
Opportunity

3rd Line

IVIG, Azathioprine, Methotrexate, or Anakinra (off-label)

Refractory Patients

4th Line

Pericardiectomy

Recurrent Pericarditis Episodes are Painful, Debilitating and Disruptive to Quality of Life

"I cannot work, walk to the mailbox, or go up/down stairs without a great deal of pain and shortness of breath. Many referred visits to the ER because of pain, where ER docs accuse me of drug seeking for pain. It's humiliating and scary." ¹

Pericarditis Flares are Burdensome for Patients...

- Significant pain with similar symptoms as heart attack that **drive patients to the ER**^{1,2,5}
- After acute pain resolves, **residual pain** and other effects can last weeks to months^{1,2}
- Elevated **risk for major complications**, such as tamponade and constrictive pericarditis^{4,6}
- Results in **hospitalization and ER visits** for large proportion of patients^{1,4,6,7,8}
- Increased **absenteeism** driven by pain and anxiety^{1,2}

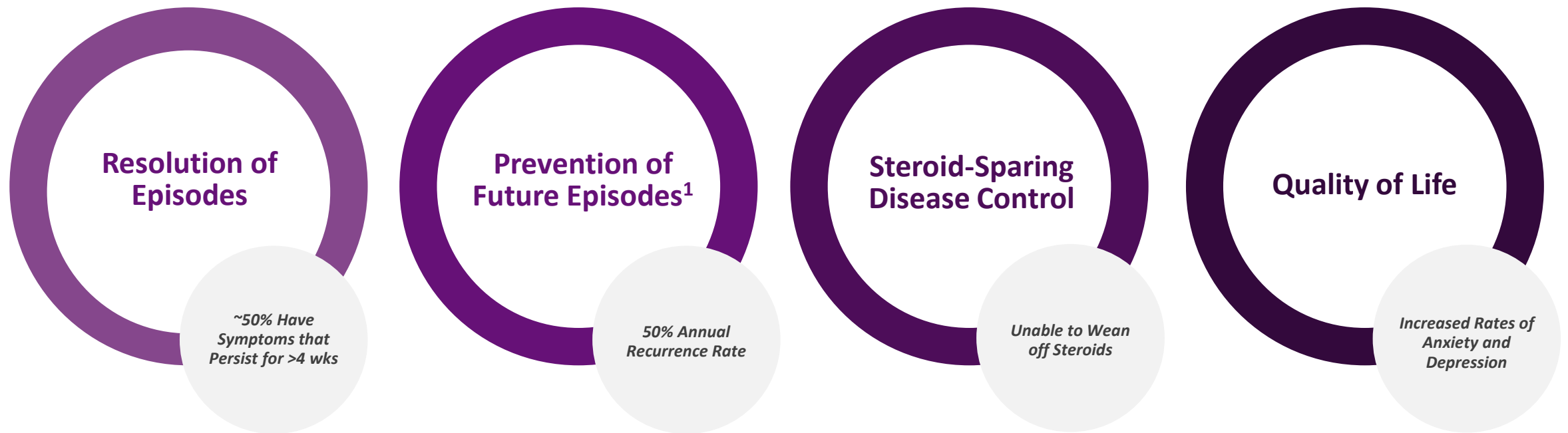
"I have gained a great deal of weight from steroids and inactivity. Exercise sets off more events, so am afraid to exercise. Pain is there constantly, just not as intense as it is during an event. [My] quality of life [is] greatly diminished." ¹

...And the Burden of the Disease Persists Even After the Flare Resolves

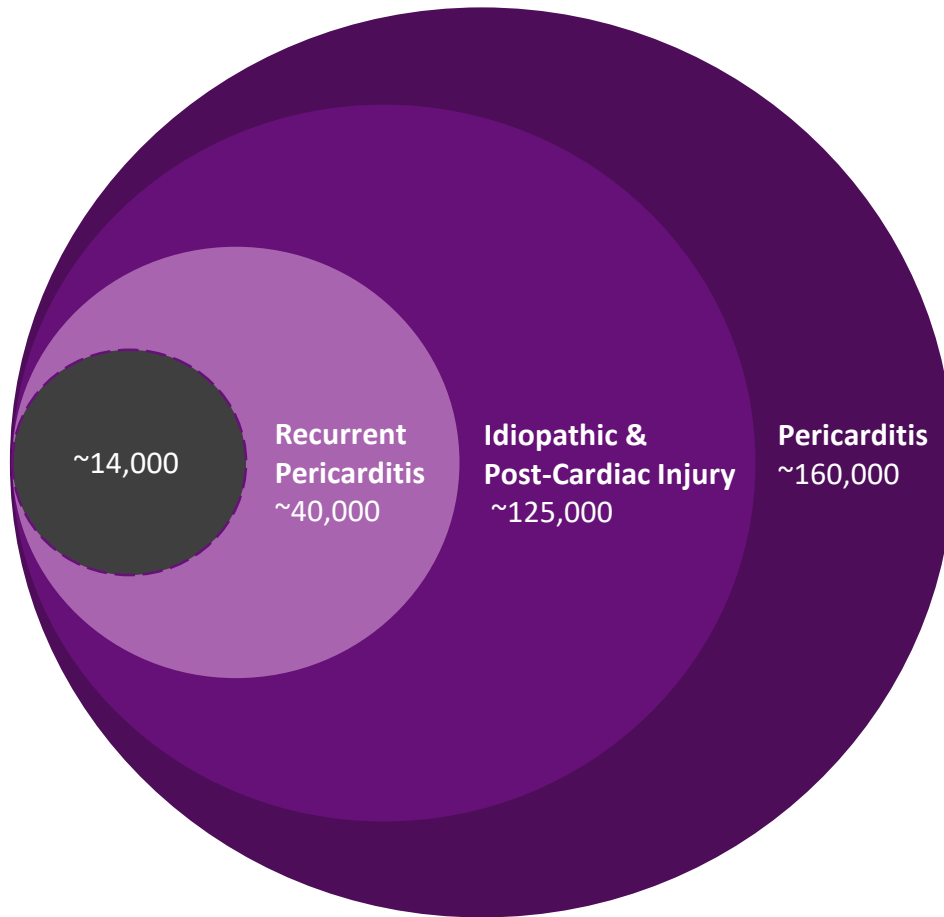
- Testimonials reveal **devastating impact on QoL** (anxiety, loss of sleep, lifestyle change, physical activity)^{1,2,5}
- Between flares, 48% of patient report their level of **fear of pericarditis** as "quite a bit" or "very much"⁹
- Corticosteroids have well known **safety and tolerability issues**, and increase recurrence rates with taper^{1,2,4,5,6,7}
- Significantly **worse QoL than general population** - Ph2 PROMIS physical and mental health³
- Increased **depression and anxiety** diagnoses seen in claims data following initial pericarditis event⁴
- 98% of patients express **need for additional therapies** that reduce the likelihood of another recurrence¹

Key Areas of Unmet Need in Patients with Recurrent Pericarditis

Recurrent pericarditis episodes: painful, debilitating and disruptive to quality of life



Pericarditis Epidemiology



All figures annual period prevalence

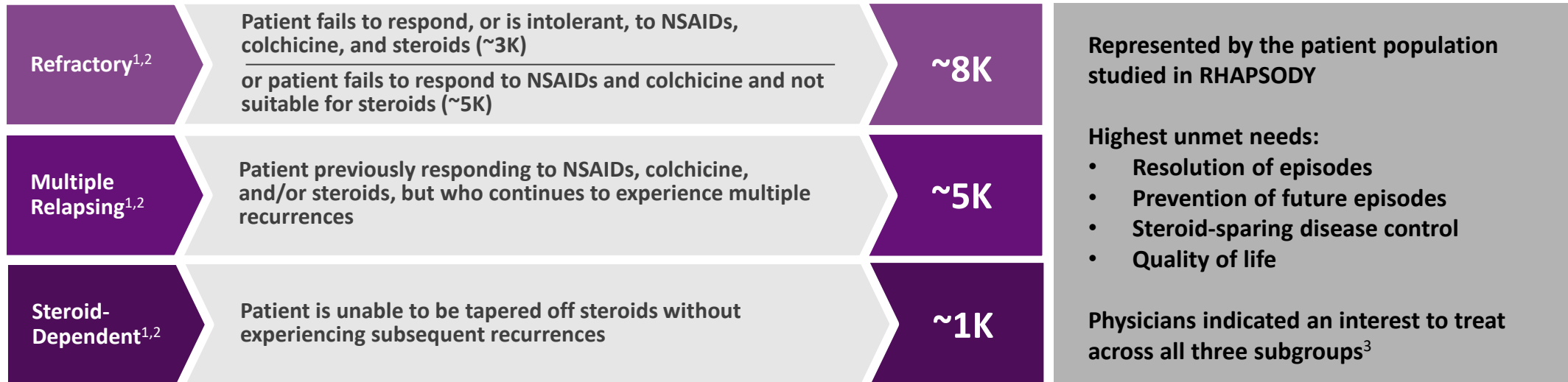
Approximately 14,000 recurrent pericarditis patients suffer from persistent underlying disease, with multiple recurrences and inadequate response to conventional therapy¹

- **~ 160,000:** Epidemiological analysis using large national surveillance databases to calculate the pooled annualized prevalence of pericarditis
(Basis for Orphan Drug Designation approval)²
- **~125,000:** Approximately 75-80% are considered idiopathic (thought to be post-viral) and post cardiac injury³⁻⁵
- **~40,000:** Up to 30% experience at least one recurrence; some recur over multiple years^{6,7}
- **~14,000:** Nearly 50% annual turnover with ~7,000 patients coming into the pool each year⁸

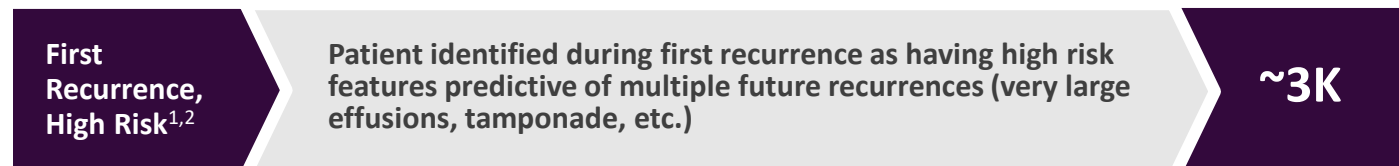
Recurrent Pericarditis U.S. Prevalence Estimated to be ~40K Patients

~14K patients with inadequate response to conventional therapy and persistent underlying disease

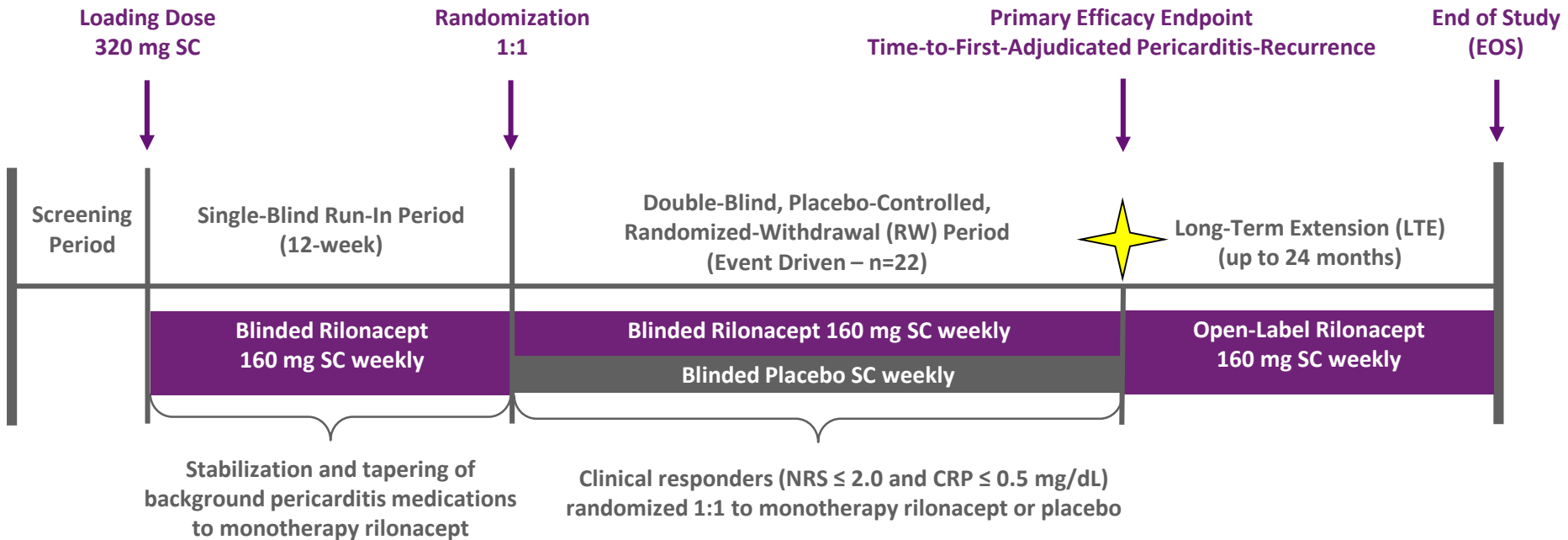
Clear Call to Action: ~14K Patients



Potential to Broaden Utilization Over Time: ~3K Patients



Design of Pivotal Phase 3 Trial of Rilonacept in Recurrent Pericarditis



Inclusion Criteria:

- All etiologies except infection and malignancy
- Present at screening with at least a third pericarditis episode, defined as at least 1 day with **NRS pain of ≥ 4** and **CRP value ≥ 1 mg/dL** within the 7-day period prior to first study drug administration
- Concomitant NSAIDs and/or colchicine and/or oral corticosteroid treatment in any combination

Primary Efficacy Endpoint :

- Time-to-first-adjudicated pericarditis-recurrence in the RW period

Major Secondary Efficacy Endpoints (16-weeks):

- Proportion of subjects who maintained Clinical Response
- Percentage of days with no or minimal pain
- Proportion of subjects with absent or minimal pericarditis symptoms

CEC Adjudication Criteria:

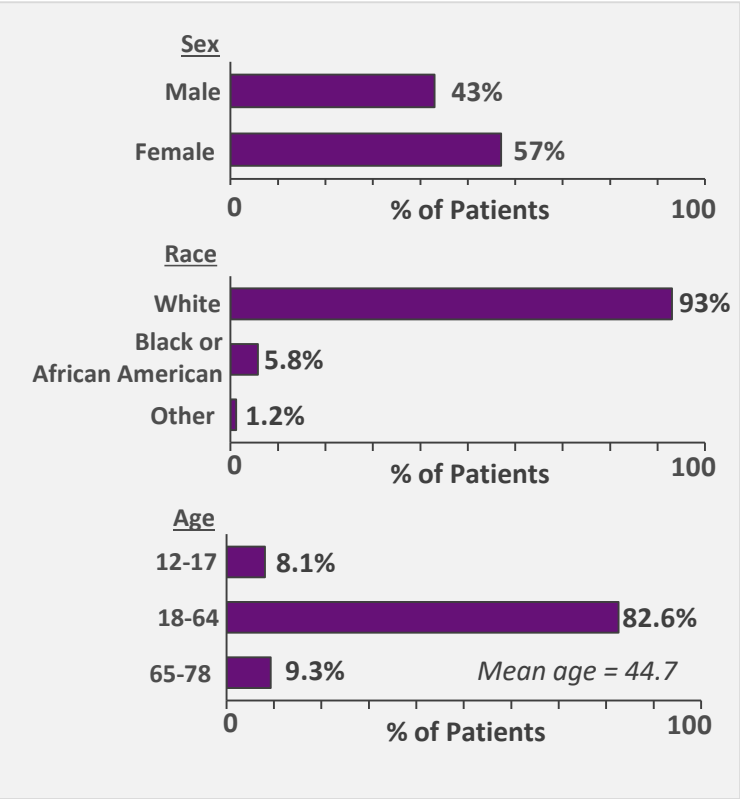
- Typical pericarditis pain (≥ 1 pain **NRS recording ≥ 4**) AND elevated **CRP (≥ 1.0 mg/dL)**, same day or ≤ 7 days
- Typical pericarditis pain (≥ 1 pain **NRS recording ≥ 4**) AND abnormal **CRP (>0.5 mg/dL)**, same day or ≤ 7 days AND ≥ 1 **supportive evidence** of pericarditis
- Typical pericarditis pain (BUT pain **NRS recording ≤ 4**) AND elevated **CRP (≥ 1.0 mg/dL)**, AND ≥ 1 **supportive evidence** of pericarditis

Baseline Demographics and Clinical Characteristics

Pivotal Phase 3 Rilonacept Data

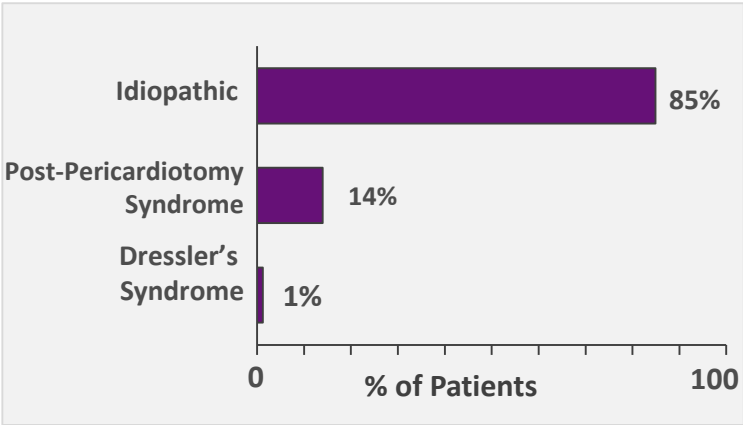


Baseline Demographics (n=86)

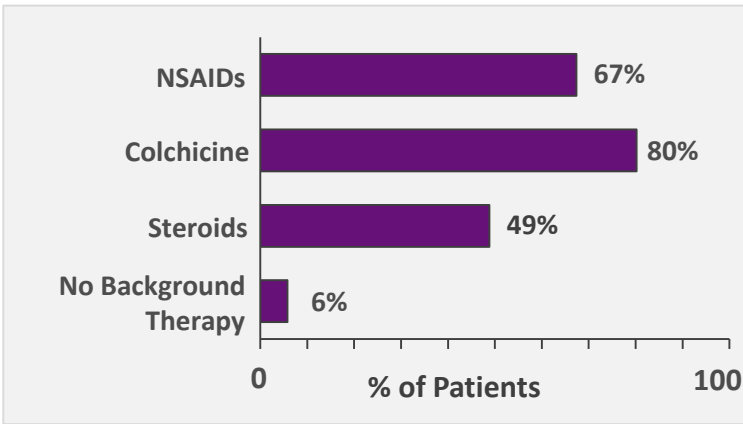


Total Number of Episodes Including Index and Qualifying Episodes	Run-in Period (n=86)
Mean	4.7

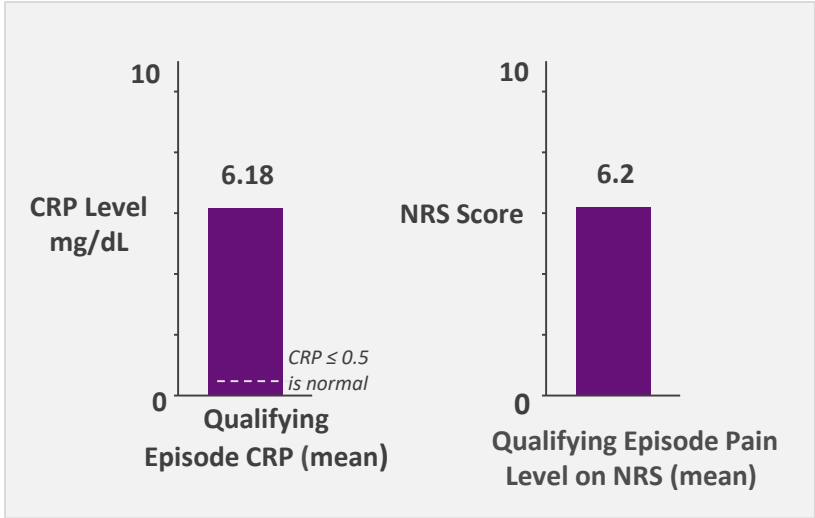
Prior Pericarditis History at Baseline (n=86)



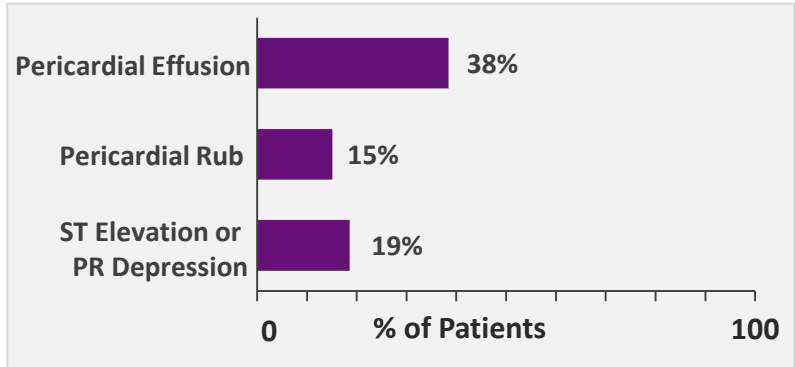
SoC Received at Qualifying Episode (n=86)



Qualifying Episode CRP & NRS (n=86)



Pericarditis Manifestations at Qualifying Episode (n=86)

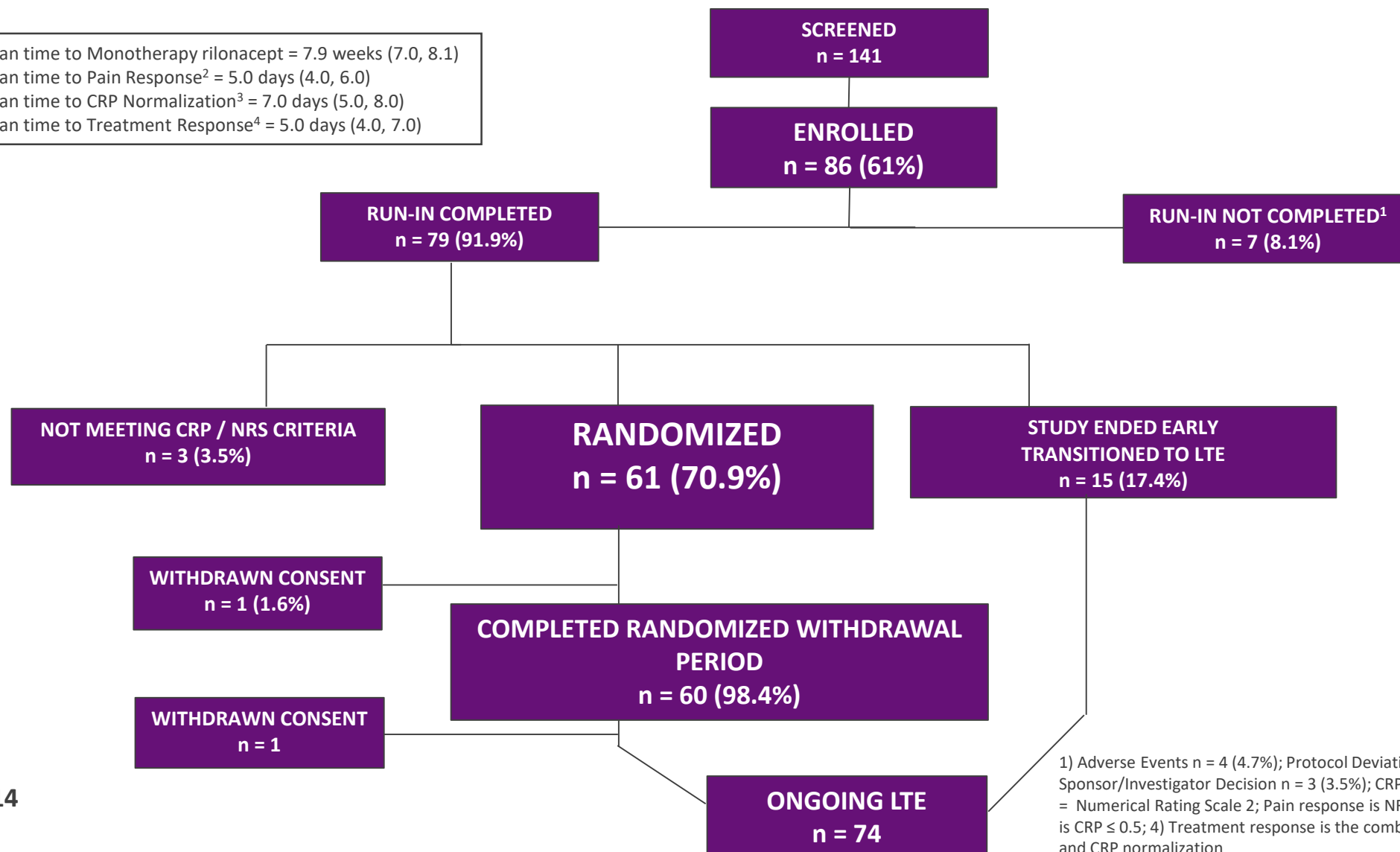


Subject Disposition

Pivotal Phase 3 Rilonacept Data

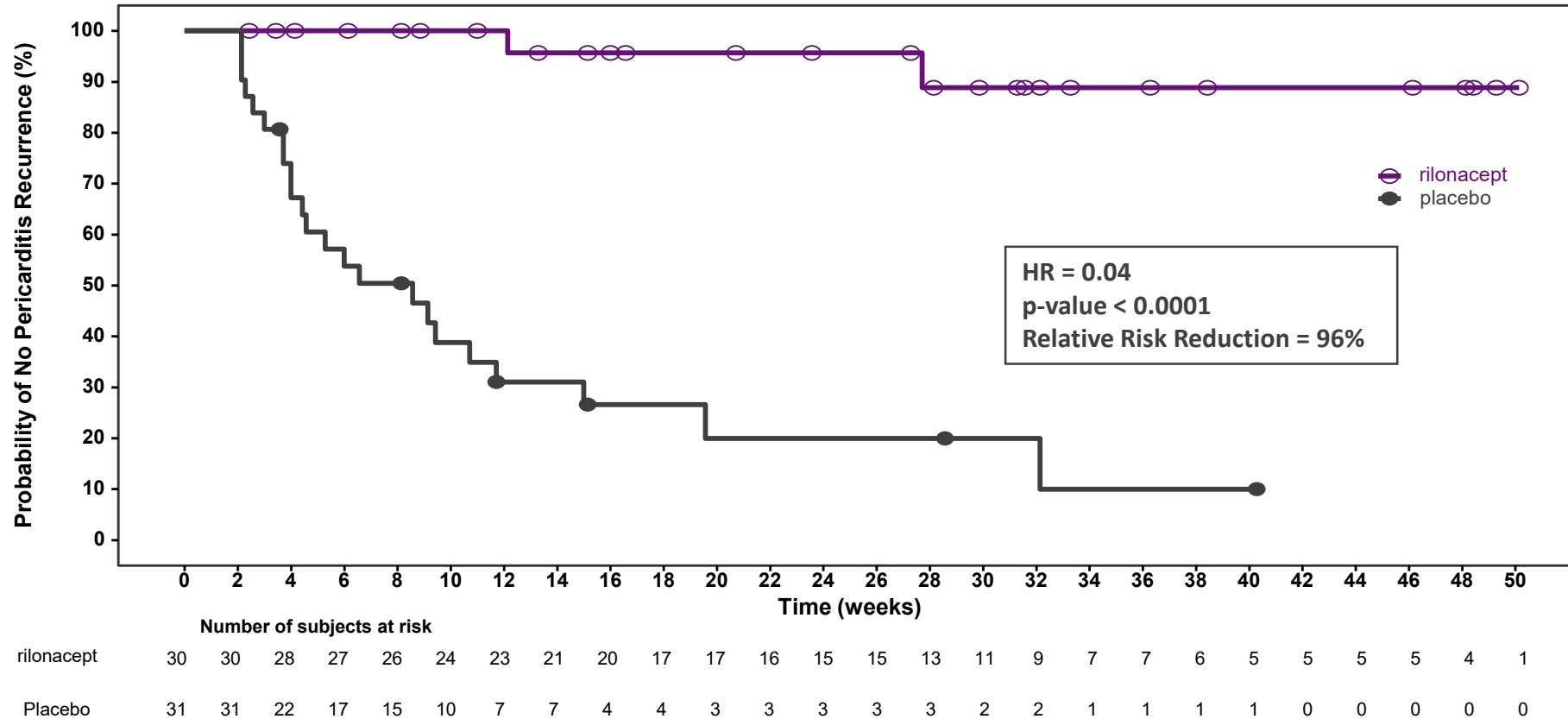


Median time to Monotherapy rilonacept = 7.9 weeks (7.0, 8.1)
Median time to Pain Response² = 5.0 days (4.0, 6.0)
Median time to CRP Normalization³ = 7.0 days (5.0, 8.0)
Median time to Treatment Response⁴ = 5.0 days (4.0, 7.0)



Primary Efficacy Endpoint: Time-to-First Adjudicated Pericarditis Recurrence

Pivotal Phase 3 Rilonacept Data



Pericarditis Recurrence Categories, n (%)	Rilonacept (N=30)	Placebo (N=31)
Number of Subjects with Events (Adjudicated Pericarditis Recurrence), n(%)	2 (6.7)	23 (74.2)
Time to First Adjudicated Pericarditis Recurrence; Median, 95% CI (Weeks)	NE (NE, NE)	8.6 (4.0, 11.7)

NE = Not Estimable

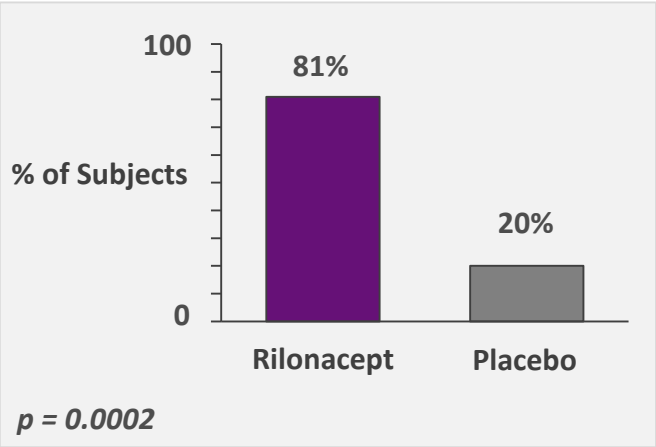


Secondary Endpoints at Week 16 of the Randomized Withdrawal Period

Pivotal Phase 3 Rilonacept Data

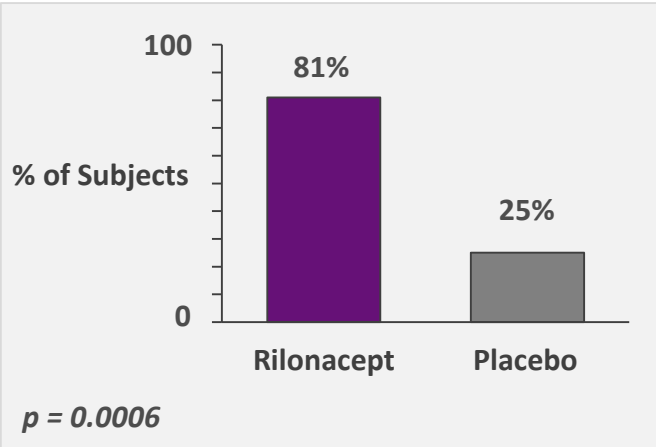


Proportion of Subjects Who Maintained Clinical Response ¹



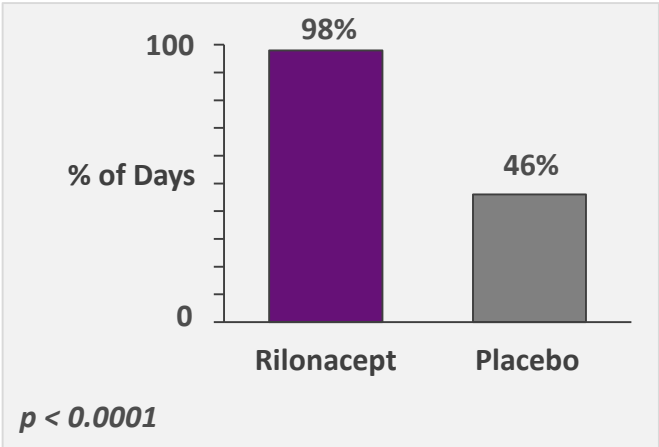
Data at Weeks 8 and 24 were consistent and statistically significant
(Week 8, $p < 0.0001$; Week 24, $p=0.0022$)

Proportion of Subjects with Absent/Minimal Pericarditis Symptoms based on the 7-point PGIPS ²



Data at Weeks 8 and 24 were consistent and statistically significant
(Week 8, $p < 0.0001$; Week 24, $p=0.0002$)

Percent of Days with No or Minimal Pain in First 16 Weeks (ITT Week 16) ³



Data at Weeks 8 and 24 were consistent and statistically significant
(Week 8, $p < 0.0001$; Week 24, $p < 0.0001$)

1) Clinical Response is defined as a weekly average of daily pericarditis pain of ≤ 2.0 on the 11-point NRS, CRP level ≤ 0.5 mg/dL, and on monotherapy of randomized study drug in that week. Subjects who had recurrence, or used bailout rilonacept, or used rescue medication, discontinued double-blinded treatment, or lost to follow-up before the week will be considered as non-responders;

2) PGIPS = Patient Global Impression of Pericarditis Severity baseline;

3) No or minimal pain is defined as non-missing daily NRS ≤ 2 . The percentage of days with no or minimal pain in the first 24, 16, and 8 weeks is calculated for each subject using 24x7, 16x7, 8x7, respectively, as the denominator. Missing values in pain diary will be counted as 0 day with no or minimal pain. On days of using ORT or corticosteroid, count as 0 day with no or minimal pain. If bailout rilonacept was used, each administration (loading dose or not) will be counted as 7 days without qualifying no or minimal pain.



Summary of Adverse Events

Pivotal Phase 3 Rilonacept Data



	Run-In Period	Randomized Withdrawal Period	
Category ¹	Rilonacept (N=86) n (%)	Rilonacept Including Bailout Rilonacept (N=30) n (%)	Placebo Only Before Bailout Rilonacept (N=31) n (%)
All Adverse Events	69 (80.2)	24 (80.0)	13 (41.9)
TEAEs ²	69 (80.2)	24 (80.0)	13 (41.9)
TEAEs by Maximum severity ³			
Mild	52 (60.5)	16 (53.3)	9 (29.0)
Moderate	15 (17.4)	8 (26.7)	4 (12.9)
Severe	2 (2.3)	0	0
Drug-Related TEAEs ⁴	46 (53.5)	10 (33.3)	1 (3.2)
Serious TEAEs (SAE) ⁵	1 (1.2)	1 (3.3)	1 (3.2)
TEAEs Leading to Death	0	0	0
Drug-Related SAE ⁴	0	0	0
TEAEs Leading to Dose Interruption	0	1 (3.3)	0
TEAEs Leading to Study Drug Discontinuation	4 (4.7) ⁶	0	0
TEAEs of Special Interest (Malignancy) ⁷	0	1 (3.3)	0
TEAEs of Injection Site Reaction	28 (32.6)	6 (20.0)	0
TEAEs of Injections and Infestations	14 (16.3)	12 (40.0)	3 (9.7)

	Run-In Period	Randomized Withdrawal Period	
Category ¹	Rilonacept (N=86) n (%)	Rilonacept Including Bailout Rilonacept (N=30) n (%)	Placebo Only Before Bailout Rilonacept (N=31) n (%)
Bronchitis	0	1 (3.3)	0
Conjunctivitis	0	1 (3.3)	0
Ear infection	0	0	0
Gastroenteritis	0	0	1 (3.2)
Gastroenteritis viral	0	0	0
Gastroenteritis viral infection	0	1 (3.3)	1 (3.2)
Hordeolum	1 (1.2)	0	0
Influenza	1 (1.2)	0	1 (3.2)
Nasopharyngitis	6 (7.0)	2 (6.7)	0
Oral herpes	1 (1.2)	1 (3.3)	0
Otitis media	0	1 (3.3)	0
Pharyngitis	1 (1.2)	0	0
Pharyngitis streptococcal	0	0	0
Rhinitis	1 (1.2)	0	0
Sinusitis	1 (1.2)	3 (10.0)	0
Subcutaneous abscess	1 (1.2)	0	0
Upper respiratory tract infection	2 (2.3)	1 (3.3)	0
Urinary tract infection	1 (1.2)	3 (10.0)	0
Vaginal infection	0	1 (3.3)	0
Viral upper respiratory tract infection	2 (2.3)	1 (3.3)	0

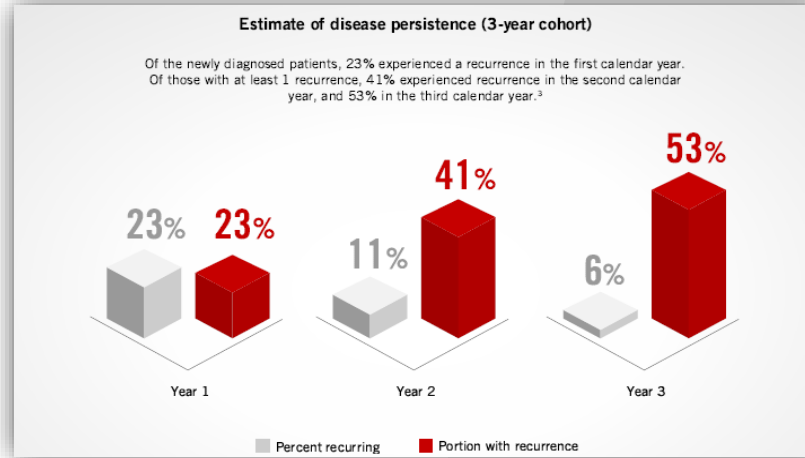
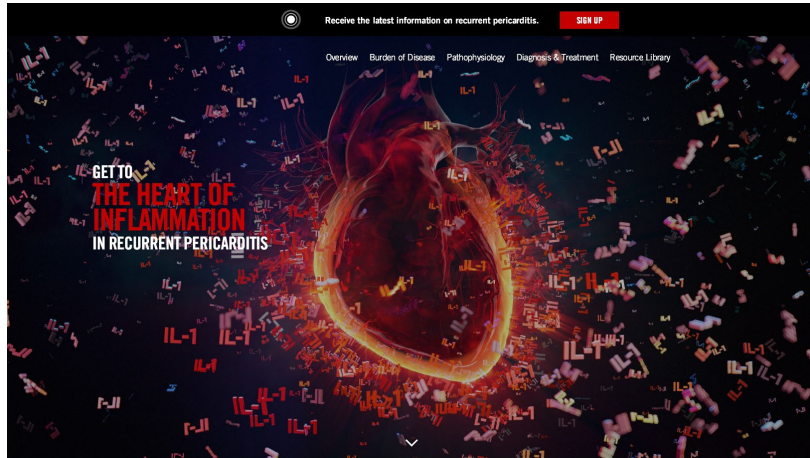
Strategic Imperatives for Commercial Launch of Rilonacept in Recurrent Pericarditis

Successful execution to physician adoption of rilonacept

	Unmet Need	Standard of Care	Payer Reimbursement	Patient Support
	Recurrent pericarditis is viewed as a serious, debilitating disease mediated primarily by IL-1	Aim for rilonacept to be the product of choice for the treatment and prevention of recurrent pericarditis	Broad patient access at a price that reflects rilonacept's value as a first-in-class IL-1 inhibitor of inflammation	Optimize the patient and customer experience with rilonacept and Kiniksa
Strategy	<ul style="list-style-type: none"> • Drive awareness and understanding of recurrent pericarditis and the role of inappropriate IL-1 production • Characterize and communicate burden of recurrent pericarditis on patients 	<ul style="list-style-type: none"> • Help ensure there is an understanding of the benefit/risk of rilonacept • Demonstrate scientific evidence that rilonacept targets the primary mediator of recurrent pericarditis disease pathophysiology (IL-1 overproduction) 	<ul style="list-style-type: none"> • Demonstrate product benefits, establish rapid payer coverage, and navigate potential access barriers • Implement scalable operations to support customers 	<ul style="list-style-type: none"> • Establish robust patient support programs • Provide a seamless experience for patients starting on rilonacept & support ongoing adherence
Tactics	<ul style="list-style-type: none"> • 'Heart of Inflammation' disease awareness campaign and website • Continued presence at scientific congresses • Virtual patient advisory boards, podcasts and videos 	<ul style="list-style-type: none"> • Specialty cardiovascular sales force • Efficient digital marketing • Peer to Peer speaker program • Patient support network • Scientific Congress Exhibits and Symposia (ACC, ESC, AHA) 	<ul style="list-style-type: none"> • Compelling value proposition and supportive tools (value dossier and budget impact model) • Comprehensive payer engagement plan • Specialty pharmacy network distribution network 	<ul style="list-style-type: none"> • High-touch patient support, reimbursement services, patient financial assistance, initiation support (Quick Start), injection training • Partner with the pericarditis community to improve advocacy, education and support for affected patients

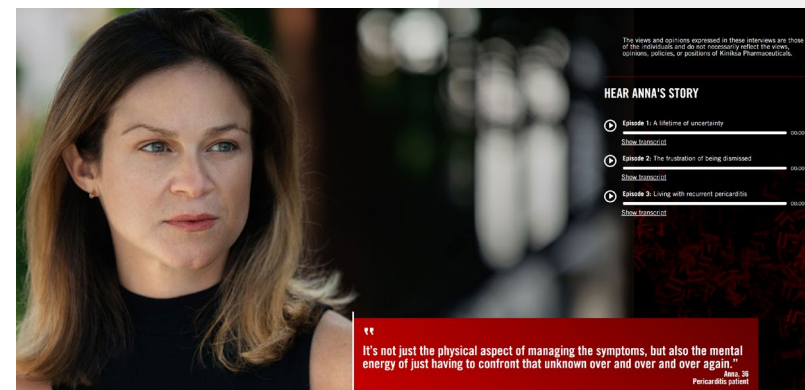
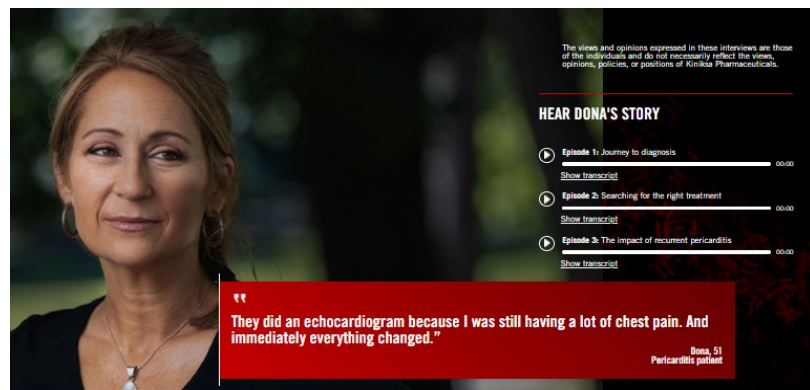
Unmet Need: 'Heart of Inflammation' Disease Awareness Campaign

Advancing physicians' perceptions of recurrent pericarditis and treatment behaviors



'Heart of Inflammation'

- Disease Overview
 - Epidemiology
 - Disease progression
 - Risk factors
- Burden of Disease
 - Patient podcasts
 - Health-related quality of life
- IL-1 Pathophysiology
 - Role of IL-1
- Diagnostics & Treatment
- Resource Library



Unmet Need: Multi-Channel Patient Support Network

Providing resources to help ensure an understanding of the benefit/risk of treatment

Peer Videos & Testimonials



Social Communication & Engagement



Patient Education



Patient Opt-In

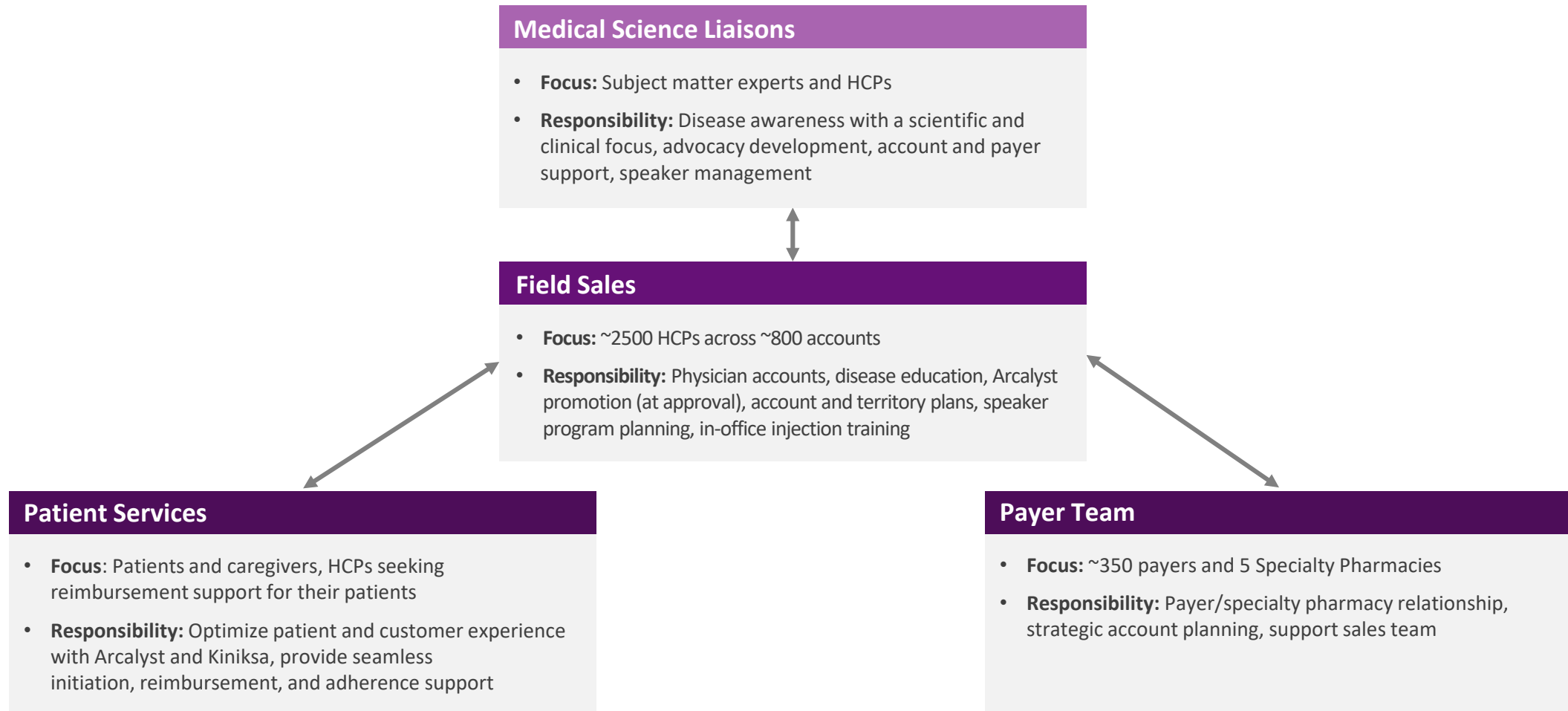
Access to Advocacy



"We are grateful to Kiniksa for taking interest in this disease and developing resources to help us. As people suffering from recurrent pericarditis, we feel alone and overlooked. We are looking to you for hope - hope that this won't last forever, hope that your drug will help us, hope that others won't have to suffer like we have. We are no longer in the dark. We now have your research and support to help us!" – Patient Advisor

Standard of Care: Kiniksa One

Building a collaborative field force to help enable rilonacept to be the product of choice for the treatment and prevention of recurrent pericarditis

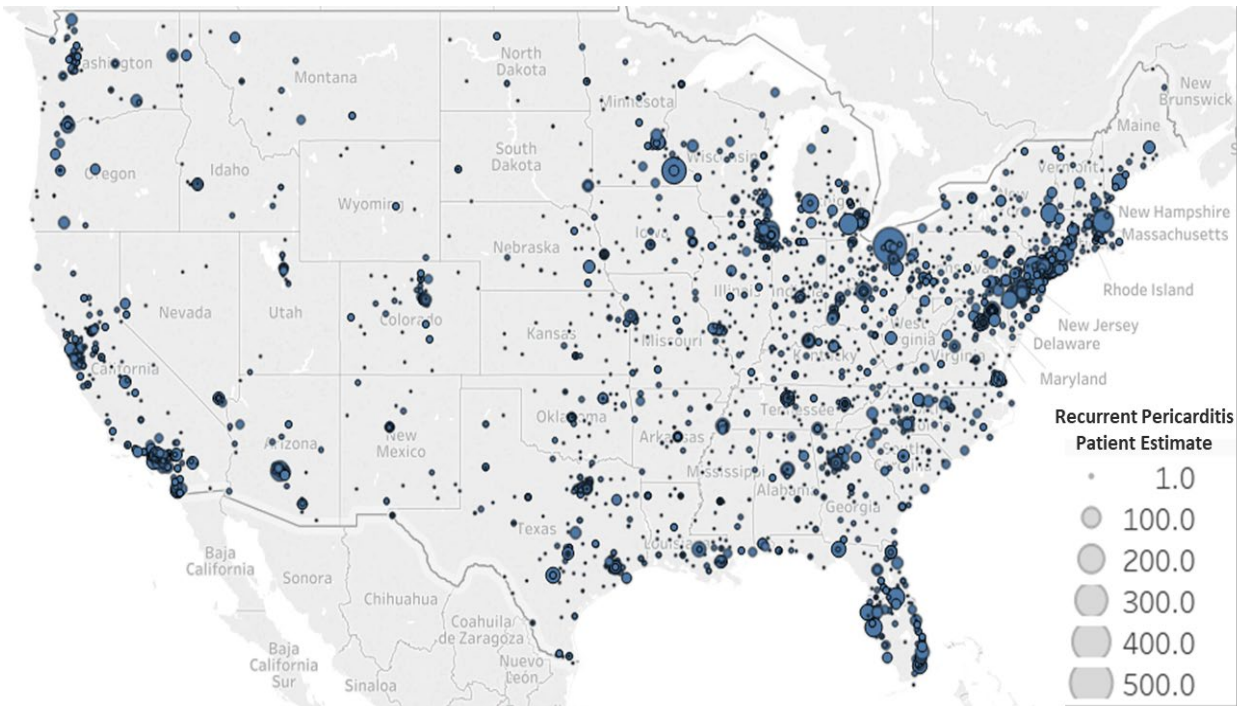


Note: Field teams will be trained to ensure compliance throughout all interactions.

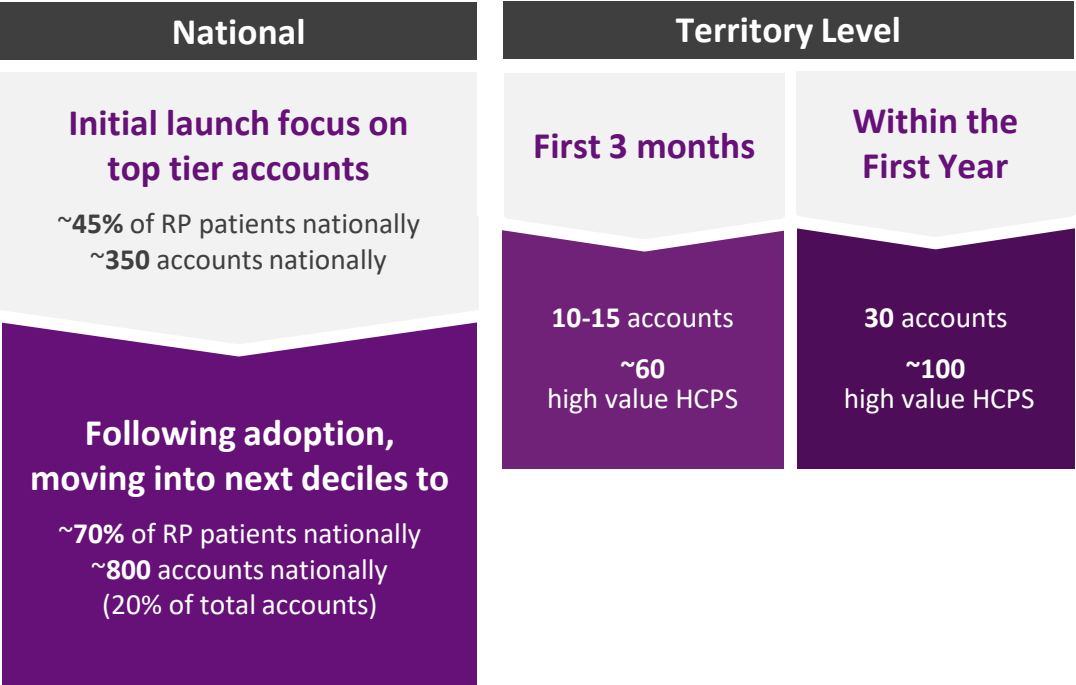
Standard of Care: Specialty Cardiovascular Sales Force

Planning to reach ~70% of recurrent pericarditis patients at top ~800 accounts

Estimated Recurrent Pericarditis Patients by Account



Focused & Targeted Sales Execution



Payer Reimbursement: Three-Phased Payer Engagement Plan

Facilitating broad access and affordability

1

Introduce Kiniksa

2

Disease Awareness

3

Support Payer Reviews

Desired Outcomes



Shortest Time Payer Review
and Coverage Policy Update



Most Favorable Formulary
Tier Means the Lowest
Patient Cost Burden



Least Burdensome
Coverage Restrictions

*Goal will be to avoid criteria that requires prior use of corticosteroids
and documented levels of C-reactive protein*

Patient Support: Programs to Help Provide a Seamless Experience

Facilitating initiation, adherence and retention



Enrollment Form & Patient
Consent Management



Adherence Program



Patient Assistance Program



Online Tools



Reimbursement, Prior Auth.
and Appeal Support



Non-Commercial
Dispensing Pharmacy



Specialty Pharmacy



Copay Card Support



Partner Integrations



Case Management



Quick Start



Data & Reporting



Injection Training



Bridge Program

Pricing and Treatment Duration Considerations

*The gross **price** for rilonacept (ARCALYST) in CAPS is \$20,000 per month based on the weekly administration; in-line with specialty biologics with Breakthrough Therapy designation, Orphan Drug designation and high unmet need*

*Our expectations are consistent with the RHAPSODY dataset; our initial assessment is that patients could be treated for at least 6 to 9 months, and the appropriate **treatment duration** for some patients may be 12 months or longer*

Inputs to Determining Optimal Treatment Duration

- **Average Duration of Recurrent Pericarditis is 2 Years¹**
 - The presence of certain baseline characteristics may identify patients who may benefit from longer-term treatment
- **Median treatment duration in RHAPSODY was 9 months, with a range up to 15 months**
 - Rilonacept treatment was associated with a 96% reduction in risk for pericarditis recurrence
 - Patients on rilonacept experienced none/minimal pericarditis pain for 98% of trial days
 - 74/75 patients continued into LTE for longer-term therapy, demonstrating a desire to continue to a duration of up to 24 months
- **Data support longer treatment duration: continued treatment resulted in continued treatment response**
 - Registry data indicate patients treated for 6 months have worse outcomes compared to patients treated for 9 months²
 - The only events in the rilonacept arm in RHAPSODY took place in the setting of temporary drug interruptions of 1-3 weeks.
 - All patients in the placebo arm who received bailout rilonacept did not experience a recurrence through the end of the RW period
- **Additional data will be available through LTE where patients are assessed for observed treatment cessation (with imaging) at 18 months³**

1) D. Lin, et al.; Recurrence Burden in Recurrent Pericarditis: A US-Based Retrospective Study of Administrative Healthcare Claims; Quality of Care and Outcomes Research (QCOR) 2020 Scientific Sessions; 2) M. Imazo, et al.; *Anakinra for corticosteroid-dependent and colchicine-resistant pericarditis: The IRAP (International Registry of Anakinra for Pericarditis) study*. European Journal of Preventative Cardiology 2019; 3) A. Klein, et al.; 2020 AHJ Reference for Phase 3 design

Summary of Rilonacept Profit Share Arrangement with Regeneron¹



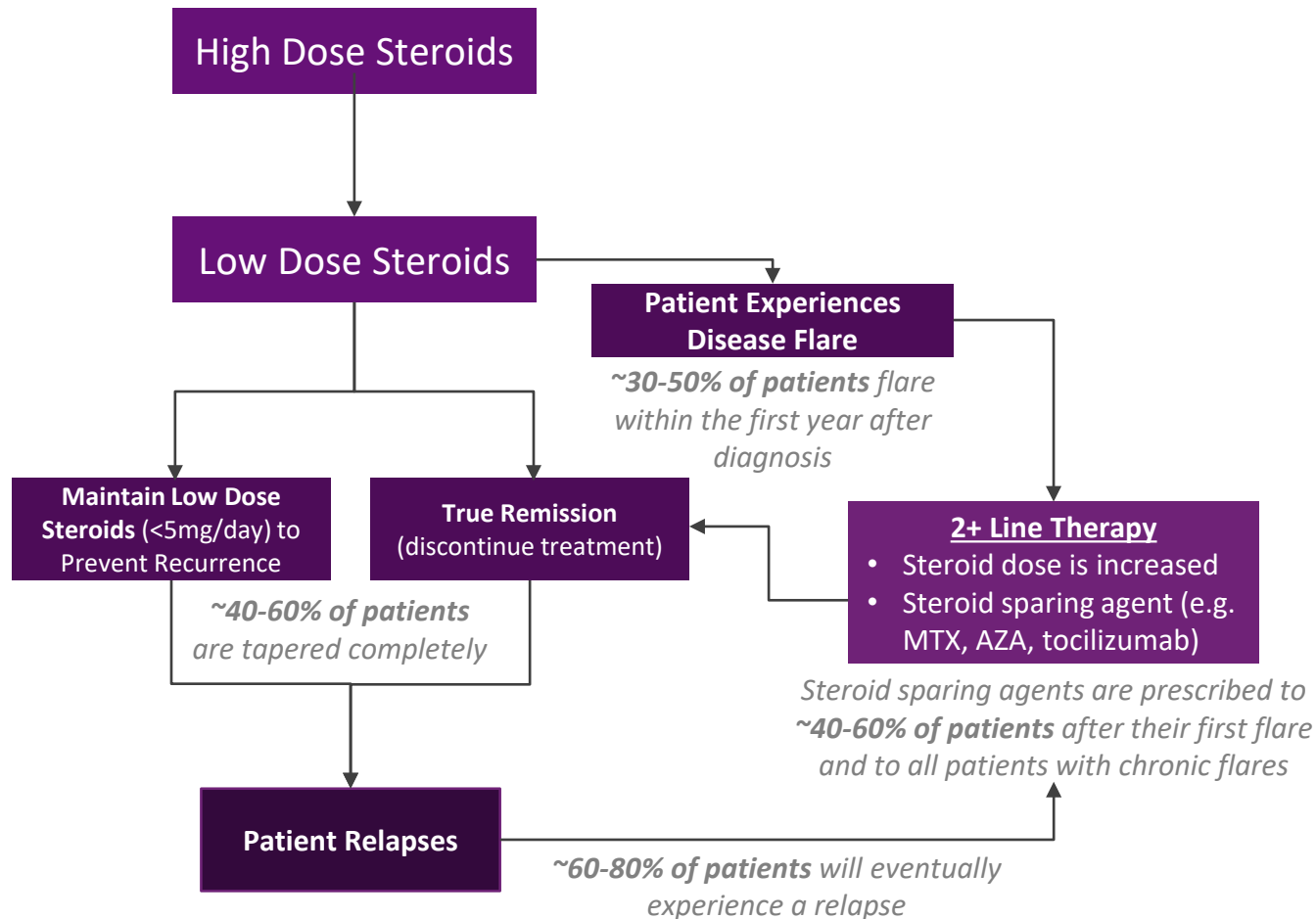
- Upfront payment: \$5 million
- Future regulatory milestones: \$27.5 million in aggregate
- Kiniksa covers 100% of development expenses related to approval of additional indications
- In the U.S. and Japan, the initial license covers all indications other than CAPS⁴, DIRA⁵, oncology, and local application for eye and inner ear
- Kiniksa has rights to develop and commercialize rilonacept in our field worldwide, with the exception of MENA⁶
- The BLA for rilonacept in CAPS is being transferred to Kiniksa following highly statistically significant Phase 3 clinical data⁷
- Upon approval for a new indication, the scope of the license expands to include CAPS and DIRA in the US and Japan, and we will assume the sales and distribution of rilonacept in these additional indications
- Profits on sales of rilonacept will be equally split after deducting certain commercialization expenses subject to specified limits

Mavrilimumab

Indications	Giant Cell Arteritis (GCA): Chronic inflammatory disease of medium-to-large arteries COVID-19 Pneumonia and Hyperinflammation
Mechanism of Action ¹	Monoclonal antibody inhibitor targeting GM-CSFR α
Scientific Rationale ²	GM-CSF is a key growth factor and cytokine in autoinflammation and autoimmunity
Prevalence	GCA ³ : ~75k - 150k prevalent in U.S.; similar prevalence in other major markets COVID-19 Pneumonia and Hyperinflammation (based on ARDS associated w/ the seasonal flu) ⁴ : ~150,000 in U.S.
Competition ⁵	Only one FDA-approved therapy for GCA and COVID-19, but unmet needs remain
Regulatory	U.S. Orphan Drug designation in GCA
Status	Phase 2 data in GCA reported in Q4 2020; Phase 2/3 in severe COVID-19 pneumonia and hyperinflammation initiated; Data from a U.S. IIS in severe COVID-19 pneumonia and hyperinflammation expected in Q4 2020
Economics	Clinical, regulatory and sales milestones; tiered royalty on annual net sales
Rights	Worldwide

1) Wicks, Roberts, Nature Review Immunology, 2015; Hamilton, Expert Review of Clinical Immunology, 11:4, 457-465; 2) Wicks & Roberts. Nature Reviews. Rheumatology, 2016; 12(1):37-48; 3) Chandran et al., Scand J Rheumatol, 2015; Trinity Consulting – HCUP/Medicare Data, Quantitative Survey (n=102 rheumatologists); 4) <https://www.cdc.gov/flu/about/burden/index.html>; <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3192778/>; <https://www.atsjournals.org/doi/pdf/10.1164/rccm.201401-0066LE>; <https://pdfs.semanticscholar.org/f3cb/d0574dc85304366dfadbd477b5eb7a271f43.pdf>; <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3198489/>; 5) Cortellis, UpToDate; Correspondence, Trial of Tocilizumab in Giant-Cell Arteritis, NEJM, 2017

Current Treatment Paradigm for GCA Involves High-Dose Steroids Upon Clinical Suspicion

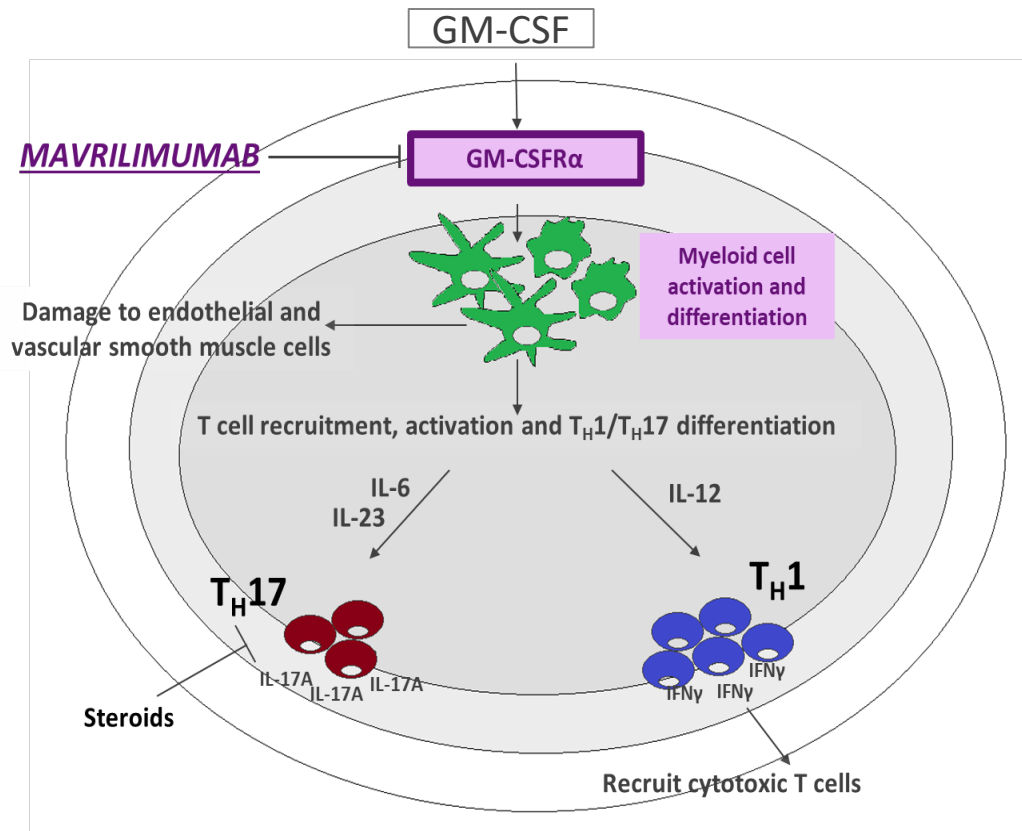


Treatment Approach:

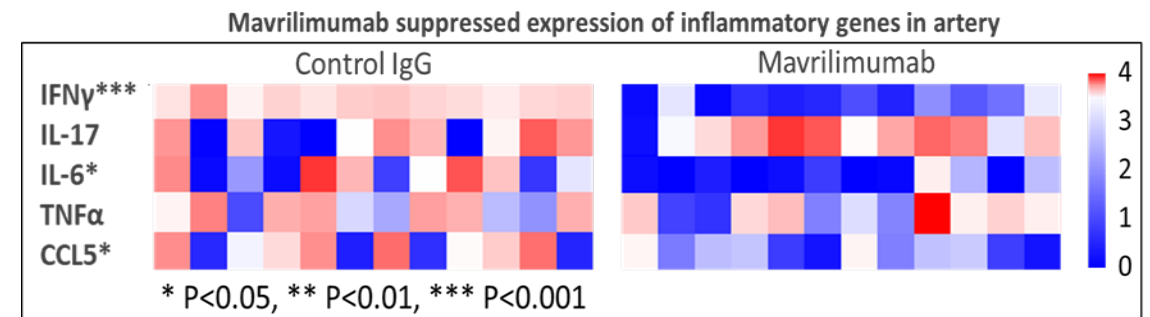
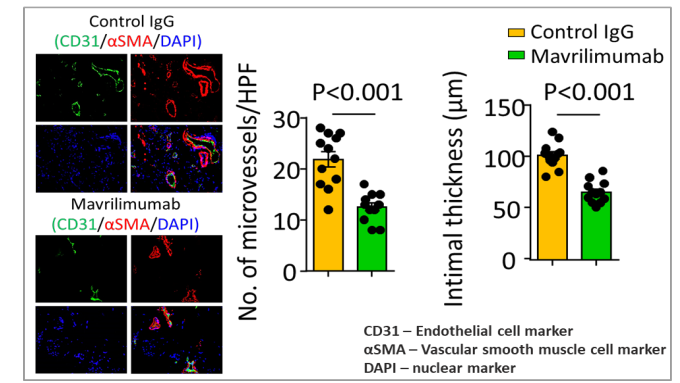
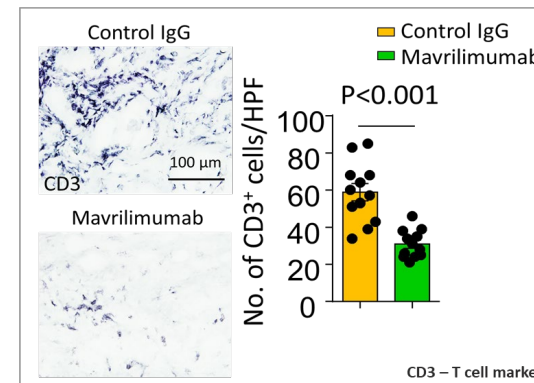
- All treated patients receive **high-dose steroids**, which are effective at preventing disease related complications; however, **they may lead to life altering side-effects** like osteoporosis and diabetes
- A few treaters initiate **steroid sparing agents** early in the treatment paradigm, relying on them more for the chronic treatment of GCA
- Others treat GCA in more of a stepwise fashion, adding new agents on top of steroids only following disease flares/relapse

Preclinical Data Support the Mechanistic Rationale of Targeting GM-CSF in GCA

GM-CSF and its receptor, GM-CSFR α , shown to be elevated in GCA biopsies compared to control¹



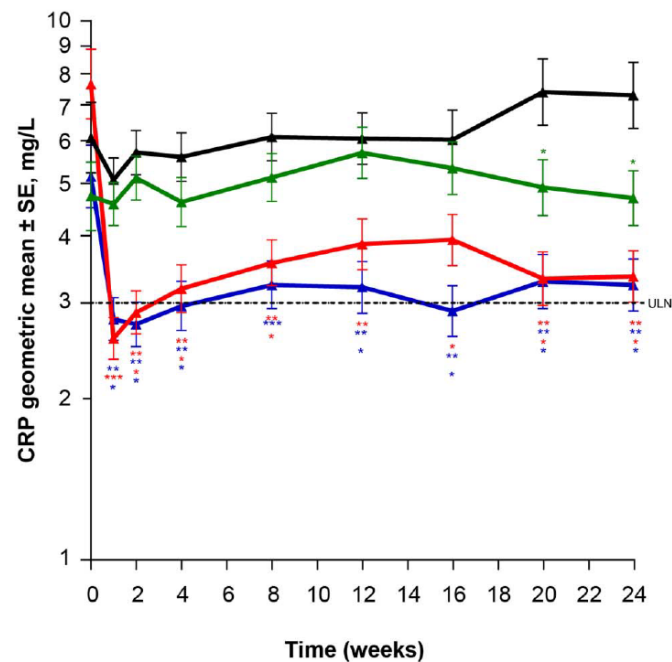
Mavrilimumab reduced arterial inflammation compared to control in an *in vivo* model of vasculitis²



In Phase 2b Rheumatoid Arthritis Study Mavrilimumab Reduced CRP and IL-6, Key Markers of Disease Activity for Giant Cell Arteritis

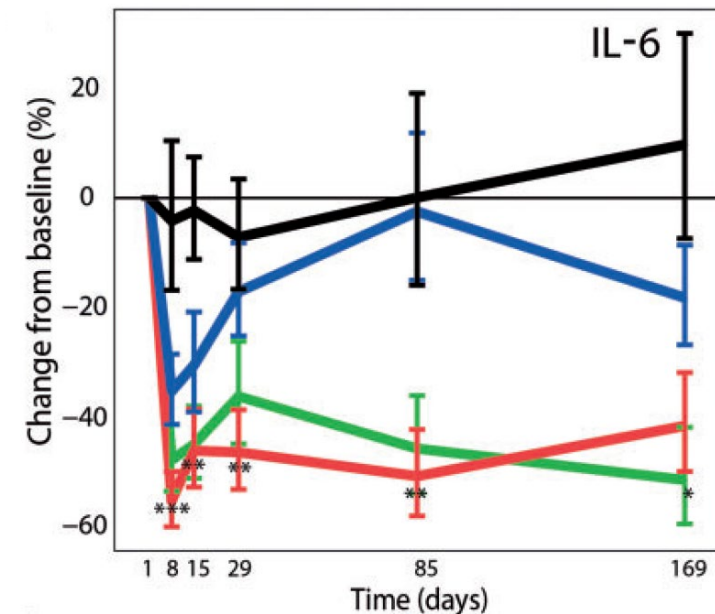
Indicative of potential broad utility across spectrum of indications with similar biomarker profiles

C-reactive Protein (CRP)¹



■ Mavrilimumab 150 mg eow (n=79) ■ Mavrilimumab 30 mg eow (n=81)
■ Mavrilimumab 100 mg eow (n=85) ■ Placebo (n=81)

Interleukin-6 (IL-6)²



■ Placebo ■ Mavrilimumab 30mg
■ Mavrilimumab 100mg ■ Mavrilimumab 150mg

Phase 2 Clinical Trial of Mavrilimumab in GCA

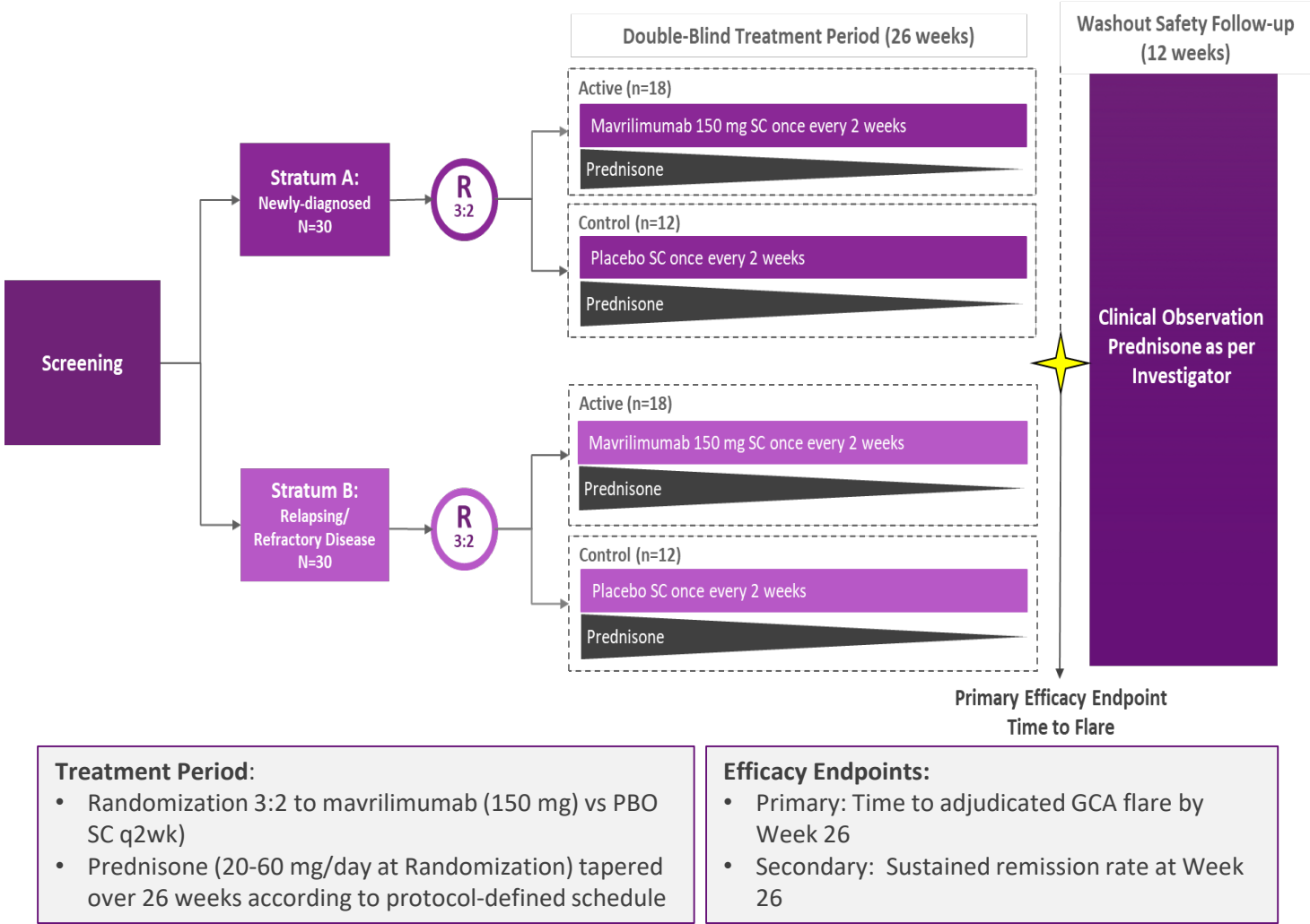
Key Inclusion Criteria:

- Age > 50 to 85 years
- Diagnosis of new-onset or relapsing/refractory GCA event within 6 wks prior to randomization (Biomarkers, Signs/Symptoms, imaging/biopsy)

Screening: Patients receive prednisone (or equivalent) at any dose required to induce remission at/before Randomization (resolution of symptoms and CRP < 20 mm in first hour)

Design Advances vs. GiACTA:

- Clinical remission at randomization adds precision to time-to-event endpoint
- 26 wk vs 52 wks shortens trial duration
- Adjudicated events require biomarkers and Signs/Symptoms/Imaging
- Adequately powered for 20-40% relative/absolute delta vs PBO in time-to-event in pooled population (trends in disease subgroups)



GCA Flare Definition (Adjudicated):

- Re-increase of CRP from normal to $\geq 1\text{mg/dL}$ and/or of ESR from $< 20\text{ mm}$ to $\geq 30\text{ mm}$
- and-
- At least one of the following signs/symptoms attributed by the Investigator to be new, worsening, or recurrent GCA:
 - Cranial symptoms (new-onset localized headache, scalp or temporal artery pain or tenderness, ischemia-related vision loss, or otherwise unexplained mouth or jaw pain upon mastication)
 - Extracranial symptoms (symptoms of polymyalgia rheumatica, claudication of the extremities)
 - Imaging (new or worsening angiographic abnormalities detected via MRI, CT/CTA, or PET-CT of the aorta or other great vessels or via ultrasound of the temporal arteries)

Mavrilimumab Phase 2 Study in Giant Cell Arteritis

Primary and Secondary Endpoints Statistically Significant

The randomized, double-blind, placebo-controlled, global Phase 2 trial consists of a 6-week screening period, a 26-week double-blind placebo-controlled treatment period, and a 12-week washout safety follow-up period

- Patients age 50 to 85 years with active GCA, confirmed by temporal artery biopsy and/or imaging, with erythrocyte sedimentation rate (ESR) ≥ 30 mm/hour or C-reactive protein (CRP) ≥ 1 mg/dL, and symptoms of GCA within 6 weeks from randomization, were included
- All patients were required to have achieved corticosteroid-induced remission (resolution of symptoms, ESR < 20 mm/hour, CRP < 1 mg/dL) prior to randomization.
- Seventy (70) patients were randomized 3:2 to mavrilimumab 150 mg or placebo biweekly injected subcutaneously, co-administered with a protocol-defined 26-week oral corticosteroid taper
- Patients were stratified by new onset (n=35) or relapsing/refractory (n=35) disease

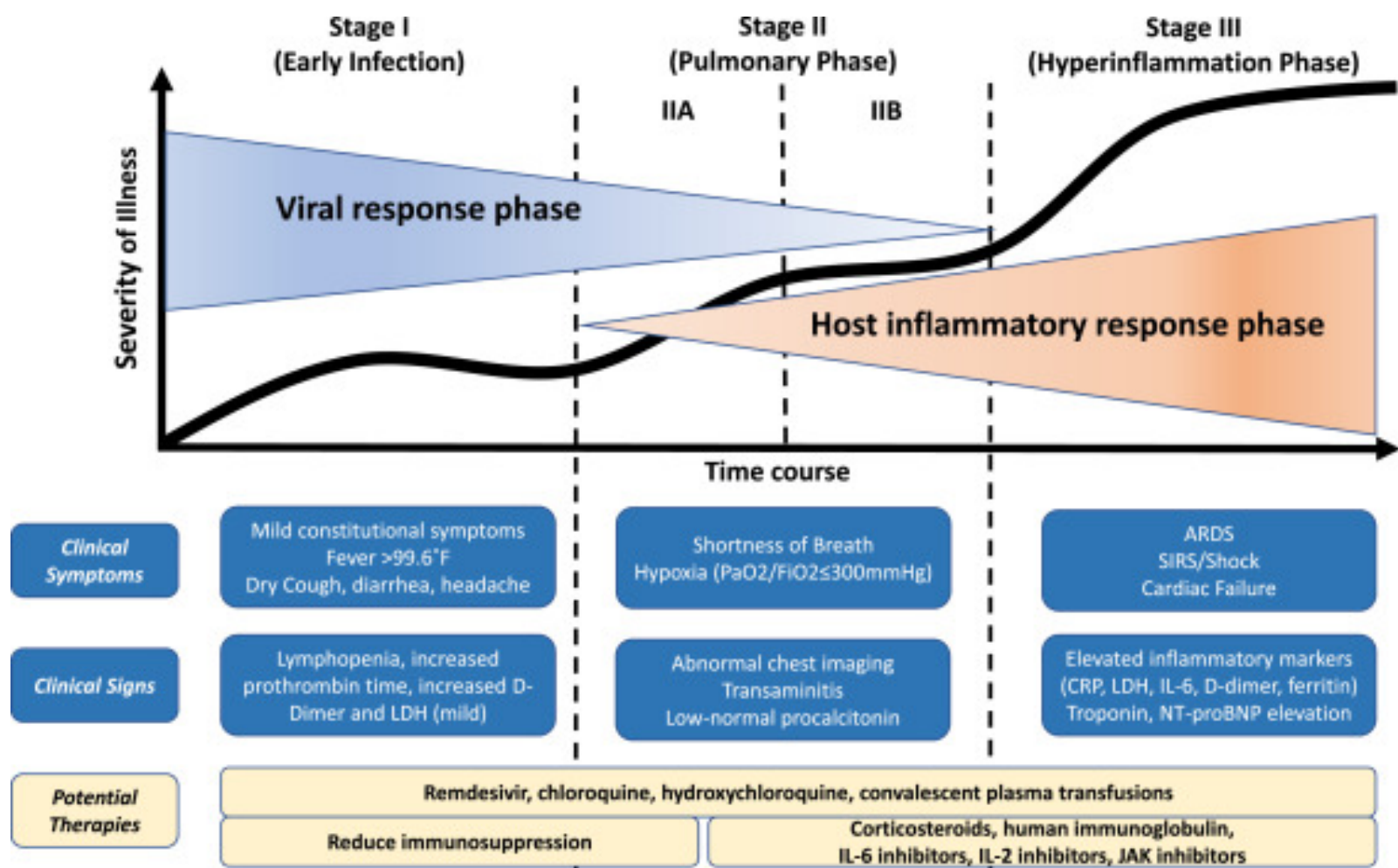
Primary Efficacy Endpoint: Time-to-first adjudicated GCA flare by Week 26 in all treated patients

Secondary Efficacy Endpoint: Sustained remission at Week 26 in all treated patients

Topline Observations:

- The primary efficacy endpoint of time-to-first adjudicated GCA flare by Week 26 in all treated patients was statistically significant (Hazard Ratio = 0.38, $p=0.0263$)
 - Median time-to-flare by Week 26 could not be estimated in mavrilimumab recipients due to the low number of flares in the mavrilimumab treatment arm. The median time-to-flare for placebo recipients was 25.1 weeks. There was a 62% lower risk of flare in mavrilimumab recipients compared to placebo recipients.
- The secondary efficacy endpoint of sustained remission at Week 26 in all treated patients was also statistically significant
 - The sustained remission rate at Week 26 was 33.3 percentage points higher in mavrilimumab recipients (83.2%) compared to placebo recipients (49.9%) ($p=0.0038$)
- Mavrilimumab was well-tolerated; there were no drug-related serious adverse events, and the rates of drug-related treatment-emergent adverse events between mavrilimumab recipients and placebo recipients were similar
- The 12-week washout safety follow-up period and additional analyses of this Phase 2 trial are ongoing. Next steps for the development program in GCA will be further informed by anticipated discussions with the U.S. Food and Drug Administration (FDA)

Escalating Phases of Disease Progression with COVID-19



Source:
Hasan K. Siddiqi MD, MSCR , Mandeep R. Mehra MD, MSc , COVID-19 Illness in Native and Immunosuppressed States: A Clinical-Therapeutic Staging Proposal, Journal of Heart and Lung Transplantation (2020), doi: <https://doi.org/10.1016/j.healun.2020.03.012>

Mavrilimumab: Potential Treatment of COVID-19 Pneumonia and Hyperinflammation

Mechanism

- GM-CSF is a key growth factor and cytokine in autoinflammation and autoimmunity¹
- Mavrilimumab is a monoclonal antibody inhibitor targeting GM-CSFR α

Rationale

- GM-CSF is implicated in the mechanism of excessive and aberrant immune cell infiltration and activation in the lungs thought to contribute significantly to mortality in COVID-19²
- Robust literature evidence showing a consistent immunophenotype and pathology of ARDS across inflammatory/infectious etiologies (influx of neutrophils and upregulation of immature, pro-inflammatory macrophages)³

Clinical Data

- Evidence of treatment response with mavrilimumab observed in an open-label treatment protocol in Italy in 13 non-mechanically ventilated patients with severe COVID-19 pneumonia and hyperinflammation⁴

Differentiation

- Mavrilimumab is believed to be the only GM-CSF receptor blocker; other anti-GM-CSF therapeutic approaches inhibit the ligand
- GM-CSFR α blockade potentially prevents pathogenic cells from infiltrating into the target tissue, and suppresses multiple markers of inflammation (e.g., IL-2R α , IL-6, CRP)^{5,6,7}
- Once hyperinflammation and CRS have begun, anti-virals may be less effective⁸
- Vaccines likely to provide incomplete population immunity + limited supply/access; vaccine does not help once virus occurs⁹

Development Status

- The safety of mavrilimumab has been evaluated in a Phase 2 trial: Mavrilimumab was dosed in over 550 patients with rheumatoid arthritis through Phase 2b by MedImmune in Europe and achieved prospectively-defined primary safety and efficacy endpoints
- Adaptive design Phase 2/3 clinical trial of mavrilimumab in severe COVID-19 pneumonia and hyperinflammation enrolling; Data expected from placebo-controlled investigator-initiated study in the U.S. in Q4 2020

1) Wicks, Roberts, Nature Review Immunology, 2015; Hamilton, Expert Review of Clinical Immunology, 11:4, 457-465; 2) Zhou et al. bioRxiv. 2020; 3) Huang et al. 2018; Huang et al 2005; Rosseau et al 2000; Thompson et al., NEJM 2017; 4) Data as of 4/28/2020; 5) De Alessandris et al., J Leukoc Biol. 2019; 6) Sterner et al., Blood 2019; 7) Guo et al., Rheumatology 2017; 8) Darwish, Muvareka, Liles. Expert Rev. Anti Infect: Ther. 9(7), 2011; 9) Osterholm et al., The Lancet Infectious Diseases, 2012; ARDS = Acute Respiratory Distress Syndrome; CRS = Cytokine Release Syndrome

Mavrilimumab Treatment Protocol in COVID-19 Pneumonia and Hyperinflammation

Improved clinical outcomes compared to matched contemporaneous controls, including earlier weaning from supplemental oxygen, shorter hospitalizations, and no deaths

The mavrilimumab open-label treatment protocol was a prospective, interventional, single-active-arm, single-center pilot experience in Italy.

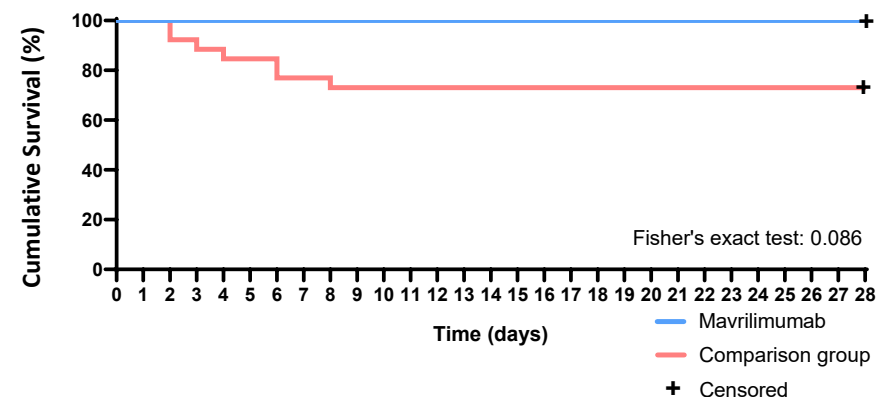
- Thirteen non-mechanically ventilated patients with severe COVID-19 pneumonia and hyperinflammation were treated with a single intravenous dose of mavrilimumab upon admission to the hospital.
- Twenty-six contemporaneous non-mechanically ventilated patients with severe COVID-19 pneumonia and hyperinflammation and with similar characteristics upon admission to the hospital, including comorbidities, baseline inflammatory markers and respiratory dysfunction, were evaluated as a control group.
- All patients in the treatment protocol received optimum local standard of care, including protease inhibitors and antiviral therapies.

Main outcome: Time to clinical improvement (defined as improvement ≥ 2 categories on a 7-point scale for assessment of clinical status)

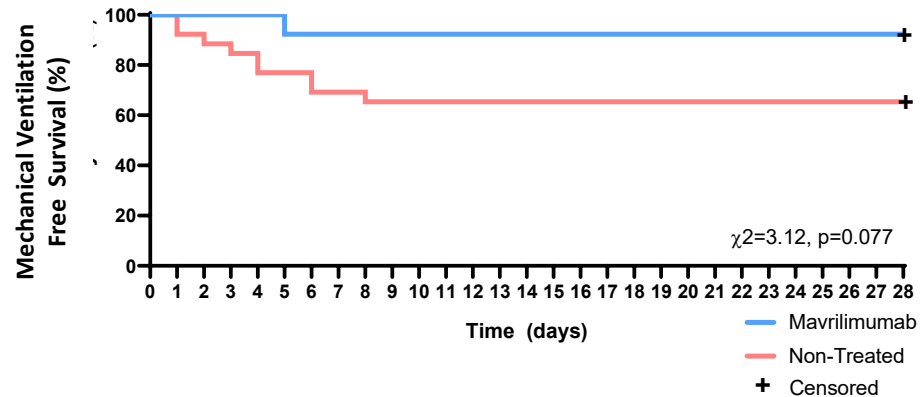
Clinical Outcomes:

- Over the course of the 28-day follow-up period, mavrilimumab-treated patients experienced greater and earlier clinical improvements than control-group patients, including earlier weaning from supplemental oxygen, shorter hospitalizations, and no deaths.
 - Death occurred in 0% (n=0/13) of mavrilimumab-treated patients by Day 28, compared to 27% (n=7/26) of control-group patients (p=0.086).
 - 8% (n=1/13) of mavrilimumab-treated patients progressed to mechanical ventilation by Day 28, compared to 35% (n=9/26) of control-group patients who progressed to mechanical ventilation or died (p=0.077).
 - 100% (n=13/13) of mavrilimumab-treated patients and 65% (n=17/26) of control-group patients attained the clinical improvement endpoint (defined as improvement of ≥ 2 categories on a 7-point scale for assessment of clinical status) by Day 28 (p=0.0001).
 - Fever resolved in 91% (n=10/11 febrile patients) of mavrilimumab-treated patients by Day 14, compared to 61% (n=11/18 febrile patients) of control-group patients (p=0.0093).
 - Representative mavrilimumab-treated patients showed significant improvement in lung opacification on computerized tomography (CT) scans, consistent with the overall improvement in their clinical status.
- Mavrilimumab was well-tolerated in all patients, without infusion reactions. P-values above are unadjusted for multiplicity.

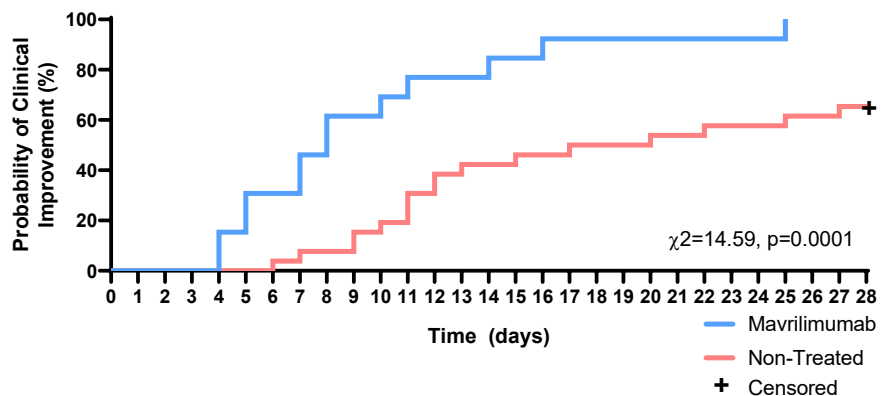
Mavrilimumab Treatment Protocol in Patients with COVID-19 Pneumonia & Hyperinflammation Showed Improved Clinical Outcomes Compared to Matched Contemporaneous Controls¹



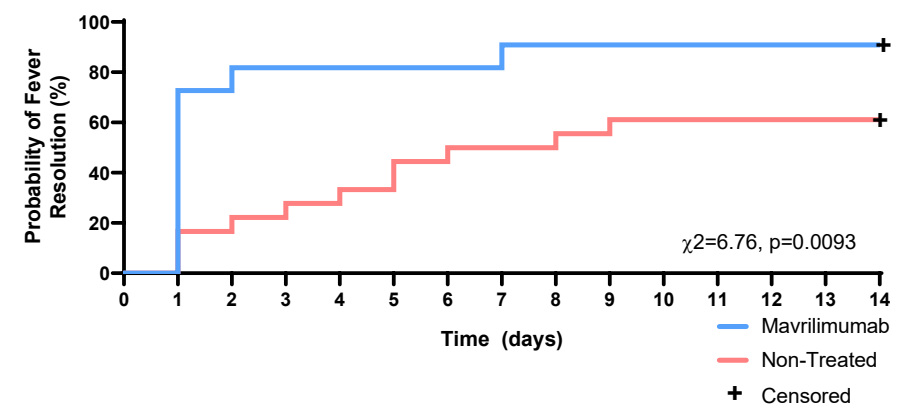
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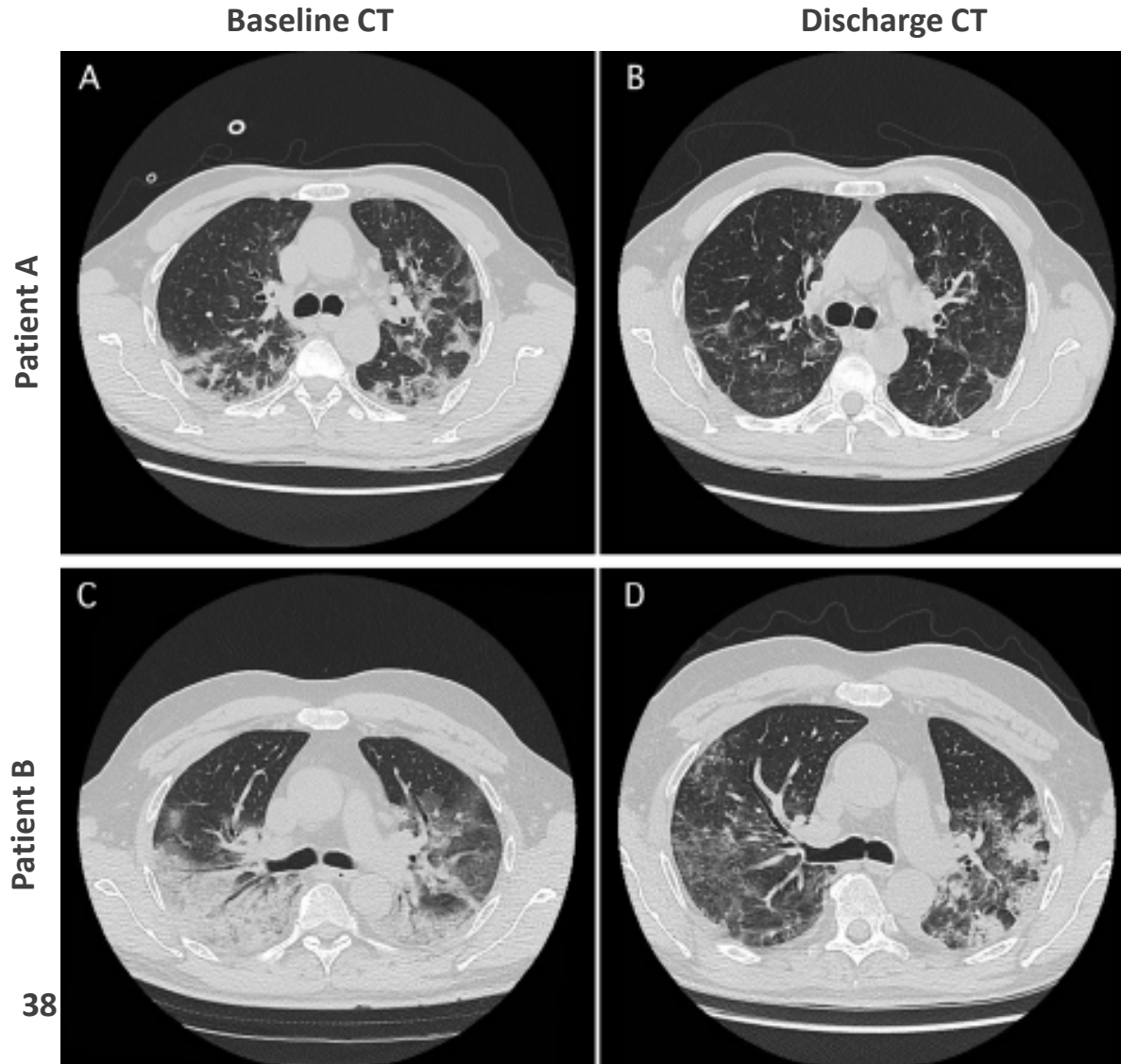


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Fever resolved in 91% (n=10/11 febrile patients) of mavrilimumab-treated patients by Day 14, compared to 61% (n=11/18 febrile patients) of control-group patients (p=0.0093)

Representative mavrilimumab-treated patients showed significant improvement in lung opacification on computerized tomography (CT) scans, consistent with the overall improvement in their clinical status



Patient A: 58 year old male.

- At day 0: febrile, receiving O₂ through a facemask; FiO₂ 0.4, PaO₂ 86 mmHg, lactic acid dehydrogenase (LDH) 374 U/L, C-reactive protein (CRP) 100 mg/L.
- At day 7: afebrile, on room air, SpO₂ 98%, LDH normalized, CRP 12.5 mg/L.

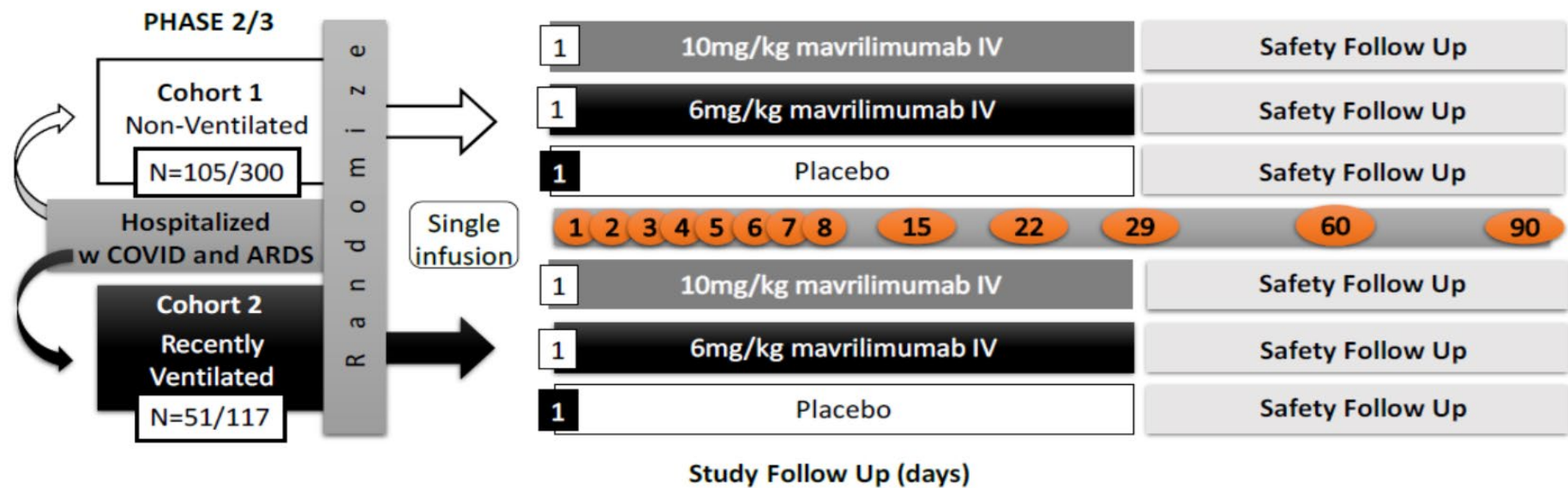
Patient B: 56 year old male

- At day 0: febrile, receiving high-low O₂ through a facemask with reservoir bag + 12 hours/day of CPAP, PaO₂ 176 mmHg, LDH 944 U/L, CRP 177 mg/L.
- At day 14: afebrile, on room air, SpO₂ 98%, LDH normalized, CRP 28.2 µg/mL (28.2 mg/L).

Adaptive Design Phase 2/3 Clinical Trial of Mavrilimumab in Severe COVID-19 Pneumonia and Hyperinflammation

Key Inclusion Criteria:

- Positive COVID-19 test within 14 days prior to randomization
- Hospitalized for COVID-19
- Bilateral pneumonia on chest x-ray or computed tomography
- Active fever or recently documented fever within 72 hours prior to randomization
- Clinical laboratory results indicative of hyper-inflammation
- Cohort 1: Non-ventilated; requiring supplemental oxygen to maintain oxygen saturation (SpO2) ≥ 92% and not-intubated
- Cohort 2: Recently ventilated with mechanical ventilation prior to randomization



Primary Efficacy Endpoints:

Cohort 1:

- Proportion of patients alive and without respiratory failure at Day 15.
- Respiratory failure is defined as the need for high flow oxygen, non-invasive ventilation, invasive mechanical ventilation, or extracorporeal membrane oxygenation.

Cohort 2:

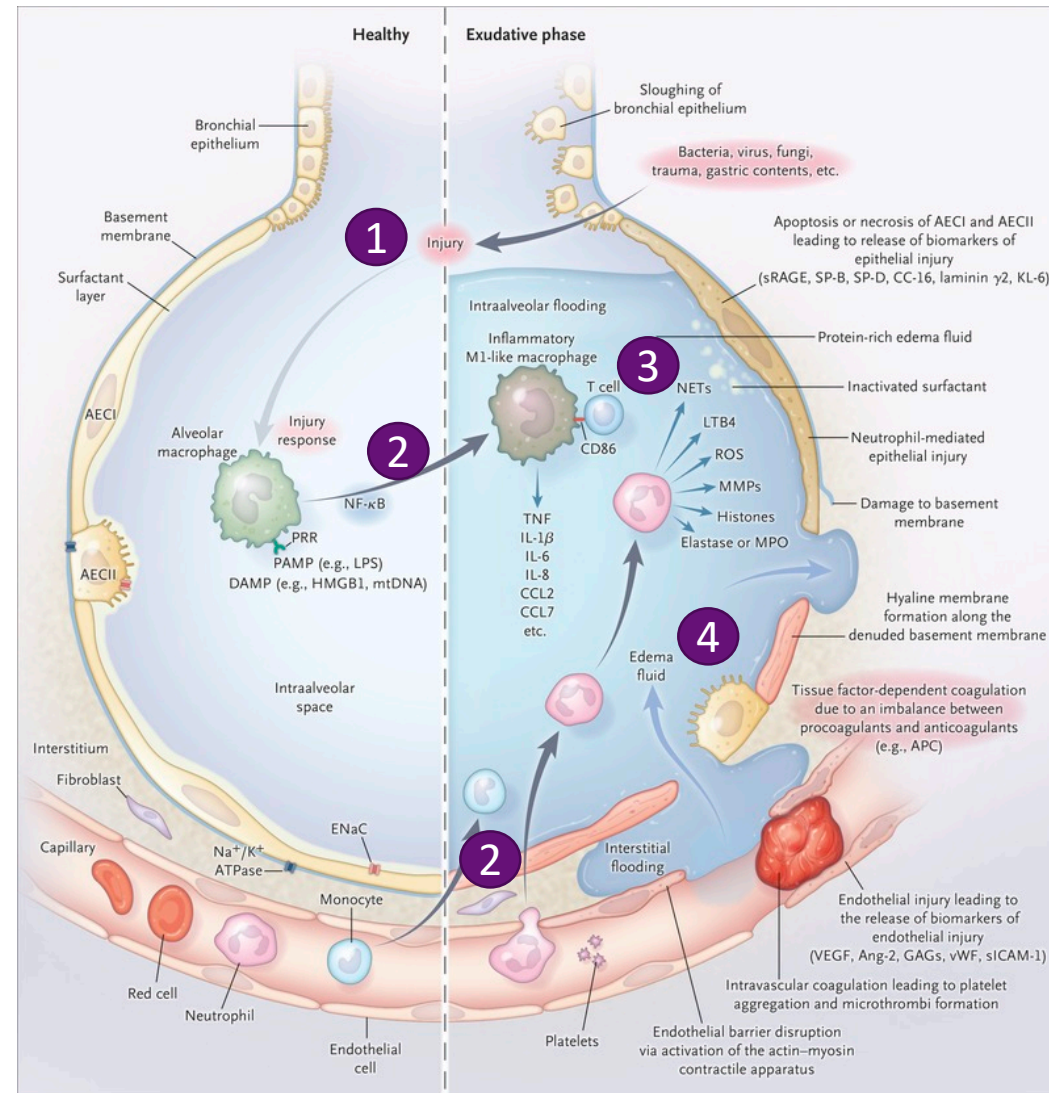
- Mortality rate at Day 15

Cytokine Cascade Amplification System in the Pathophysiology of ARDS

Pathophysiology of ARDS (Exudative Phase)

- 1 • Inflammatory insults, either locally from the lungs or systemically from extra-pulmonary sites, affect bronchial epithelium, alveolar macrophages, and vascular endothelium

- 4 • Extensive damage to lung epithelia and endothelia results in an impaired alveolar-capillary barrier.
• Disruption of this barrier allows protein-rich fluid to enter the alveoli causing fluid accumulation in alveolar spaces (pulmonary edema) interfering with gas exchange



- 2 • Resident alveolar macrophages secrete proinflammatory cytokines, leading to **neutrophil** and **monocyte** or **macrophage** recruitment, as well as activation of **alveolar epithelial cells** and **effector T cells**, to promote and sustain inflammation and tissue injury.
- 3 • Hyperactivation of myeloid cells and T-cells produce large amounts of inflammatory cytokines, which in turn lead to **endothelial activation** and microvascular injury ultimately leading to barrier disruption in ARDS which can worsened by mechanical stretch.

The Role of Mavrilimumab Throughout the Immune System and its Potential to Treat COVID-19 Pneumonia and ARDS More Broadly

Mechanisms driving ARDS pathophysiology	Targetable by Mavrilimumab ⁽⁴⁻¹⁴⁾	Targetable by anti-IL-6 ⁽¹⁵⁻²⁰⁾	Targetable by anti-IL-1β ⁽²¹⁻²⁶⁾
Recruitment of neutrophils	✓	✓	✓
Neutrophil longevity	✓	Conflicting evidence	
Formation of neutrophil extra cellular traps (NET)	✓		
Activation of AM & polarization to M1-like phenotype	✓		
Th1 inflammation ⁽¹⁻³⁾	✓		
Th17 inflammation ⁽¹⁻³⁾	✓	✓	✓

Evidence of targetable pathways by anti-IL-6

¹Wu J Microbiol, Immunol and Infection (2020), ² Xu Lancet Respir Med (2020), ³ Huang Lancet (2020).

Evidence of targetable pathways by anti-IL-6

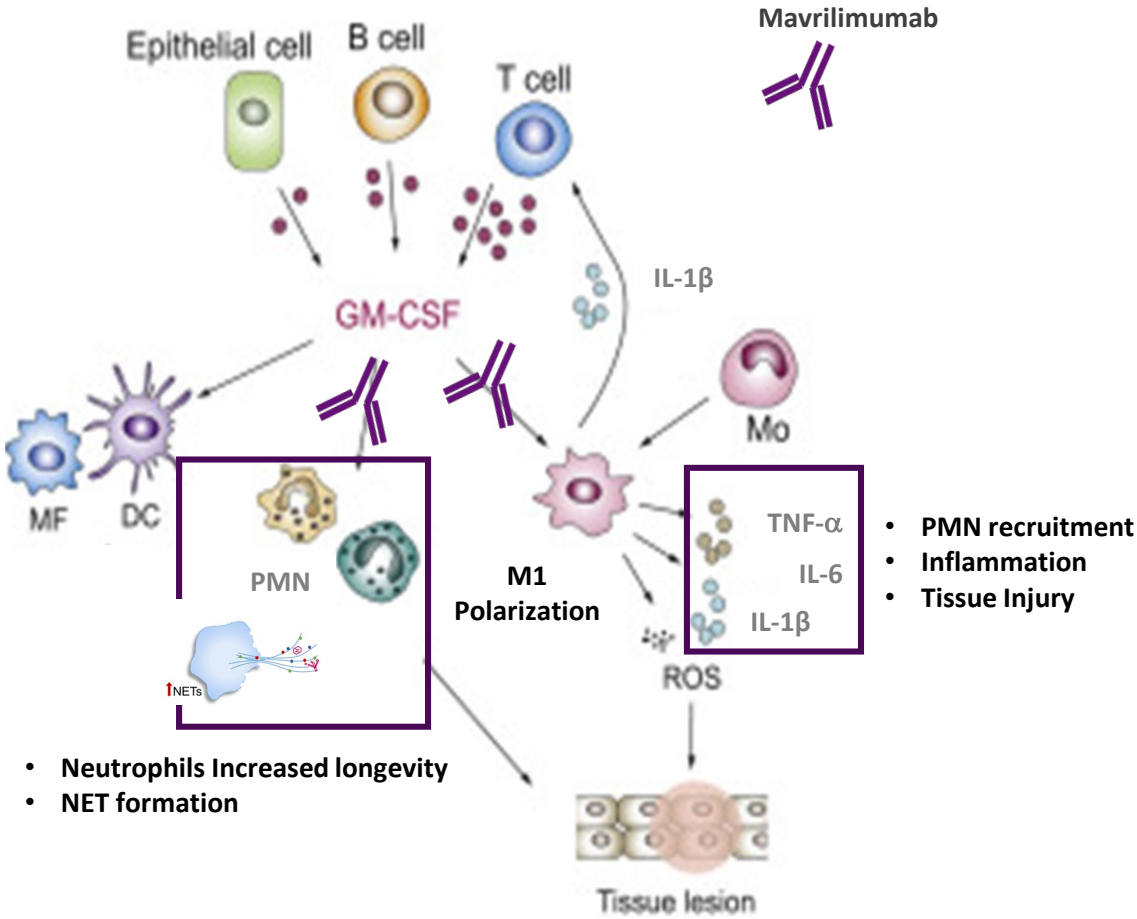
⁴ De Alessandris JLB (2019), ⁵ Matute-Bello Am J Resp Crit Care Med (1997), ⁶ Juss Am J Resp Crit Care Med 1997 (2016), ⁷ Yousefi Cell Death and Differentiation (2009), ⁸ Gray Thorax (2018), ⁹ Fleetwood JI (2007), ¹⁰ Dalrymple BMC Immunol. (2013), ¹¹ Benmerzoug Sci Rep (2018), ¹² Krausgruber Nat Imm (2011), ¹³ Shiomi JI (2014), ¹⁴ Shiomi Med Inflamm (2015).

Evidence of targetable pathways by anti-IL-6

¹⁵ Jones J Infect Dis (2006), ¹⁶ Wright Rheumatology (2014), ¹⁷ Afford JBC (1992), ¹⁸ Biffi JLB (1995), ¹⁹ Oh J Exp Med (2011), ²⁰ Yan Sci Rep (2016).

Evidence of targetable pathways by anti-IL-1β

²¹ Sichelstiel PLOS One (2014), ²² Jones AJRCB (2014), ²³ Ganter Circ Res (2008), ²⁴ Frank Thorax (2008), ²⁵ Wu JI (2013), ²⁶ Gasse PLOS One (2011).



Vixarelimab

Indication	Prurigo Nodularis (PN): Chronic inflammatory skin disease with pruritic lesions
Mechanism of Action¹	Monoclonal antibody inhibitor targeting OSMR β
Scientific Rationale^{2,5,6}	OSMR β is a key receptor subunit shared by IL-31 and OSM; cytokines implicated in chronic pruritic diseases
Prevalence³	PN: ~300k prevalent in U.S.
Competition⁴	No FDA-approved therapies for PN
Status^{5,6}	Phase 2a data in PN achieved statistical significance in both reduction in weekly-average WI-NRS and attainment of PN-IGA 0/1 score at Week 8 ⁵ ; dose-ranging Phase 2b initiation expected in Q4 2020
Economics	Clinical, regulatory and sales milestones; tiered royalty on annual net sales
Rights	Worldwide

1) Trinity Qualitative Interviews; 2) Dillon SR, Sprecher C, Hammond A, Bilsborough J, Rosenfeld-Franklin M, Presnell SR, et al. Interleukin 31, a cytokine produced by activated T cells, induces dermatitis in mice. Nat Immunol. 2004; 5(7):752-60; Weigelt N, et al. J Cutan Pathol . 2010;37:578-86. 3) Trinity Consulting - HCUP/Medicare Data 2012/2013; Quantitative Survey (n=100 dermatologists); Dantas, 2015, "Prevalence of dermatoses in dermatologic evaluation requests from patients admitted to a tertiary hospital for 10 years"; Mortz et al., British Journal of Dermatology, 200; 4) Journal of the American Academy of Dermatology - Analysis of Real-World Treatment Patterns in Patients with Prurigo Nodularis: [https://www.jaad.org/article/S0190-9622\(19\)32744-6/pdf](https://www.jaad.org/article/S0190-9622(19)32744-6/pdf) ; 5) Vixarelimab Phase 2a data in prurigo nodularis (www.investors.kiniksa.com); 6) Vixarelimab exploratory Phase 2 data in diseases characterized by chronic pruritus (www.investors.kiniksa.com); WI-NRS = Worst-Itch Numeric Rating Scale; PN-IGA = prurigo nodularis-investigator's global assessment



Prurigo Nodularis is Typically Treated by Dermatologists Through a Combination of Medications and Behavioral Therapies; Treatment is Usually Unsuccessful

Diagnosis of Prurigo Nodularis By Dermatologists

1 st Line	~100%	Emollients + Antipruritic Creams + Topical Corticosteroids + Antihistamines	
2 nd Line	~60-70%	Low-Dose Oral Corticosteroids, Intralesional Steroids, Occlusive Steroid Wrap	Vixarelimab may initially slot after steroids
3 rd Line	~25-30%	UV Phototherapy	
4 th Line	~20-30%	Other Systemic Therapy (e.g. MTX, Cyclosporine, Doxepin, Thalidomide)	

Note: none of the above therapies are approved specifically for prurigo nodularis



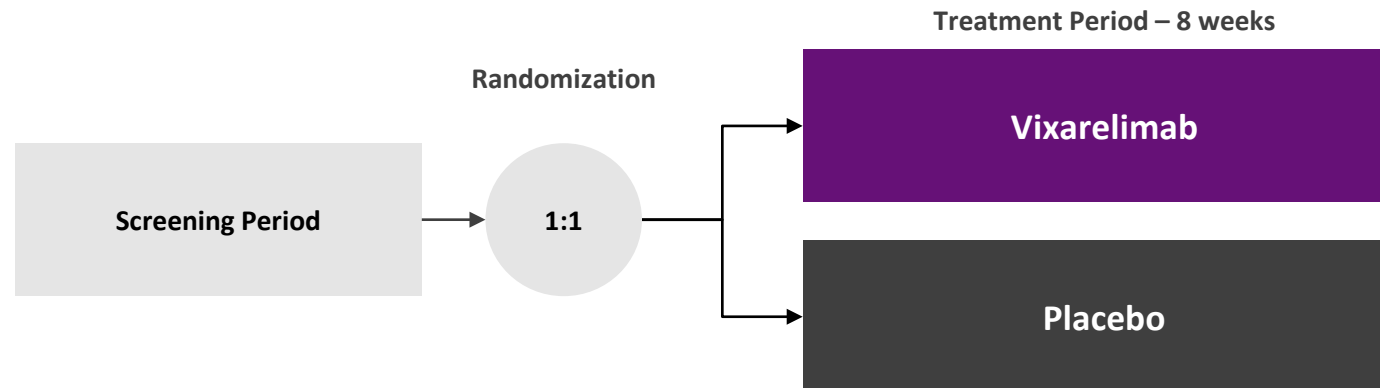
Vixarelimab Phase 2a Study in Prurigo Nodularis

Phase 2a Proof-of-Concept

Objective: Assess pruritus reduction

Dose: 720 mg SC loading dose --> 360 mg single SC QW thereafter

Primary Efficacy Endpoint : % change from baseline in weekly average Worst Itch-Numeric Rating Scale (WI-NRS)



Inclusion Criteria

- Male or female aged 18 to 75 years, inclusive, at the time of consent
- Have a physician-documented diagnosis of prurigo nodularis that is confirmed by review of medical photography during the Screening Period. Duration of prurigo nodularis (since the time of first PN nodule) must be at least 6 months from the time of first PN nodule to Day 1, as affirmed by the subject
- Have at least 10 nodules of approximately 0.5 to 2 cm at the Screening Visit and Day 1. The nodules must be pruritic and present on at least 2 different anatomical locations (not be localized), involve the extremities, with extensor extremity involvement greater than the flexor extremity involvement. Nodules on the head (face and scalp) are not counted as an anatomical location for eligibility criteria. There must be normal appearing skin present in between nodules with the exception of atopic dermatitis. Each arm, each leg, and trunk are considered different anatomical locations
- Subject has moderate to severe pruritus, defined as WI-NRS ≥ 7 at the Screening Visit and a mean weekly WI-NRS ≥ 5 for each of the 2 consecutive weeks immediately prior to randomization
- Patients were required to stop antihistamines and topical treatments, including corticosteroids, for at least two weeks prior to dosing
- Prurigo nodularis treatments, other than study drug, were not allowed except for rescue

Vixarelimab Phase 2a Study Prurigo Nodularis

Statistically significant primary efficacy endpoint of reduction in weekly-average WI-NRS at Week 8

Enrolled and treated 49 patients with moderate-to-severe prurigo nodularis (mean PN- IGA of 3.4) experiencing moderate-to-severe pruritus (mean WI-NRS score of 8.3)

- Randomized 1:1 to receive a loading dose of vixarelimab 720 mg (n=23) or placebo (n=26) subcutaneous (SC) followed by vixarelimab 360 mg or placebo SC weekly
- Data includes 49 subjects through the 8-week treatment period

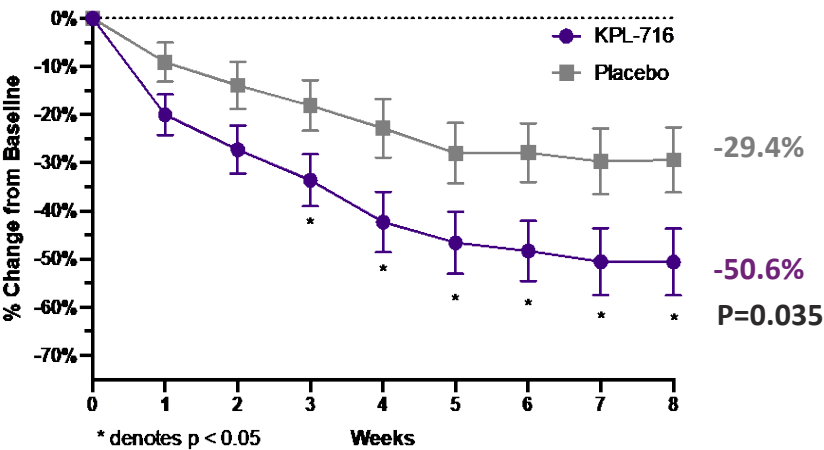
Primary Efficacy Endpoint: percent change versus baseline in weekly-average WI-NRS at Week 8 (using the last observation carried forward analysis)

Topline Observations:

- Least squares-mean change from baseline in weekly-average WI-NRS at Week 8 was -50.6% in vixarelimab recipients compared to -29.4% in placebo recipients (mean difference 21.1%; p=0.035)
- Median change from baseline in weekly-average WI-NRS at Week 8 was -69.8% in vixarelimab recipients compared to -36.1% in placebo recipients
- 30.4% of vixarelimab recipients achieved a PN-IGA score of 0/1 at Week 8 compared to 7.7% of placebo recipients (p=0.032)
- 52.2% of vixarelimab recipients demonstrated a ≥ 4 -point reduction in weekly-average WI-NRS at Week 8 compared to 30.8% of placebo recipients (p=0.109)
- In this Phase 2a trial, vixarelimab was well-tolerated by all subjects and no dose-limiting adverse experiences were observed. There were no serious adverse events or atopic dermatitis flares

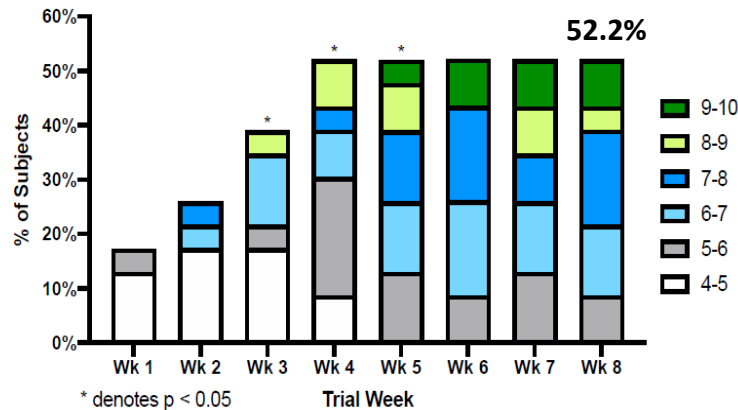
Vixarelimab Phase 2a Data in Prurigo Nodularis

LS-Mean % Change in Weekly Average WI-NRS



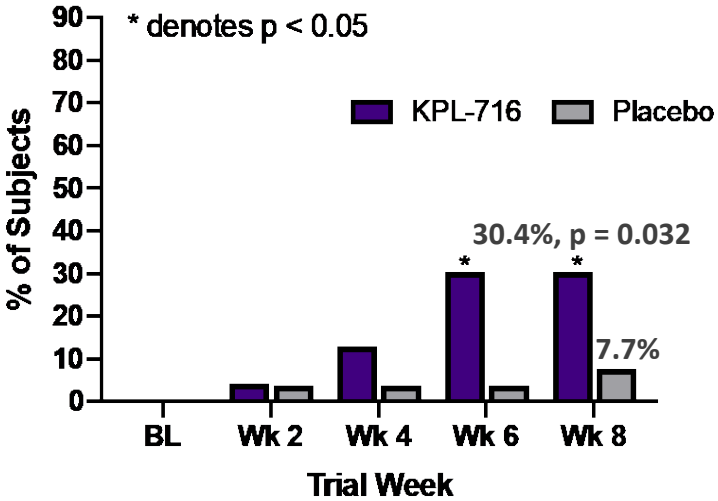
Statistically Significant Primary Efficacy Endpoint of Reduction in Weekly-Average WI-NRS at Week 8

% of Vixarelimab Subjects with a Clinically Meaningful Response in WI-NRS



Majority of Vixarelimab Recipients Showed a Clinically Meaningful ≥ 4 -Point Weekly-Average WI-NRS Reduction at Week 8

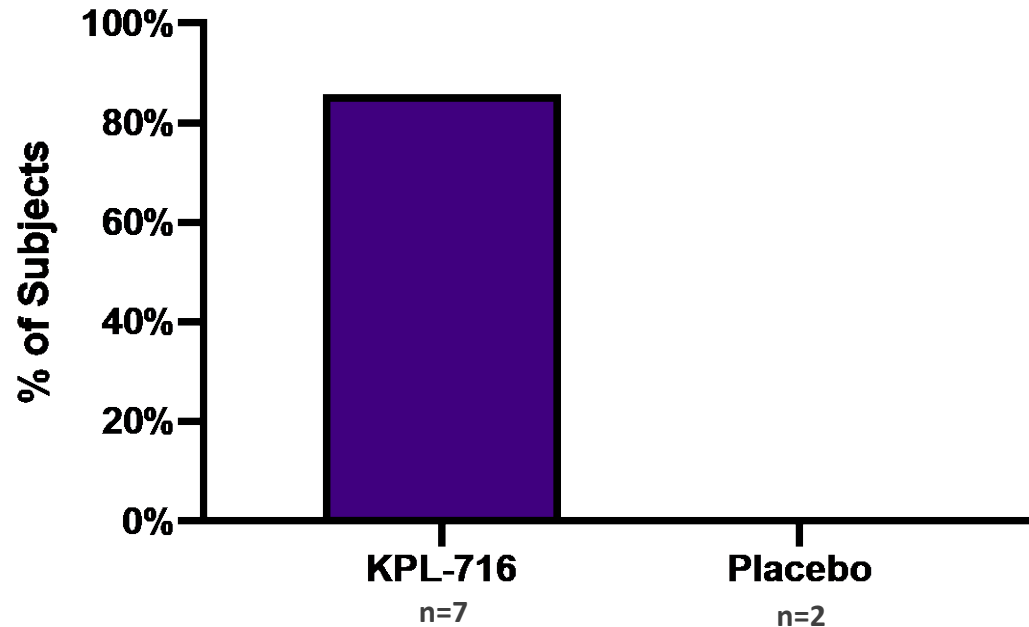
PN-IGA Score of 0 or 1



Significantly More Vixarelimab Recipients Attained A Clear/Almost Clear Lesion Score by Week 8

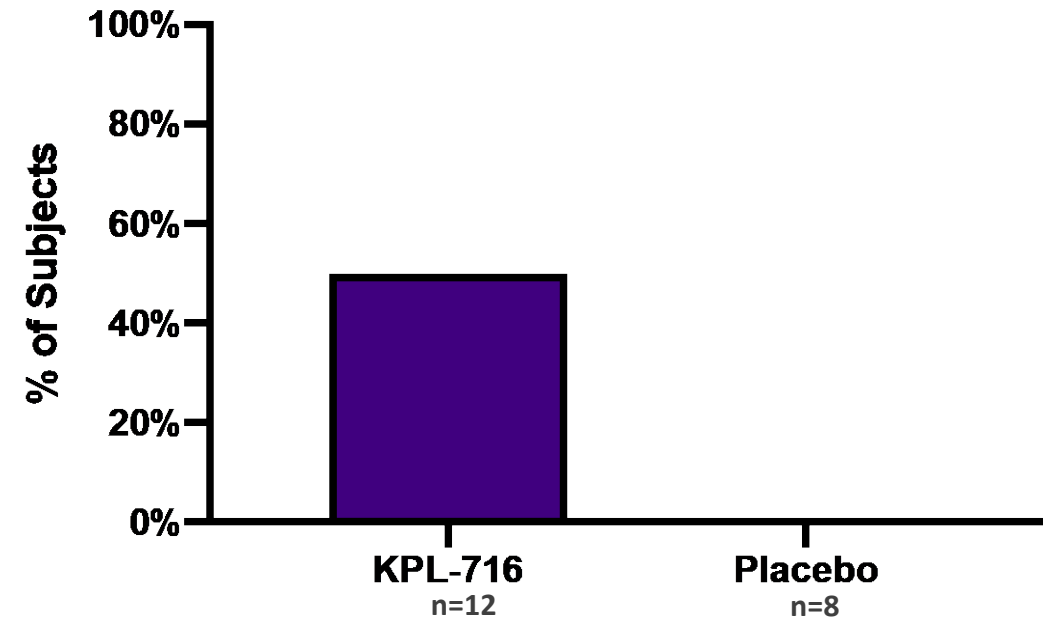
Vixarelimab Phase 2a Study in Prurigo Nodularis: Concordant Activity of Vixarelimab on PN-IGA and Pruritus

% of IGA 0-1 Subjects with ≥ 4 Point Change in WI-NRS



85.7% of the subjects who achieved 0-1 on the PN-IGA scale were also 4-point responders on WI-NRS vs. none for placebo

% of Subjects with ≥ 4 Point Change in WI-NRS and an IGA of 0-1



50% of the subjects who had a clinically meaningful reduction in itch by week 8 also had an PN-IGA score of 0-1 vs. none for placebo

Vixarelimab Phase 2a Study in Prurigo Nodularis: Representative Images of Nodule Resolution at Week 8 in Vixarelimab-Treated Subjects

Day 1

Week 8

Subject 1



Subject 2



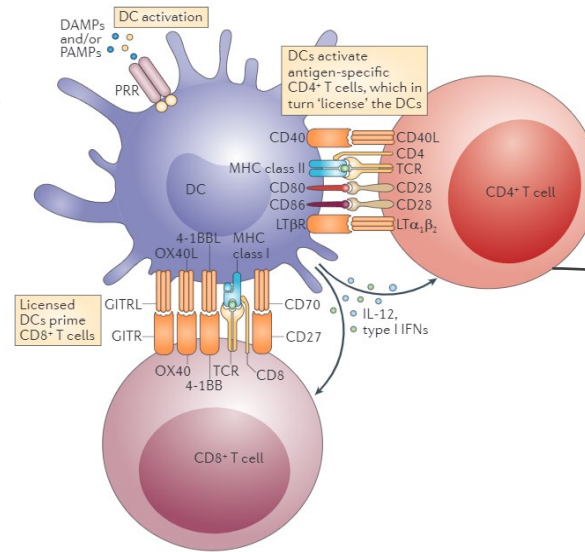
Autoimmune Diseases¹	External proof-of-concept previously established in broad range of autoimmune diseases: Sjogren's disease, systemic lupus, rheumatoid arthritis, solid organ transplant and Graves' disease ¹
Mechanism of Action²	Monoclonal antibody inhibitor of CD40-CD40L interaction
Scientific Rationale^{3,4}	Attractive target for blocking T-cell dependent, B-cell-mediated autoimmunity
Status	Enrolling first-in-human study with antigen challenge TDAR ⁵ ; Phase 1 data expected in Q4 2020
Economics	Clinical and regulatory milestones and royalty on annual net sales
Rights	Worldwide

KPL-404: Potential Molecule for Evaluation in a Broad Range of Autoimmune Diseases

Mechanism	Humanized mAb inhibitor of CD40-CD40L interaction ¹	<ul style="list-style-type: none"> Designed to inhibit CD40-CD40L, a T-cell co-stimulatory pathway critical for B-cell maturation and immunoglobulin class switching
Rationale	External POC for CD40-CD40L inhibition observed in a range of autoimmune diseases ^{2,3}	<ul style="list-style-type: none"> Published Positive Class-Related Clinical Data: Sjogren's syndrome, systemic lupus erythematosus, solid organ transplant, rheumatoid arthritis, Graves' disease Ongoing Class-Related Studies: type 1 diabetes, ulcerative colitis, lupus nephritis, hidradenitis suppurativa, kidney transplant and focal segmental glomerulosclerosis
Preclinical Data	Robust preclinical package supports development potential	<ul style="list-style-type: none"> Favorable pharmacokinetic and pharmacodynamic findings, including engagement of CD40 target and block of antigen-specific primary and secondary antibody responses in a T-cell dependent antibody response cynomolgus monkey model
Competition	Potential differentiation	<ul style="list-style-type: none"> KPL-404 at 10mg/kg achieved/maintained ~100% receptor occupancy in 7/7 non-human primates (NHP) through 4 weeks KPL-404 10mg/kg suppressed T-cell dependent antibody responses (TDAR) in NHP model to tetanus toxoid (TT) and keyhole limpet hemocyanin (KLH) for >4 weeks
Status	Enrolling first-in-human study	<ul style="list-style-type: none"> Enrolling a single-ascending-dose Phase 1 study in healthy volunteers which will provide safety data and pharmacokinetics as well as receptor occupancy and TDAR Top-line data are expected in 4Q 2020

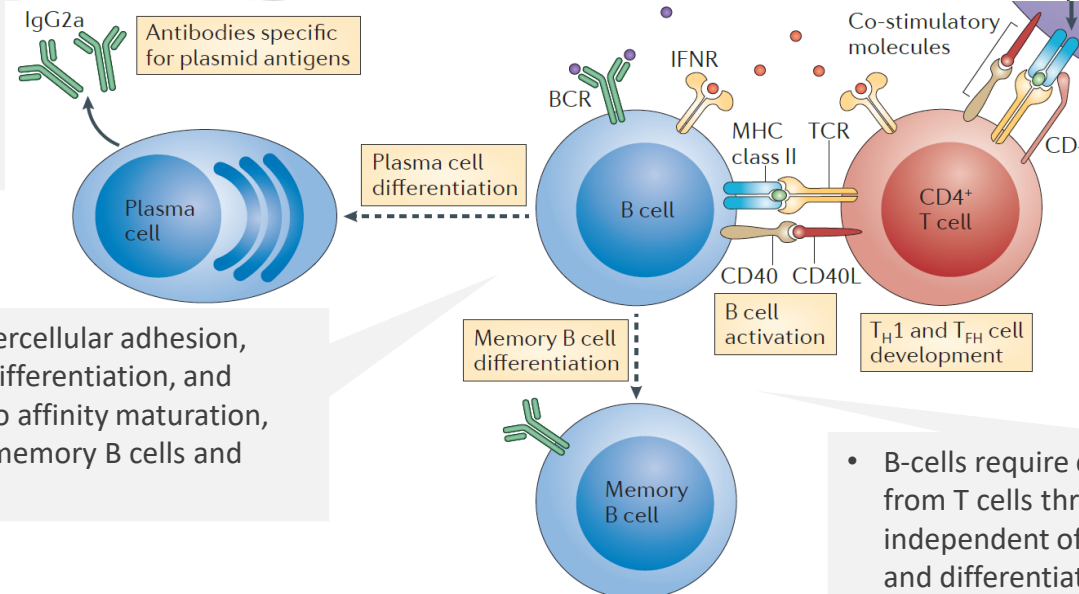
CD40/CD40L is an Essential Immune Pathway for T-Cell Priming and T-Cell Dependent B-Cell Responses

- CD40 is expressed on the surface of dendritic cells, B-cells, antigen-presenting cells and non-immune cell types
- Its ligand, CD40L (CD154), is expressed by activated T-cells, platelets, and other cell types



- CD40 ligation on DCs induces cell maturation by promoting antigen presentation and enhancing their costimulatory activity
- Mature DCs stimulate activated T-cells to increase IL-2 production that facilitates T-helper cells (Th) and cytolytic T-Lymphocyte (CTL) expansion
- CD40-stimulated DCs also secrete cytokines favoring Th1 cell differentiation and promoting Th cell migration to sites of inflammation
- CD40 ligation also provides a pro-inflammatory signal within the mononuclear phagocyte system

- Humoral immunity is dependent on a thriving B cell population and activation by Th cells; blockade of CD40/CD40L interaction has been shown to completely ablate primary and secondary TDAR response



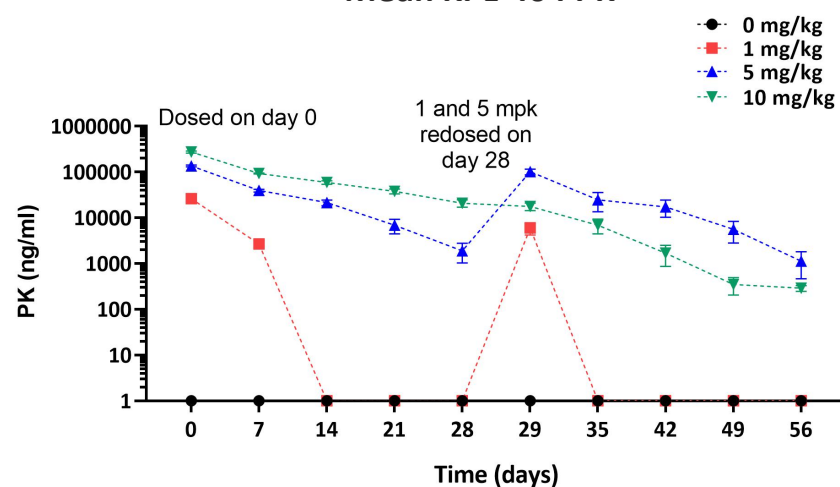
- CD40 engagement triggers B-cell intercellular adhesion, sustained proliferation, expansion, differentiation, and antibody isotype switching leading to affinity maturation, which is essential for generation of memory B cells and long-lived plasma cells

- B-cells require contact-dependent stimulus from T cells through CD40/CD40L interaction independent of cytokines to trigger growth and differentiation

Sources: Elgueta et al., Immunol Rev, 2009; Peters et al., Semin Immunol, 2009; Kambayashi et al., Nature Reviews: Immunology, 14, 2014; Desmet et al., Nature Reviews: Immunology, 12, 2012

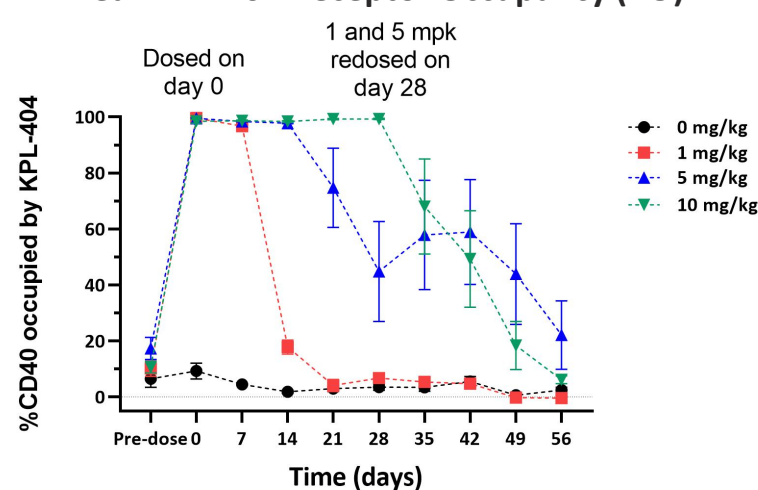
KPL-404 Showed Encouraging Results in a Non-Human Primate Model of TDAR

Mean KPL-404 PK



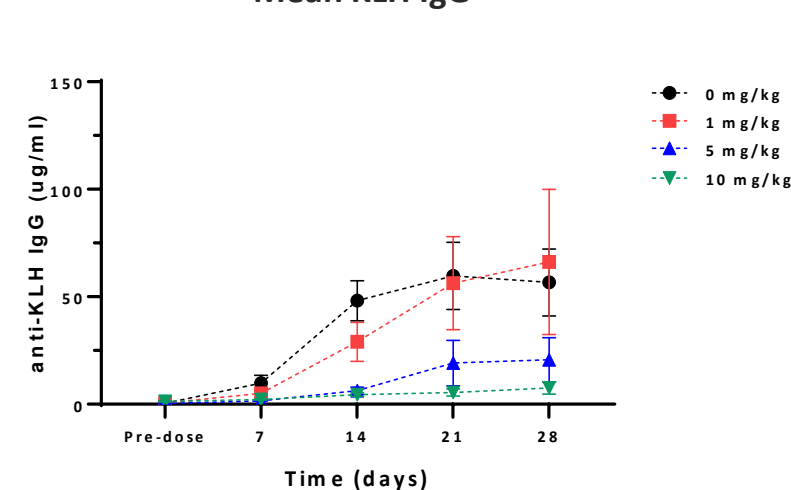
Showed linear pharmacokinetic profile with low variability between non-human primate subjects (n=7)

Mean KPL-404 Receptor Occupancy (RO)



KPL-404 achieved 100% receptor occupancy for 2 weeks in all animals at 5mg/kg and 4 weeks in all animals at 10mg/kg

Mean KLH IgG

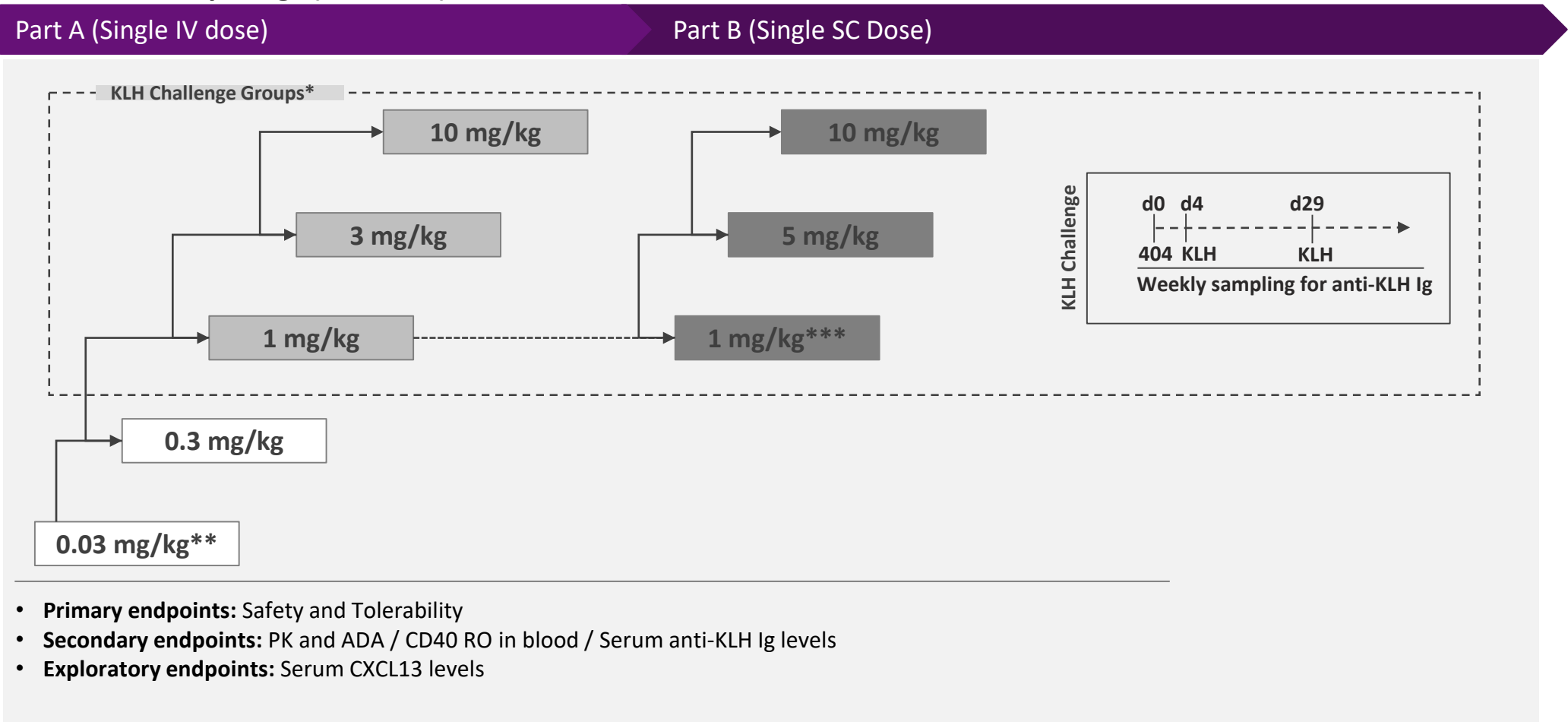


Complete suppression of primary T-cell dependent antigen response correlated with 100% receptor occupancy

KPL-404 Single-Ascending-Dose Phase 1 Study

First-in-human study to provide safety data and pharmacokinetics as well as receptor occupancy and TDAR

Phase 1 SAD Study Design (n=60 NHV)



Notes: Unless otherwise noted dose groups included 6 active/2 placebo subjects; *1° KLH challenge for all SAD dose groups except 0.03 and 0.3 mg/kg, 2° KLH re-challenge only in 1, 3, and 10 mg/kg IV; ** Cohort included 2 active and 2 placebo subjects; *** The 1 mg/kg SC dose arm will enroll after review of the 1 mg/kg IV SMC

SAD = single-ascending-dose; TDAR = T-cell dependent antibody response; KLH = keyhole limpet hemocyanin; RO = receptor occupancy; ADA = anti-drug antibodies





Immune-Modulating Product Candidates

Validated Mechanisms or Strong Biologic Rationale

Debilitating Diseases with Unmet Medical Need

~\$398M Proforma Cash Reserves* Extend into 2023

Multiple Clinical Data Readouts Expected in 2H 2020

*Kiniksa had proforma cash reserves of \$398.3 million as of June 30, 2020, which includes approximately \$252.4 million of cash, cash equivalents and short-term investments as of June 30, 2020 and approximately \$145.9 million of estimated net proceeds from our July 2020 public offering and concurrent private placement as though we had closed on these financings in the second quarter of 2020. As such our proforma cash reserves is not prepared in accordance with GAAP.



Every Second Counts!™

Appendix



Every Second Counts!™

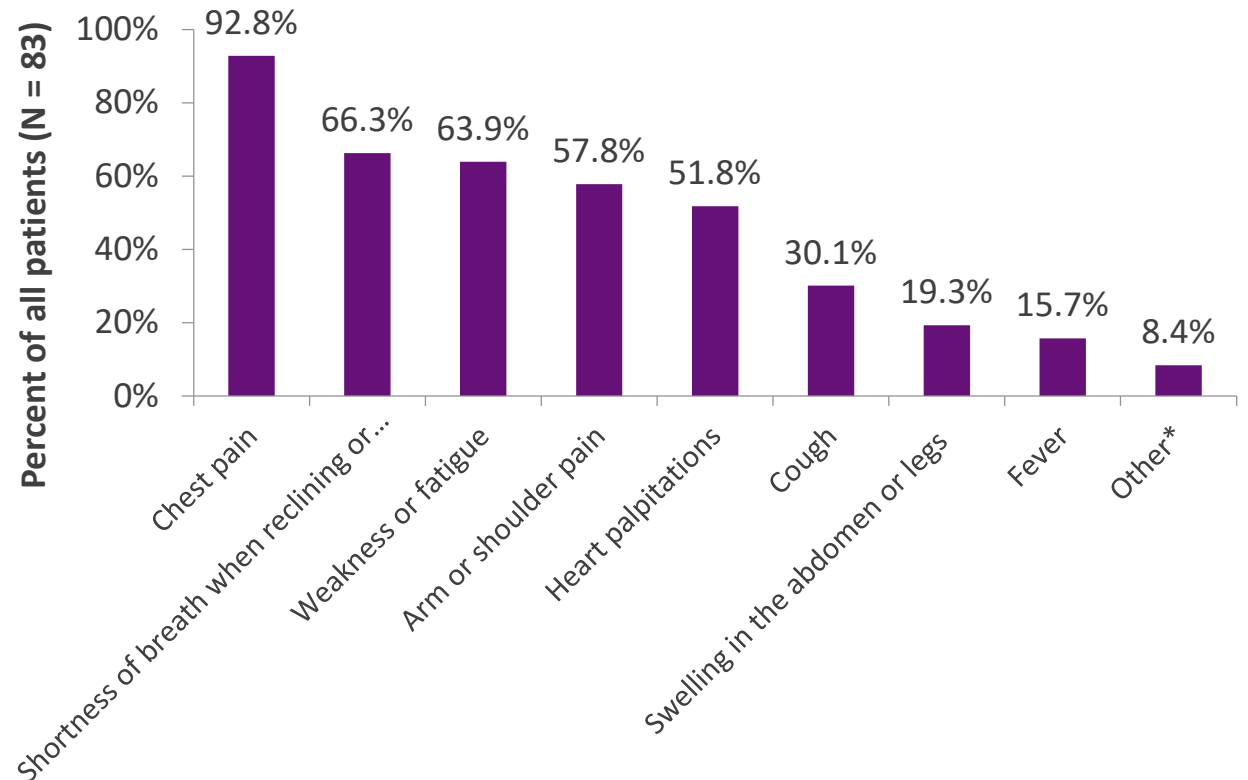
Appendix – Rilonacept

Recurrent Pericarditis Episodes are Painful, Debilitating and Disruptive to Quality of Life

"I cannot work, walk to the mailbox, or go up or down stairs without a great deal of pain and shortness of breath. Many referred visits to the ER because of pain, where ER docs accuse me of drug seeking for pain. It's humiliating and scary."
- Patient 2019

- Severe pain with similar symptoms as heart attack that **drive patients to the ER**^{1,2,5}
- Significantly **worse QoL than general population** - Ph2 PROMIS physical and mental health³
- Elevated **risk for major complications**, such as tamponade and constrictive pericarditis^{4,6}
- Results in **hospitalization and ER visits** for large proportion of patients^{1,4,6,7,8}

Symptoms during most recent pericarditis episode



* Other symptoms include difficulty swallowing (1), nausea (1), chest spasms (1), pneumonia (1), dizziness (1), headaches (1), pain when breathing (1), and upper back pain (2).

1. Results from an IRB-approved cross-sectional survey study of 80 respondents with a confirmed diagnosis of RP

Recurrent Pericarditis Episodes are Painful, Debilitating and Disruptive to Quality of Life

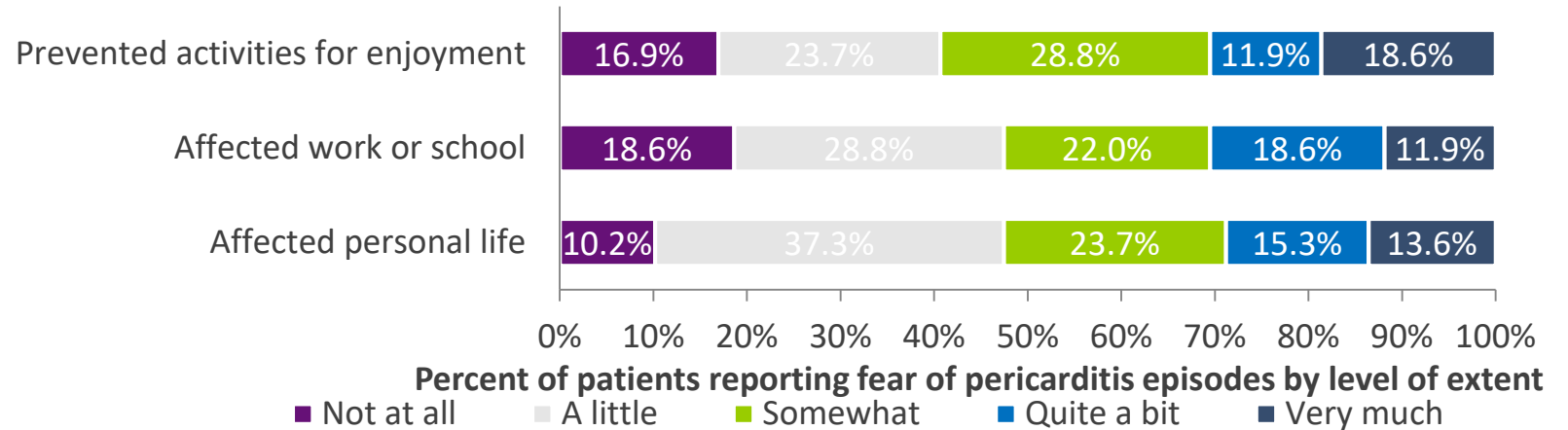
"I have gained a great deal of weight from steroids and inactivity. Exercise sets off more events, so am afraid to exercise. Pain is there constantly, just not as intense as it is during and event. [My] quality of life [is] greatly diminished." - Patient 2019

- Between flares, up to 95% of patients report some level of **fear of recurrence of pericarditis episodes**⁹
- After acute pain resolves, **residual pain** and other effects can last weeks to months^{1,2}
- Testimonials reveal **devastating impact on QoL** (anxiety, loss of sleep, lifestyle change, physical activity)^{1,2,5}
- 98% of patients express **need for additional therapies** that reduce the likelihood of another recurrence¹

Fear of recurrence of pericarditis episodes



Effect of fear of pericarditis episodes among patients who reported "a little" or more fear of pericarditis episodes (N = 59)



Recurrent Pericarditis is a Debilitating Disease with No FDA-Approved Therapies

Pericarditis is chest pain caused by pericardial inflammation

Acute Pericarditis is diagnosed in patients with two of the following:

- (1) Retrosternal, pleuritic chest pain (85-90% of cases), (2) Abnormal ECG (ST elevation or PR depression); (4) Pericardial effusion^{1,2}

Often Idiopathic Etiology:

- Absent a clear sign of infection, it is assumed that most cases are post-viral, but are termed “idiopathic”

Recurrent Pericarditis:

- Diagnosed if there is recurrence after initial episode of acute pericarditis, with a symptom-free interval of > 4-6 weeks → First recurrence is followed by more recurrences between 20% - 30% of the time^{1,2}

Involvement of IL-1 in Idiopathic Recurrent Pericarditis:

- IL-1 has been implicated by several case reports and the AIRTRIP Study in idiopathic pericarditis

Recurrent pericarditis causes significant impairment of quality of life

Recurrent Disease Creates Burden on QoL:

- Although pericarditis is rarely life-threatening, patients may have significant impairment on quality of life due to chest pain:
 - Interference with sleep, as chest pain worsens while reclining
 - Lower productivity at work or school
 - Some patients may be on disability or close to it
 - Standard of care treatments have significant AEs

Complications Are Rare but Severe:

- Complications of pericarditis are rare (i.e., effusion, tamponade, constrictive pericarditis), but, when they occur, they can be life threatening and often require invasive therapy

Summary of Adverse Events

Pivotal Phase 3 Rilonacept Data



	Run-In Period	Randomized Withdrawal Period	
Category ¹	Rilonacept (N=86) n (%)	Rilonacept Including Bailout Rilonacept (N=30) n (%)	Placebo Only Before Bailout Rilonacept (N=31) n (%)
Subjects with Any TEAEs	69 (80.2)	24 (80.0)	13 (41.9)
Blood and lymphatic system disorders	2 (2.3)	0	0
Eosinophilia	1 (1.2)	0	0
Lymphadenopathy	1 (1.2)	0	0
Cardiac disorders	5 (5.8)	0	2 (6.5)
Angina pectoris	1 (1.2)	0	0
Aortic valve incompetence	0	0	1 (3.2)
Atrial fibrillation	1 (1.2)	0	0
Cardiac flutter	0	0	1 (3.2)
Palpitations	1 (1.2)	0	0
Sinus tachycardia	1 (1.2)	0	0
Tachycardia	1 (1.2)	0	0
Ventricular dyssynchrony	1 (1.2)	0	0
Ear and labyrinth disorders	1 (1.2)	0	0
Middle ear effusion	0	0	0
Vertigo	1 (1.2)	0	0
Endocrine disorders	0	1 (3.3)	0
Hypothyroidism	0	1 (3.3)	0
Eye disorders	1 (1.2)	0	0
Diplopia	0	0	0
Eye inflammation	1 (1.2)	0	0
Gastrointestinal disorders	14 (16.3)	2 (6.7)	2 (6.5)

	Run-In Period	Randomized Withdrawal Period	
Category ¹	Rilonacept (N=86) n (%)	Rilonacept Including Bailout Rilonacept (N=30) n (%)	Placebo Only Before Bailout Rilonacept (N=31) n (%)
Abdominal distension	2 (2.3)	0	0
Abdominal pain	0	0	1 (3.2)
Abdominal tenderness	0	1 (3.3)	0
Aphthous ulcer	0	1 (3.3)	0
Constipation	1 (1.2)	0	0
Diarrhea	5 (5.8)	0	0
Gastric ulcer	1 (1.2)	0	0
Gastritis	1 (1.2)	0	0
Gastrointestinal disorder	1 (1.2)	0	0
Gastroesophageal reflux disease	1 (1.2)	1 (3.3)	0
Gingival pain	1 (1.2)	0	0
Haemorrhoids	0	0	1 (3.2)
Ileus	0	0	0
Nausea	2 (2.3)	0	0
Tongue ulceration	0	1 (3.3)	0
Vomiting	1 (1.2)	0	0
General disorders and administration site conditions	30 (34.9)	10 (33.3)	1 (3.2)
Asthenia	2 (2.3)	0	0
Chest discomfort	1 (1.2)	1 (3.3)	0
Chills	1 (1.2)	0	0
Fatigue	2 (2.3)	2 (6.7)	0
Feeling abnormal	1 (1.2)	0	0

Summary of Adverse Events

Pivotal Phase 3 Rilonacept Data



	Run-In Period	Randomized Withdrawal Period	
Category ¹	Rilonacept (N=86) n (%)	Rilonacept Including Bailout Rilonacept (N=30) n (%)	Placebo Only Before Bailout Rilonacept (N=31) n (%)
Feeling hot	2 (2.3)	0	0
Injection site bruising	1 (1.2)	0	0
Injection site discolouration	2 (2.3)	0	0
Injection site erythema	18 (20.9)	6 (20.0)	0
Injection site inflammation	1 (1.2)	0	0
Injection site nodule	1 (1.2)	0	0
Injection site pain	4 (4.7)	0	0
Injection site pruritus	5 (5.8)	5 (16.7)	0
Injection site rash	3 (3.5)	0	0
Injection site reaction	2 (2.3)	0	0
Injection site swelling	5 (5.8)	1 (3.3)	0
Non-cardiac chest pain	1 (1.2)	3 (10.0)	1 (3.2)
Oedema peripheral	0	1 (3.3)	0
Pain	1 (1.2)	1 (3.3)	0
Pyrexia	1 (1.2)	0	0
Immune system disorders	1 (1.2)	0	1 (3.2)
Drug hypersensitivity	1 (1.2)	0	0
Hypersensitivity	1 (1.2)	0	0
Seasonal allergy	0	0	1 (3.2)
Infections and infestations	14 (16.3)	12 (40.0)	3 (9.7)
Bronchitis	0	1 (3.3)	0
Conjunctivitis	0	1 (3.3)	0

	Run-In Period	Randomized Withdrawal Period	
Category ¹	Rilonacept (N=86) n (%)	Rilonacept Including Bailout Rilonacept (N=30) n (%)	Placebo Only Before Bailout Rilonacept (N=31) n (%)
Ear infection	0	0	0
Gastroenteritis	0	0	1 (3.2)
Gastroenteritis viral	0	0	0
Gastrointestinal viral infection	0	1 (3.3)	1 (3.2)
Hordeolum	1 (1.2)	0	0
Influenza	1 (1.2)	0	1 (3.2)
Nasopharyngitis	6 (7.0)	2 (6.7)	0
Oral herpes	1 (1.2)	1 (3.3)	0
Otitis media	0	1 (3.3)	0
Pharyngitis	1 (1.2)	0	0
Pharyngitis streptococcal	0	0	0
Rhinitis	1 (1.2)	0	0
Sinusitis	1 (1.2)	3 (10.0)	0
Subcutaneous abscess	1 (1.2)	0	0
Upper respiratory tract infection	2 (2.3)	1 (3.3)	0
Urinary tract infection	1 (1.2)	3 (10.0)	0
Vaginal infection	0	1 (3.3)	0
Viral upper respiratory tract infection	2 (2.3)	1 (3.3)	0
Injury, poisoning and procedural complications	6 (7.0)	3 (10.0)	1 (3.2)
Epicondylitis	0	1 (3.3)	0
Fall	2 (2.3)	0	0
Humerus fracture	0	0	1 (3.2)

Summary of Adverse Events

Pivotal Phase 3 Rilonacept Data



	Run-In Period	Randomized Withdrawal Period	
Category ¹	Rilonacept (N=86) n (%)	Rilonacept Including Bailout Rilonacept (N=30) n (%)	Placebo Only Before Bailout Rilonacept (N=31) n (%)
Joint injury	0	1 (3.3)	0
Limb injury	0	0	1 (3.2)
Muscle strain	1 (1.2)	0	0
Post procedural contusion	0	1 (3.3)	0
Post-traumatic pain	2 (2.3)	0	0
Procedural dizziness	1 (1.2)	0	0
Investigations	12 (14.0)	7 (23.3)	0
Bacterial test	0	0	0
Blood cholesterol increased	0	1 (3.3)	0
Blood glucose decreased	0	1 (3.3)	0
Blood glucose increased	1 (1.2)	0	0
Blood pressure increased	1 (1.2)	1 (3.3)	0
Blood triglycerides increased	0	1 (3.3)	0
Body temperature decreased	1 (1.2)	0	0
C-reactive protein increased	1 (1.2)	2 (6.7)	0
Eosinophil count increased	1 (1.2)	0	0
Haemoglobin decreased	1 (1.2)	0	0
Heart rate increased	1 (1.2)	1 (3.3)	0
Hepatic enzyme increased	1 (1.2)	1 (3.3)	0
Heart density lipoprotein decreased	1 (1.2)	0	0
Heart density lipoprotein increased	0	3 (10.0)	0
Lipids increased	0	2 (6.7)	0

	Run-In Period	Randomized Withdrawal Period	
Category ¹	Rilonacept (N=86) n (%)	Rilonacept Including Bailout Rilonacept (N=30) n (%)	Placebo Only Before Bailout Rilonacept (N=31) n (%)
Liver function test increased	1 (1.2)	0	0
Low density lipoprotein increased	1 (1.2)	0	0
Mean cell volume increased	0	1 (3.3)	0
Smear cervix abnormal	1 (1.2)	0	0
Weight increased	1 (1.2)	0	0
Metabolism and nutrition disorders	0	1 (3.3)	0
Hyperlipidaemia	0	1 (3.3)	0
Musculoskeletal and connective tissue disorders	26 (30.2)	6 (20.0)	4 (12.9)
Arthralgia	8 (9.3)	1 (3.3)	0
Arthritis	0	1 (3.3)	0
Axillary mass	0	1 (3.3)	0
Back pain	3 (3.5)	1 (3.3)	0
Groin pain	1 (1.2)	0	0
Joint stiffness	2 (2.3)	0	0
Musculoskeletal chest pain	3 (3.5)	1 (3.3)	4 (12.9)
Musculoskeletal pain	3 (3.5)	0	0
Myalgia	9 (10.5)	1 (3.3)	0
Neck pain	1 (1.2)	0	1 (3.2)
Osteoarthritis	1 (1.2)	0	0
Pain in extremity	1 (1.2)	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	1 (1.2)	2 (6.7)	0
Acrochordon	1 (1.2)	0	0

Summary of Adverse Events

Pivotal Phase 3 Riloncept Data



	Run-In Period	Randomized Withdrawal Period	
Category ¹	Riloncept (N=86) n (%)	Riloncept Including Bailout Riloncept (N=30) n (%)	Placebo Only Before Bailout Riloncept (N=31) n (%)
Lipoma	0	1 (3.3)	0
Squamous cell carcinoma	0	1 (3.3)	0
Nervous system disorders	14 (16.3)	2 (6.7)	0
Carpal tunnel syndrome	1 (1.2)	0	0
Cerebrovascular accident	1 (1.2)	0	0
Dizziness	2 (2.3)	1 (3.3)	0
Dysgeusia	1 (1.2)	0	0
Head discomfort	0	1 (3.3)	0
Headache	7 (8.1)	0	0
Migraine	1 (1.2)	0	0
Presyncope	1 (1.2)	0	0
Somnolence	1 (1.2)	0	0
Psychiatric disorders	1 (1.2)	0	1 (3.2)
Insomnia	0	0	1 (3.2)
Sleep disorder	1 (1.2)	0	0
Renal and urinary disorders	0	1 (3.3)	1 (3.2)
Nephrolithiasis	0	1 (3.3)	0
Renal colic	0	0	1 (3.2)
Reproductive system and breast disorders	1 (1.2)	1 (3.3)	1 (3.2)
Ovarian cyst	1 (1.2)	0	0
Uterine haemorrhage	0	1 (3.3)	0
Uterine polyp	0	0	1 (3.2)

	Run-In Period	Randomized Withdrawal Period	
Category ¹	Riloncept (N=86) n (%)	Riloncept Including Bailout Riloncept (N=30) n (%)	Placebo Only Before Bailout Riloncept (N=31) n (%)
Respiratory, thoracic and mediastinal disorders	15 (17.4)	7 (23.3)	1 (3.2)
Alveolitis allergic	1 (1.2)	0	0
Cough	5 (5.8)	1 (3.3)	0
Dysphonia	0	1 (3.3)	0
Dyspnoea	1 (1.2)	1 (3.3)	0
Epistaxis	1 (1.2)	0	0
Nasal congestion	0	0	0
Oropharyngeal pain	1 (1.2)	3 (10.0)	0
Pharyngeal hypoaesthesia	1 (1.2)	0	0
Respiratory tract congestion	2 (2.3)	0	1 (3.2)
Rhinorrhoea	1 (1.2)	0	0
Sinus congestion	2 (2.3)	2 (6.7)	0
Skin and subcutaneous tissue disorders	11 (12.8)	0	1 (3.2)
Acne	1 (1.2)	0	0
Alopecia	1 (1.2)	0	0
Angioedema	1 (1.2)	0	0
Erythema	2 (2.3)	0	0
Pruritus	2 (2.3)	0	0
Pruritus generalised	2 (2.3)	0	1 (3.2)
Rash	1 (1.2)	0	0
Rash macular	3 (3.5)	0	0
Social circumstances	0	1 (3.3)	0

Summary of Adverse Events

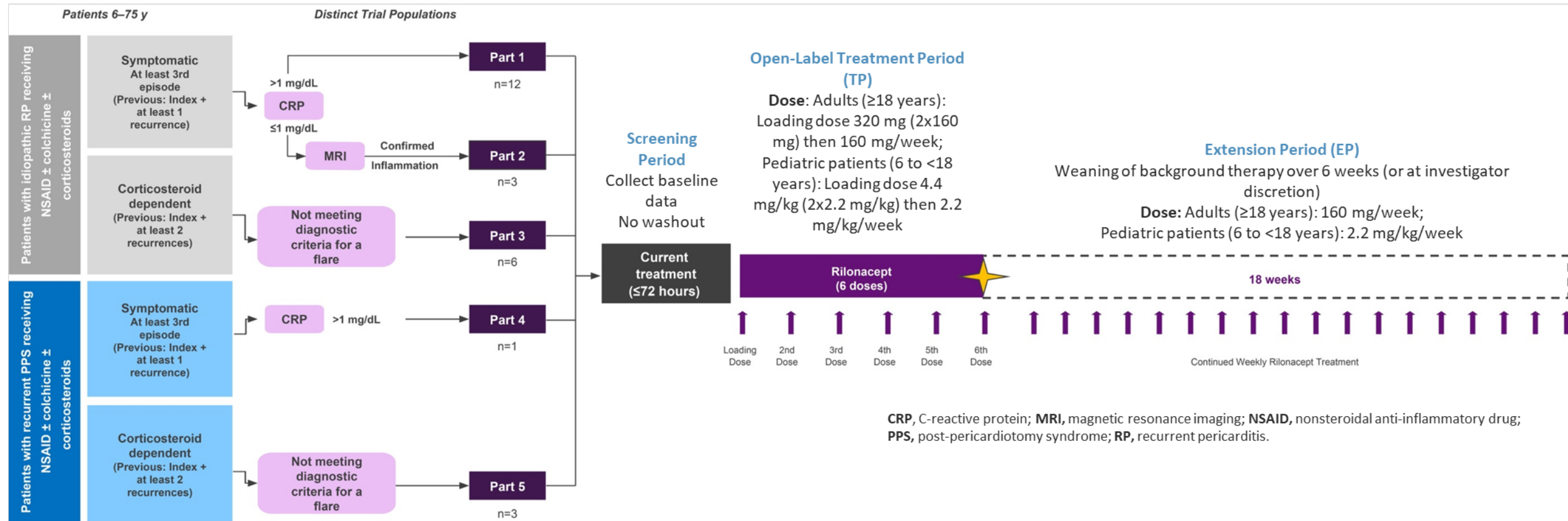
Pivotal Phase 3 Rilonacept Data



	Run-In Period	Randomized Withdrawal Period	
Category ¹	Rilonacept (N=86) n (%)	Rilonacept Including Bailout Rilonacept (N=30) n (%)	Placebo Only Before Bailout Rilonacept (N=31) n (%)
Menopause	0	1 (3.3)	0
Vascular disorders	2 (2.3)	1 (3.3)	1 (3.2)
Hypertension	2 (2.3)	1 (3.3)	1 (3.2)

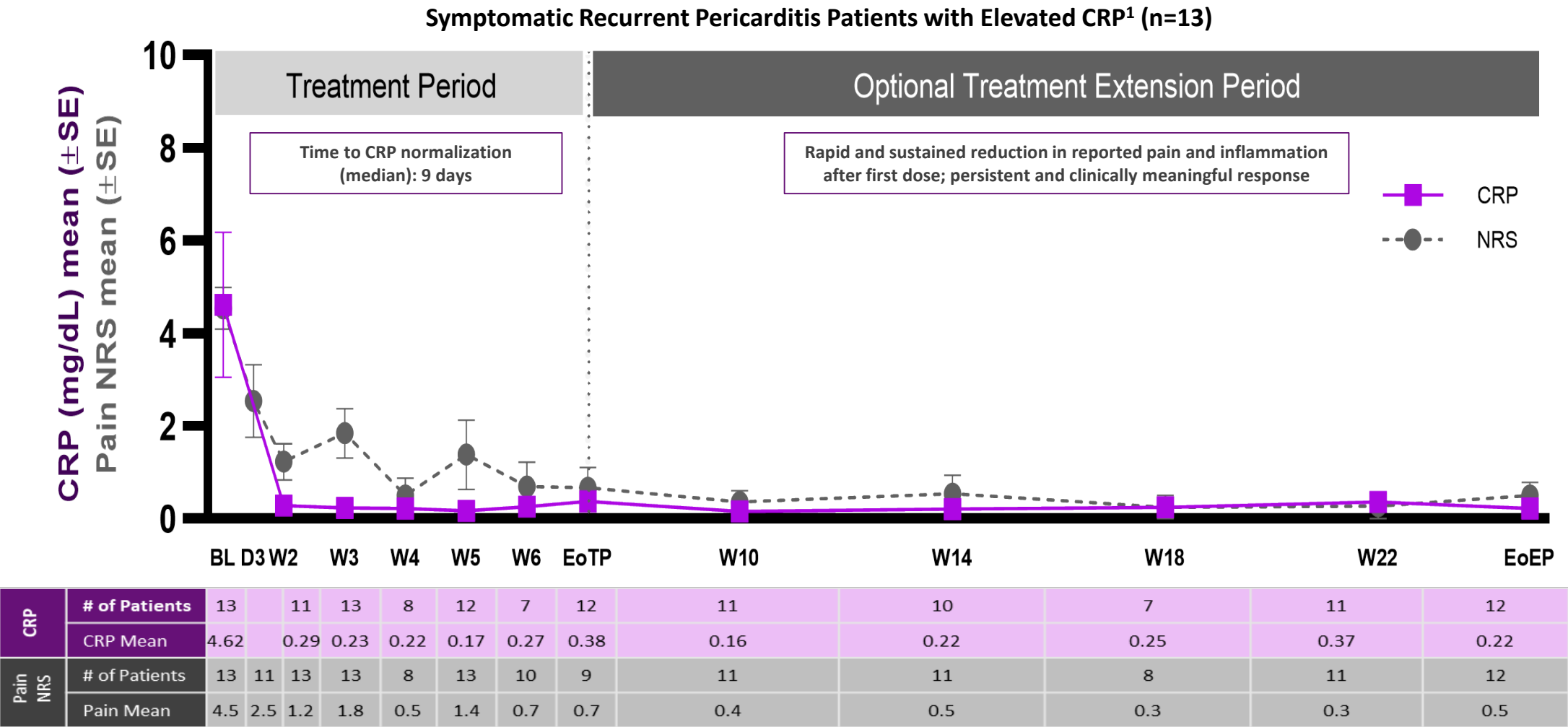
	Run-In Period	Randomized Withdrawal Period	
Category ¹	Rilonacept (N=86) n (%)	Rilonacept Including Bailout Rilonacept (N=30) n (%)	Placebo Only Before Bailout Rilonacept (N=31) n (%)
Subjects with Any Serious TEAE	1 (1.2)	1 (3.3)	1 (3.2)
Cardiac disorders	0	0	1 (3.2)
Cardiac flutter	0	0	1 (3.2)
Gastrointestinal disorders	0	0	0
Ileus	0	0	0
General disorders and administration site conditions	0	0	0
Pyrexia	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0	1 (3.3)	0
Squamous cell carcinoma	0	1 (3.3)	0
Nervous system disorders	1 (1.2)	0	0
Cerebrovascular accident	1 (1.2)	0	0

Open-Label Phase 2 Clinical Trial of Rilonacept in Pericarditis Populations



Phase 2 Rilonacept Data

Resolution of pericarditis episodes in symptomatic patients (parts 1 and 4)



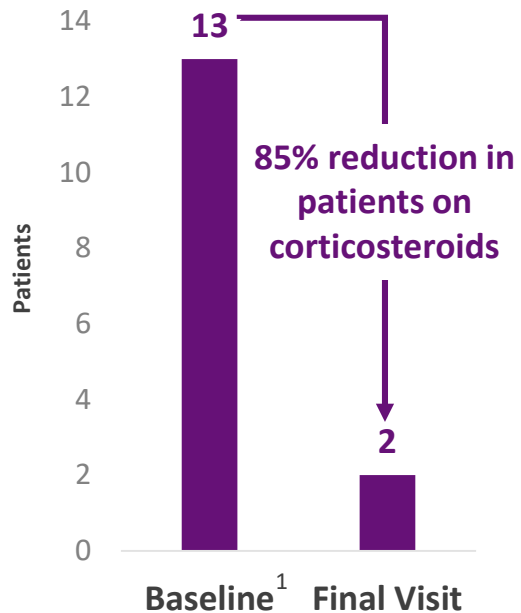
1) Patients with elevated CRP and symptomatic disease (Parts 1 and 4) are most representative of real-world recurrent pericarditis. Inclusion and exclusion criteria for the ongoing Phase 3 study RHAPSODY align with this patient population (clinicaltrials.gov/NCT03737110). EoTP = end of treatment period; EoEP = end of extension period; CRP = C-Reactive Protein; NRS = Numeric Rating Scale



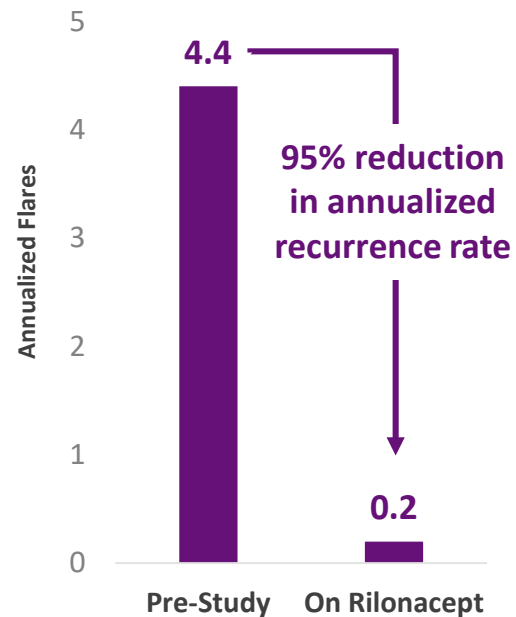
Phase 2 Rilonacept Data

Discontinuation of corticosteroids, decrease in incidence of pericarditis episodes while on treatment and improvement in quality of life scores

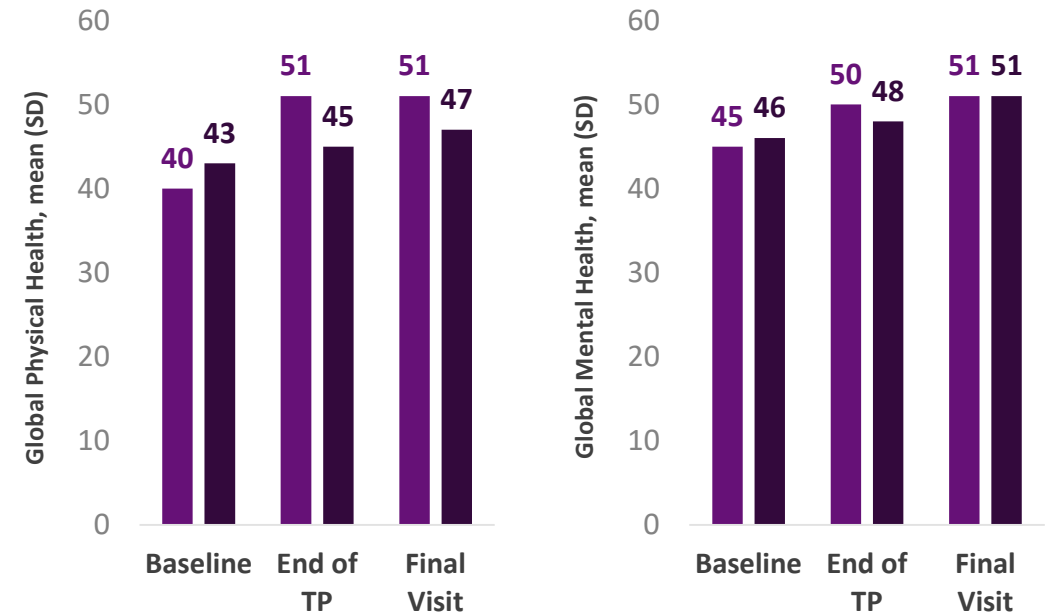
Discontinuation of Corticosteroids Without Pericarditis Recurrence



Decrease in Annualized Incidence of Pericarditis Episodes While on Treatment



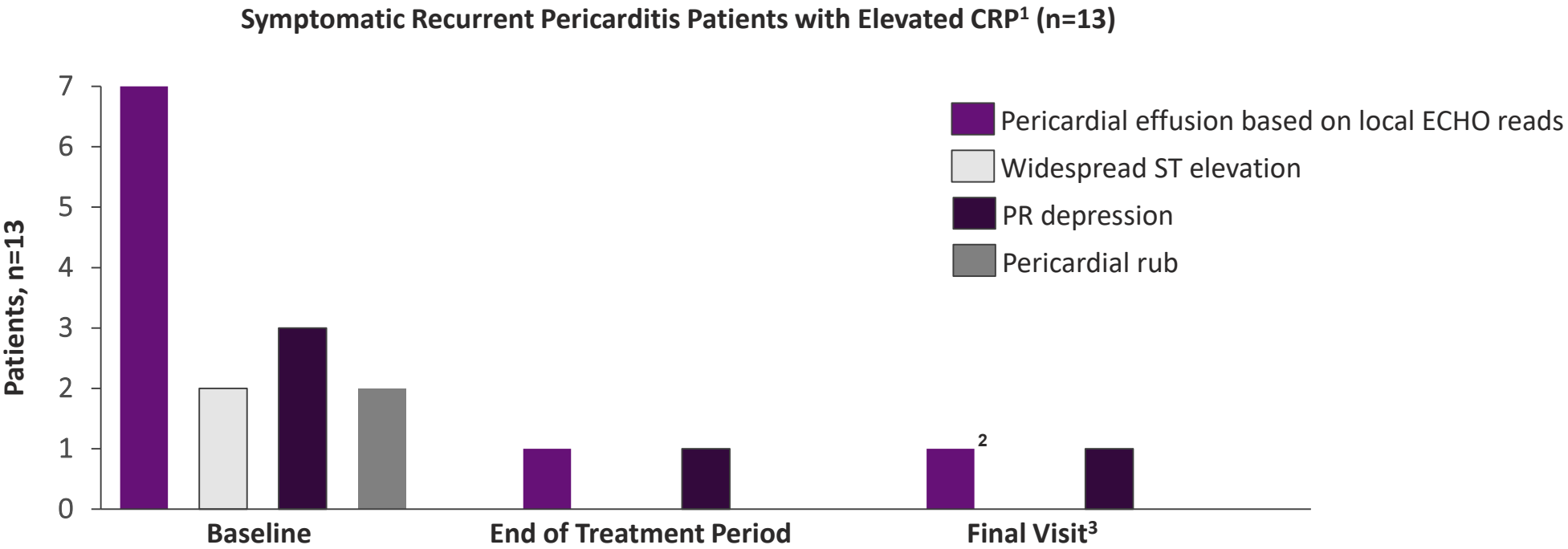
Improved Quality of Life Scores²



Idiopathic or PPS: ■ Active³ (n=16) ■ CS-dependent⁴ (n=9)

Phase 2 Rilonacept Data

Pericardial signs resolved or improved in all patients (parts 1 and 4)

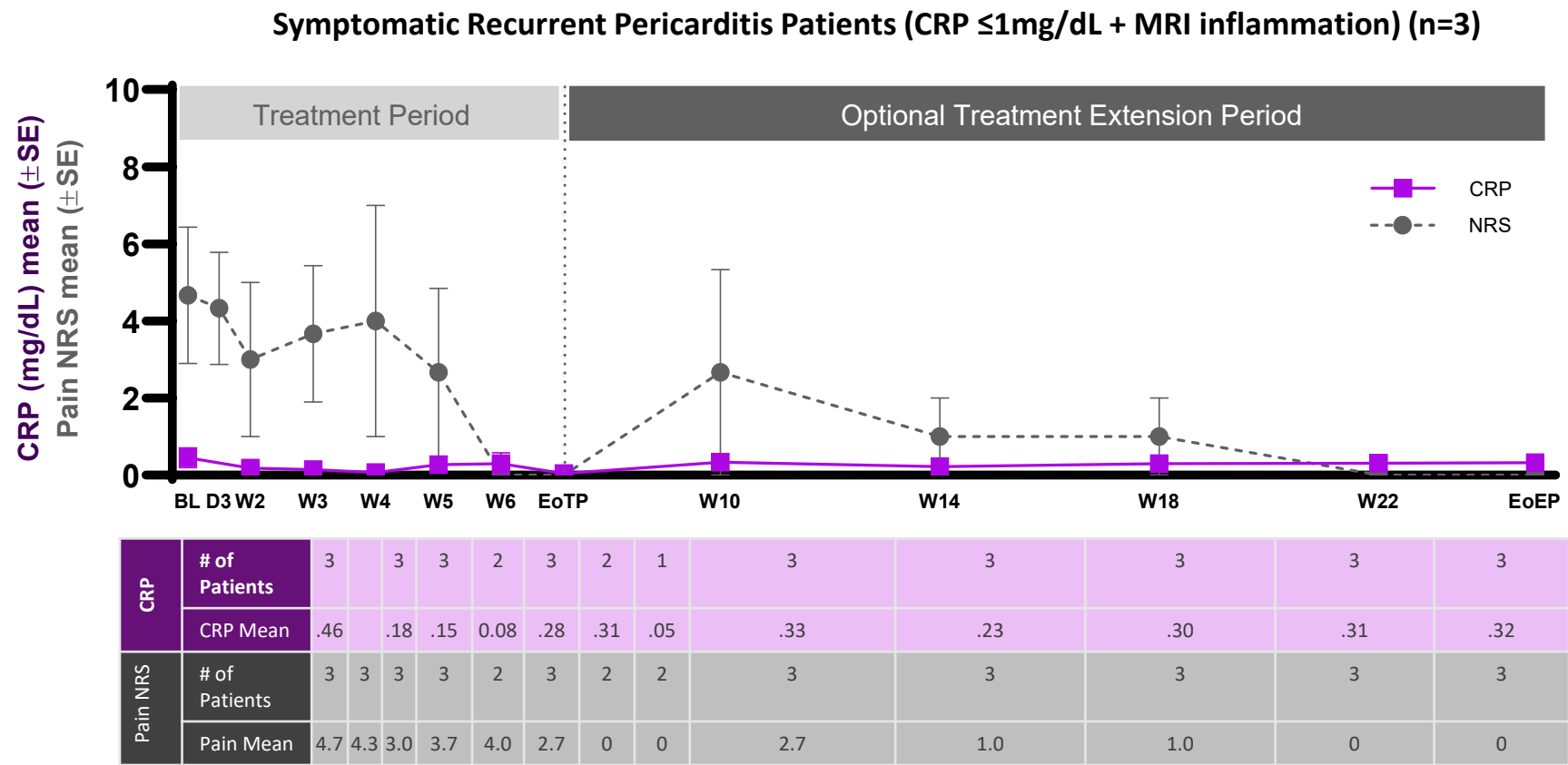


1) Patients with elevated CRP and symptomatic disease (Parts 1 and 4) are most representative of real-world recurrent pericarditis. Inclusion and exclusion criteria for the ongoing Phase 3 study RHAPSODY align with this patient population (clinicaltrials.gov/NCT03737110); 2) patient with effusion at baseline, no effusion at EoT Visit and trivial effusion (not pathological) at Final Visit; 3) n=12; one patient discontinued study drug in TP due to SAE; no effusion at baseline or EoT Visit; CRP = C-Reactive Protein



Phase 2 Rilonacept Data

Reduction in both reported pain and inflammation in symptomatic patients without elevated CRP and with MRI inflammation (Part 2)



Phase 2 Rilonacept Data

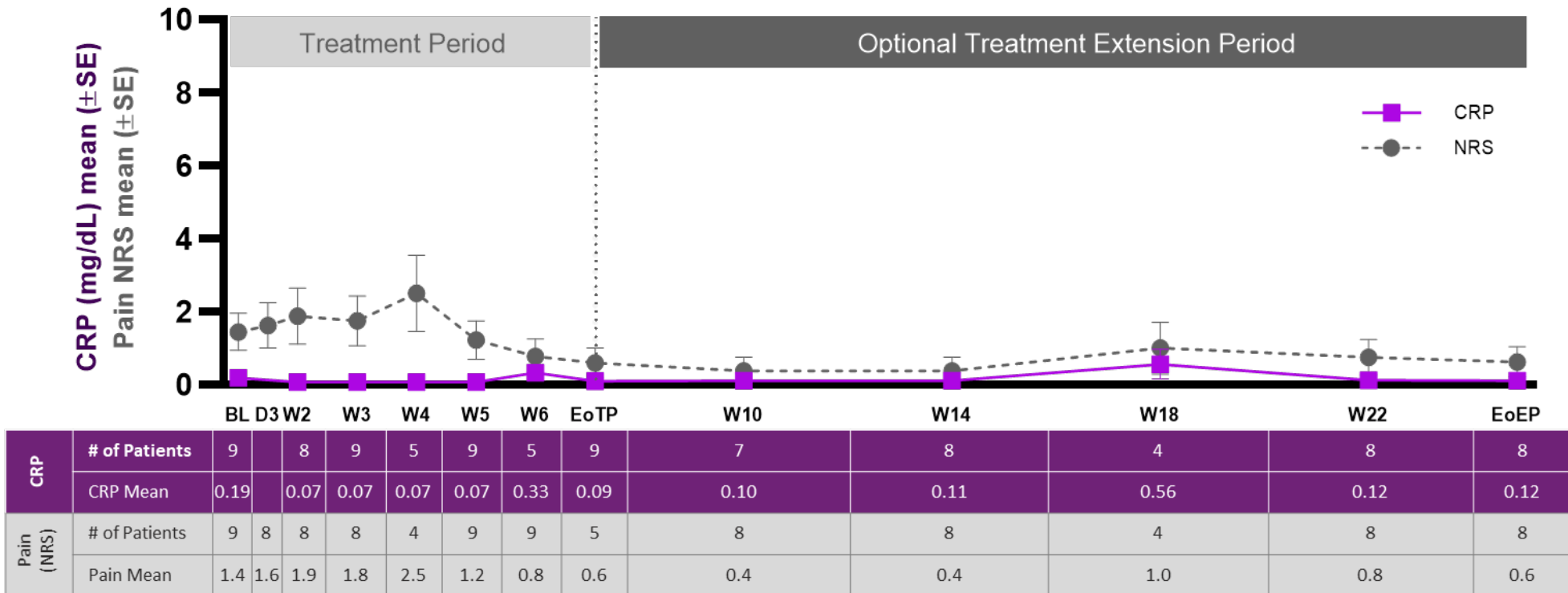
Corticosteroid tapering in corticosteroid-dependent patients (Parts 3 and 5)

Corticosteroid-Dependent Patients (Parts 3 and 5): Pericarditis Medications During TP and EP Combined						
n/N (%)	<u>Medications</u>					
	At least 1	Analgesics	Aspirin	NSAIDs	Colchicine	CS
Dose stopped	7/8 (87.5)	0/0	0/1	2/5 (40.0)	1/7 (14.3)	7/8 (87.5)
Dose decreased	4/8 (50)	0/0	1/1 (100)	2/5 (40)	1/7 (14.3)	1/8 (12.5)
Dose increased	0/8	0/0	0/1	0/5	0/7	0/8
Starting new	0/8	0/8	0/8	0/8	0/8	0/8
CS, corticosteroid; NSAID, nonsteroidal anti-inflammatory drugs						

Phase 2 Rilonacept Data

Pericarditis pain scores and CRP in corticosteroid-dependent patients (Parts 3 and 5)

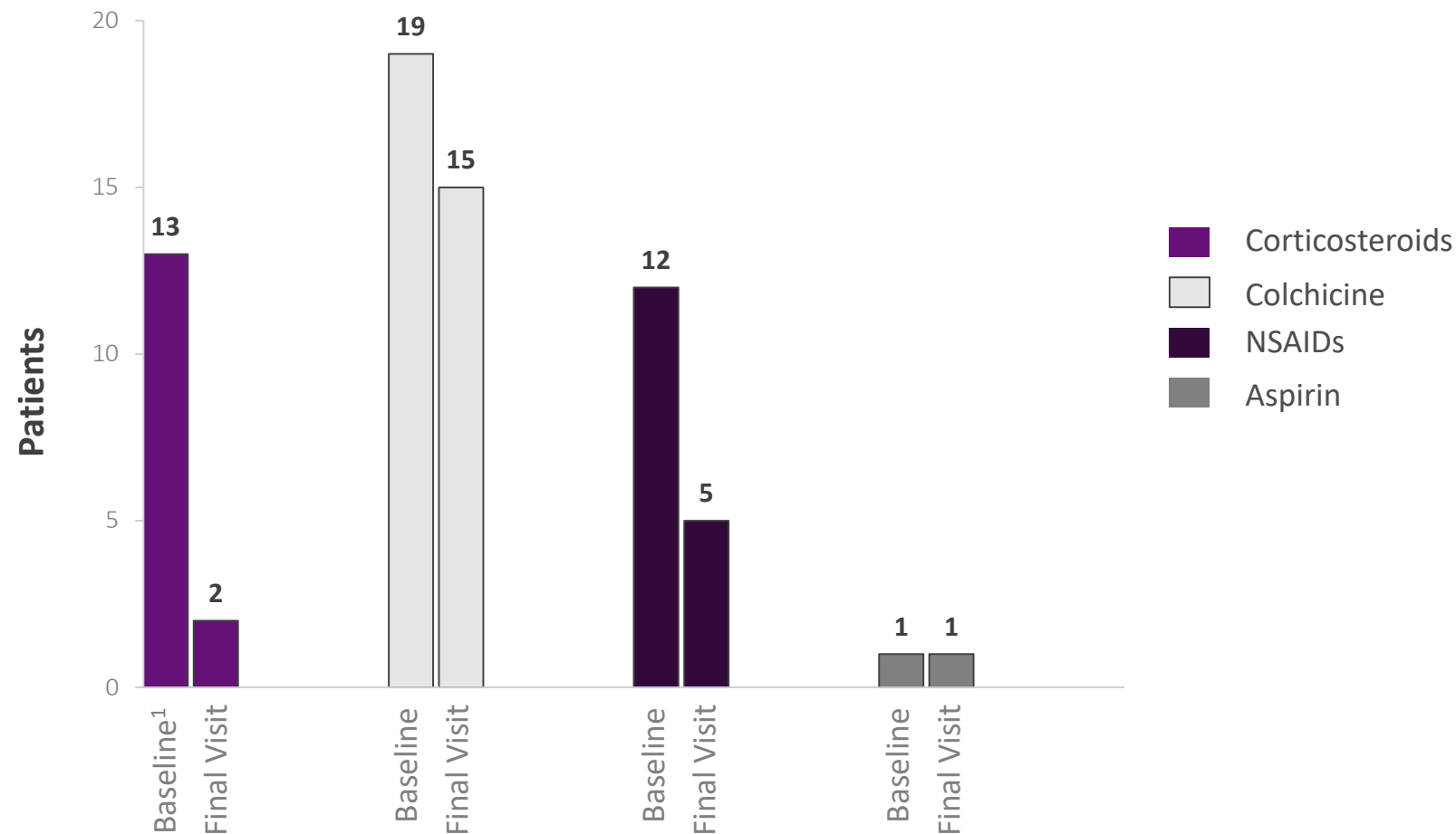
NRS Scores (Pain) and CRP Levels Non-Active CS-Dependent Patients (n=9) During TP and Throughout EP (Parts 3 and 5)



Phase 2 Rilonacept Data

All patients on corticosteroids (CS) at baseline who completed 24 weeks of treatment stopped or tapered CS during rilonacept treatment without experiencing a recurrence

No patients had pericarditis recurrence in investigators' judgement after stopping concomitant pericarditis medication while on rilonacept treatment



1) 15 recurrent pericarditis patients on corticosteroids at baseline enrolled in the 6-week base treatment period, and 13 continued into the optional 18-week extension treatment period and completed 24 weeks of treatment



Phase 2 Rilonacept Data

Of 13 patients on corticosteroids (CS) at baseline who completed 24 weeks of treatment, 11 discontinued CS and the CS dose was successfully tapered in the remaining 2 patients

	Idiopathic			PPS		Idiopathic or PPS
Disease Status:	Active ¹	Active ²	CS-dep ³	Active ⁴	CS-dep ⁵	All ¹⁻⁵
CRP requirement (mg/dL):	>1	≤1	N/A	>1	N/A	N/A
N:	12	3	6	1	3	25
Baseline						
Patients on prednisone ⁶ , n	4	2	6	0	3	15
Mean dose (mg/day)	8.4	40.0	8.9	0	7.7	12.7
Min	1.0	30.0	2.5	0	3.0	1.0
Max	12.5	50.0	30	0	15.0	50.0
Corticosteroid Changed During TP and EP Combined						
Prednisone dose decreased ^{7,8}	0/3	1/2 (50.0)	1/5 (20.0)	0/0	0/3	2/13 (15.4)
Prednisone stopped ^{8,9}	3/3 (100)	1/2 (50.0)	4/5 (80.0)	0/0	3/3 (100)	11/13 (84.6)
Prednisone dose increased ⁷	0/3	0/2	0/5	0/0	0/3	0/13
Prednisone initiated ⁹	0/11	0/3	0/5	0/1	0/3	0/23

1) Part 1; 2) Part 2; 3) Part 3; 4) Part 4; 5) Part 5; 6) 2 patients on prednisone at baseline did not enter EP (one in Part 1 and in Part 3) 7) Refers to patients who entered the study on prednisone; 8) 1 patient decreased prednisone dose in TP, and 1 stopped prednisone in TP (both in Part 2); 9) Refers to all patients in EP; CRP= C-reactive protein; CS-dep = corticosteroid-dependent; PPS = post-pericardiotomy syndrome; TP = treatment period; EP = extension period

Phase 2 Rilonacept Data

Annualized incidence of pericarditis episodes decreased during rilonacept treatment in the study

Disease Status: CRP requirement (mg/dL): N:	Idiopathic			PPS	
	Active ¹	Active ²	CS-dep ³	Active ⁴	CS-dep ⁵
	>1	≤1	N/A	>1	N/A
	12	3	6	1	3
Prior to the study ⁶					
Pericarditis episodes per year, mean (SD)	4.4 (4.68)	2.0 (1.75)	4.5 (2.58)	1.3 (N/A)	3.7 (3.02)
During the study ⁷					
Patients with pericarditis episodes, n	1 ^h	0	0	0	0
Pericarditis episodes per year, mean (SD)	0.18 (0.62)	0	0	0	0

1) Part 1; 2) Part 2; 3) Part 3; 4) Part 4; 5) Part 5; 6) Episodes at enrollment include index, prior recurrences, and current episode; 7) Episodes during the study include recurrences during TP and EP combined. Pericarditis recurrence during the study was based on Investigator’s judgement; ^hPatient had a mild pericarditis recurrence in TP, 5 days duration, with NRS pain increase from 0 to 2, CRP 0.10 mg/dL, not requiring addition of new medication to treat pericarditis; CRP = C-reactive protein; CS-dep = corticosteroid-dependent; PPS = post-pericardiotomy syndrome



Phase 2 Rilonacept Data

Rilonacept treatment resulted in improvement of quality of life scores¹

	Idiopathic or PPS	
	Active ¹ (n=16)	CS-dependent ² (n=9)
Global Physical Health, mean (SD)		
Baseline	39.94 (8.941)	43.3 (5.311)
End of TP	51.35 (7.962)	45.09 (4.057)
Final Visit	51.32 (6.564)	46.81 (9.266)
Global Mental Health, mean (SD)		
Baseline	44.5 (10.484)	46.49 (7.767)
End of TP	50.13 (11.325)	47.91 (5.509)
Final Visit	50.54 (10.995)	50.66 (6.299)

1) PROMIS® = Patient Reported Outcomes Measurement Information System. The higher the score, the better global health is. US national average score for Global Physical and Mental Health is 50 (SD 10); 1) Part 1, 2, and 4; 2) Part 3 and 5



Case Study: Treatment/Retreatment of Recurrent Pericarditis with Rilonacept

- **Patient**

- 50-year-old female with idiopathic pericarditis and 1 prior recurrence, enrolled in Part 1 during her third episode (pain NRS 6/10; CRP 8.85 mg/dL; pericardial effusion on echocardiography) while receiving colchicine 0.6 mg bid.

- **Pain and CRP Reduction During the Study**

- Addition of rilonacept to colchicine background rapidly reduced pain (week 2 pain NRS 1/10; week 24 pain NRS 0/10), decreased CRP (week 2 CRP 0.66 mg/dL; week 24 CRP 0.09 mg/dL), and resolved pericardial effusion.

- **Safety**

- Mild, transient injection site reactions occurred for 21 of 24 rilonacept injections; the patient also had reported mild AEs of heartburn, common cold, worsening of elevated LFTs, elevated cholesterol, elevated HDL, intermittent chest discomfort and elevated CK

- **After Completing the EP**

- Approximately 8 weeks after rilonacept discontinuation, while continuing on colchicine 0.6 mg bid, the patient presented with pericarditis symptoms requiring addition of celecoxib 200 mg/day. Ten weeks later the patient developed frank pericarditis recurrence (pain NRS 7/10; CRP 23.1 mg/dL) and cardiac tamponade requiring pericardiocentesis. The patient was re-enrolled in the study.

- **Pain and CRP Normalized and Pericardial Effusion Resolved with Rilonacept Retreatment**

- Rapid improvements in pain and CRP were observed after the first rilonacept administration (week 2 pain NRS 0/10; CRP 0.57 mg/dL). At the week 7 visit, NRS pain was 1/10, CRP was 0.09 mg/dL, and there was no evidence of pericardial effusion on echocardiography. At the last study evaluation available (1 month EP), NRS pain was 0/10 and CRP remained normal (0.08 mg/dL). At the Final Visit NRS pain was 0/10 and CRP remained normal (0.14 mg/dL).

- **Safety**

- Mild, transient injection site reactions occurred in 17 out of 24 rilonacept administrations; the patient also developed mild AEs of hypokalemia, decreased WBC count, and increased lipids.

Phase 2 Rilonacept Data

Baseline demographics and clinical characteristics

Baseline Demographics

General Characteristics	All Patients (n=25)
Unique patients, n	25
Mean age (range), yrs	42.8 (26-62)
Sex (male/female)	10/15
Race (white/African American)	22/3
Mean pericarditis episodes at enrollment ¹ (range)	4.3 (3-10)
Mean disease duration (range), yrs	2.2 (0.2-7.9)

1) Includes index, recurrent, and qualifying (if applicable) episodes

Clinical Characteristics

Disease Status: CRP requirement (mg/dL): N:	Idiopathic RP			PPS	
	Active ^a	Active ^b	CS-dep ^c	Active ^d	CS-dep ^e
	>1	≤1	N/A	>1	N/A
Mean NRS ^f (SD)	4.6 (1.7)	4.7 (3.1)	1.2 (0.8)	4.0 (N/A)	2.0 (2.7)
Mean CRP (SD), mg/dL	4.9 (5.8)	0.5 (0.4)	0.2 (0.1)	1.1 (N/A)	0.1 (0.1)

Phase 2 Rilonacept Data

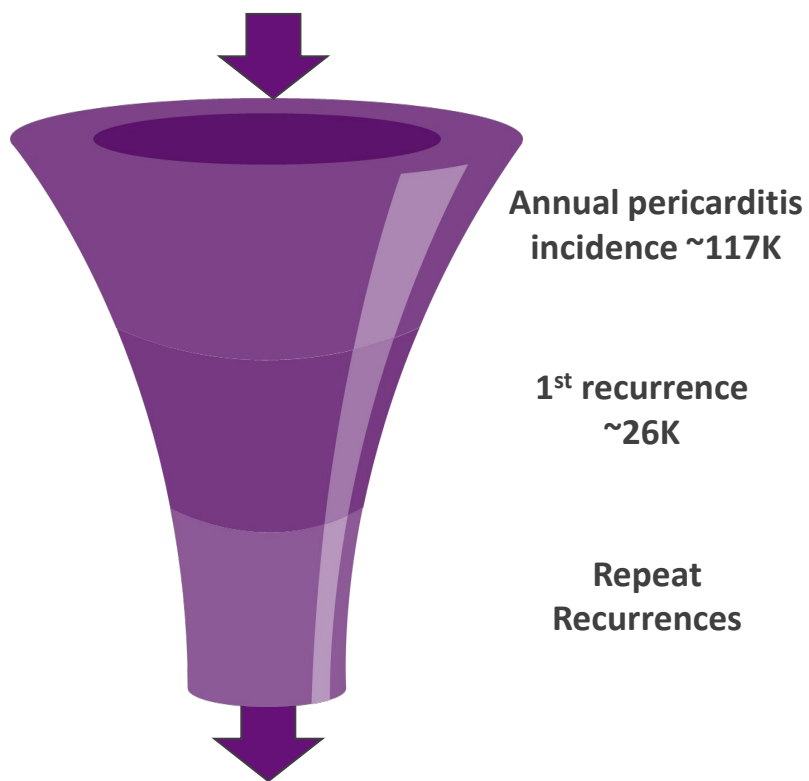
Summary of adverse events

Disease Status:	Idiopathic			PPS		Idiopathic or PPS		
	Active ¹	Active ²	CS-dep ³	Active ⁴	CS-dep ⁵	Active ^{1,2,4}	CS-dep ^{3,5}	All ¹⁻⁵
CRP requirement (mg/dL):	>1	≤1	N/A	>1	N/A	N/A	N/A	N/A
N:	12	3	6	1	3	16	9	25
≥1 TEAE, n (%)	12 (100)	3 (100)	6 (100)	1 (100)	3 (100)	16 (100)	9 (100)	25 (100)
≥1 treatment-related TEAE, n (%)	9 (75)	2 (66.7)	3 (50)	1 (100)	2 (66.7)	12 (75)	5 (55.6)	17 (68)
≥1 serious TEAE, n (%)	2 (16.7)	0	0	0	0	2 (12.5)	0	2 (8)
≥1 treatment-related serious TEAE, n (%)	1 (8.3)	0	0	0	0	1 (6.3)	0	1 (4)
≥1 TEAE leading to treatment discontinuation, n (%)	1 (8.3)	0	0	0	0	1 (6.3)	0	1 (4)
≥1 TEAE leading to death, n (%)	0	0	0	0	0	0	0	0
TEAEs by severity, n (%)								
Mild	9 (75)	3 (100)	4 (66.7)	1 (100)	2 (66.7)	13 (81.3)	6 (66.7)	19 (76)
Moderate	2 (16.7)	0	2 (33.3)	0	0	2 (12.5)	2 (22.2)	4 (16)
Severe	1 (8.3)	0	0	0	1 (33.3)	1 (6.3)	1 (11.1)	2 (8)
Reactions at injection site ⁶ , n (%)	5 (41.7)	1 (33.3)	3 (50)	1 (100)	2 (66.7)	7 (43.8)	5 (55.6)	12 (48)

- There were 2 serious treatment-emergent AEs reported in Part 1, both of which resolved
 - 1 patient with subcutaneous abscess (possibly related to study drug) that resolved with medical management discontinued rilonacept treatment
 - 1 patient with atypical chest pain (not related to study drug) continued rilonacept treatment
- AEs observed with rilonacept treatment are consistent with the known safety profile of rilonacept
- The most common AEs were observed in the general disorders and administration site conditions (injection site reactions), infections and infestations, and musculoskeletal and connective tissue disorders classes

Addressable U.S. Opportunity of Rilonacept Estimated to be ~14K Patients

~7K new patients with multiple recurrences enter target pool annually



Year	-4	-3	-2	-1	0
Incident case of acute pericarditis (1 st episode) ¹	117K	117K	117K	117K	117K
Incidence of initial RP patients (1 st recurrence) ²	26K	26K	26K	26K	26K
Ongoing recurrent from year-1 ³				7K	
Ongoing recurrent from year-2 ³			7K	3.5K	
Ongoing recurrent from year-3 ³		7K	3.5K	1.8K	
Ongoing recurrent from year-4 ³	7K	3.5K	1.8K	0.9K	
Ongoing recurrent from year-5 ³	3.5K	1.8K	0.9K	0.5K	
Ongoing recurrent from year-6 ³	1.8K	0.9K	0.5K	0.2K	
Ongoing recurrent from year-7 ³					0.1K

Addressable Opportunity in U.S.

1: Prevalence estimate from Imazio, et al. (2008); includes all etiologies (~80% idiopathic)
 2: Mid point of 15-30% of initial recurrence rate published in ESC Guidelines given higher colchicine use today
 3: Estimate for recurrence rate of subsequent recurrences from ESC Guidelines and Claims Analysis



Every Second Counts!™

Appendix – Mavrilimumab

GCA is a Serious Condition Characterized by Inflammation of Medium-to-Large Arteries

1

Chronic inflammation of medium-to-large arteries

- GCA is characterized by inflammation of medium-to-large arteries with **predisposition for the cranial branches of the carotid artery** and is typically **found in patients over 50 years old**
- Due to the impact on the carotid arteries, GCA is **often characterized by temporal specific symptoms like headaches**, jaw claudication and scalp tenderness

2

If left untreated, GCA can cause serious complications

- While the onset of symptoms tends to be subacute, patients can experience **acute events including permanent vision loss (~10-20% of patients)** and/or aneurysms/dissections (~1-6% of patients)
- Due to the threat of these more serious complications, giant cell arteritis is **considered a medical emergency**

3

GCA variants associated with unique presentations

- **LV-GCA**, characterized by the involvement of the aorta and its major proximal branches, is estimated to be involved in anywhere from **~30-80% of patients**
- **~40-50%** of GCA patients **suffer from polymyalgia rheumatica**, a rheumatic disease characterized by widespread aching and stiffness; symptoms are relieved immediately upon starting on low-dose steroids

“There is an urgency of treatment with these patients, compared to other conditions it’s serious.”

– Rheumatologist

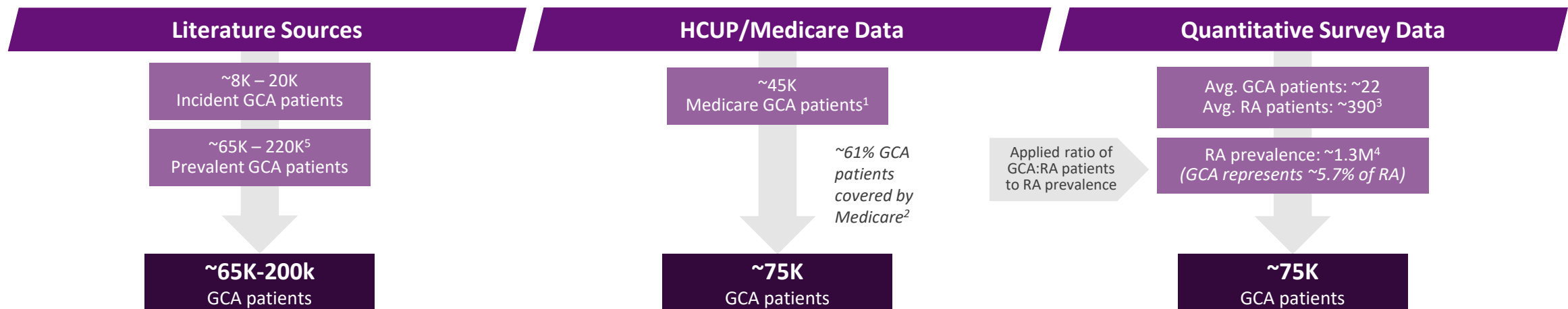
“There are people out there that need to get this disease under control, but they never receive the correct treatment, this is life threatening!”

– Rheumatologist

“I hate steroids, the long –term side effects are sometimes worse than the disease but, I definitely don’t want patients to go blind.”

– Rheumatologist

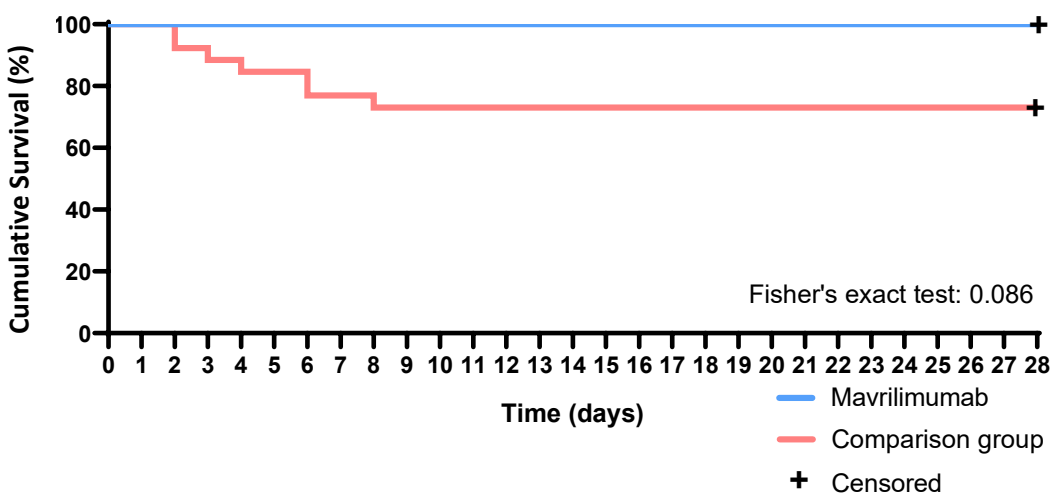
GCA U.S. Prevalence Estimated to be ~75-150k Patients



Key Considerations to Market Sizing Approach

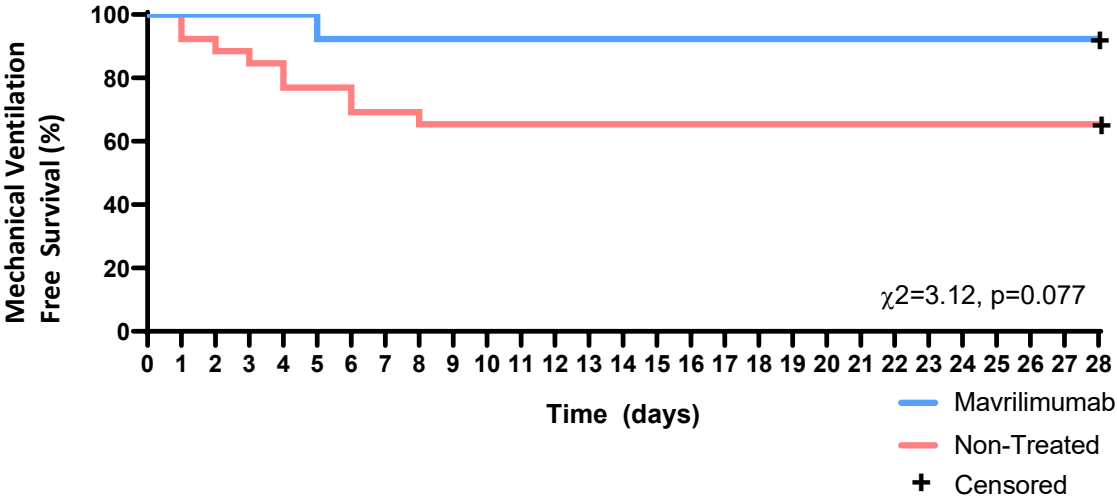
Wide Range	Under-Representation	Under-Representation
<p>High geographic variation</p> <p>GCA prevalence estimates vary across geographies with Northern European populations showing the highest rates and Asian populations the lowest</p>	<p>Represents Actively Managed Patients</p> <p>Medicare analysis does not capture GCA patients who were not actively managed within a given year; thus, the estimate from this analysis will exclude some remission patients or patients likely to relapse</p>	<p>Represents patients actively seen by a Rheum</p> <p>Rheumatologists reported the number of GCA patients they manage. Patients who are not actively managed would likely be excluded from these estimates</p>
<p>Weighted by US demographics</p> <p>Given the demographic breakdown of the US, prevalence of GCA is likely ~75-150k (less than that of purely Northern Europeans, but more than estimates from Asian countries)</p>		

Mavrilimumab Treatment Protocol in Patients with COVID-19 Pneumonia & Hyperinflammation Showed Improved Clinical Outcomes Compared to Matched Contemporaneous Controls¹



Patients at Risk	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
Mavrilimumab	13	13	13	13	13	13	13	13	13	13	13	13	13	13	13	13	13	13	13	13	13	13	13	13	13	13	13	13	13
Comparison group	26	26	26	24	23	22	22	20	20	19	19	19	19	19	19	19	19	19	19	19	19	19	19	19	19	19	19	19	19

Death occurred in 0% (n=0/13) of mavrilimumab-treated patients by Day 28, compared to 27% (n=7/26) of control-group patients (p=0.086)



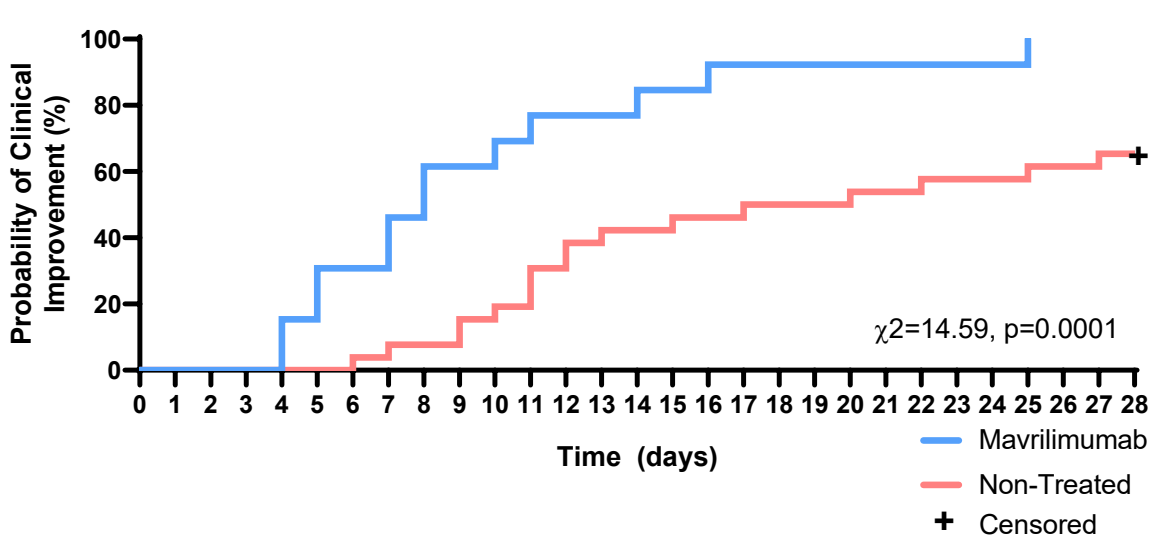
Patients at Risk	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
Mavrilimumab	13	13	13	13	13	13	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
Comparison group	26	26	24	23	22	20	20	18	18	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17

8% (n=1/13) of mavrilimumab-treated patients progressed to mechanical ventilation by Day 28, compared to 35% (n=9/26) of control-group patients who progressed to mechanical ventilation or died (p=0.077)

1) De Luca G. et al. GM-CSF blockade with mavrilimumab in severe COVID-19 pneumonia and systemic hyperinflammation: a single-centre, prospective cohort study. Lancet Rheumatol 2020 Published Online June 16, 2020 [https://doi.org/10.1016/S2665-9913\(20\)30170-3](https://doi.org/10.1016/S2665-9913(20)30170-3); The treatment protocol with the investigational drug mavrilimumab was conducted by Professor Lorenzo Dagna, MD, FACP, Head, Unit of Immunology, Rheumatology, Allergy and Rare Diseases IRCCS San Raffaele Scientific Institute and Vita-Salute San Raffaele University in Milan, Italy within a COVID-19 Program directed by Professor Alberto Zangrillo, Head of Department of Anesthesia and Intensive Care of the Scientific Institute San Raffaele Hospital and Professor in Anesthesiology and Intensive Care, Università Vita-Salute San Raffaele; p-values above are unadjusted for multiplicity.

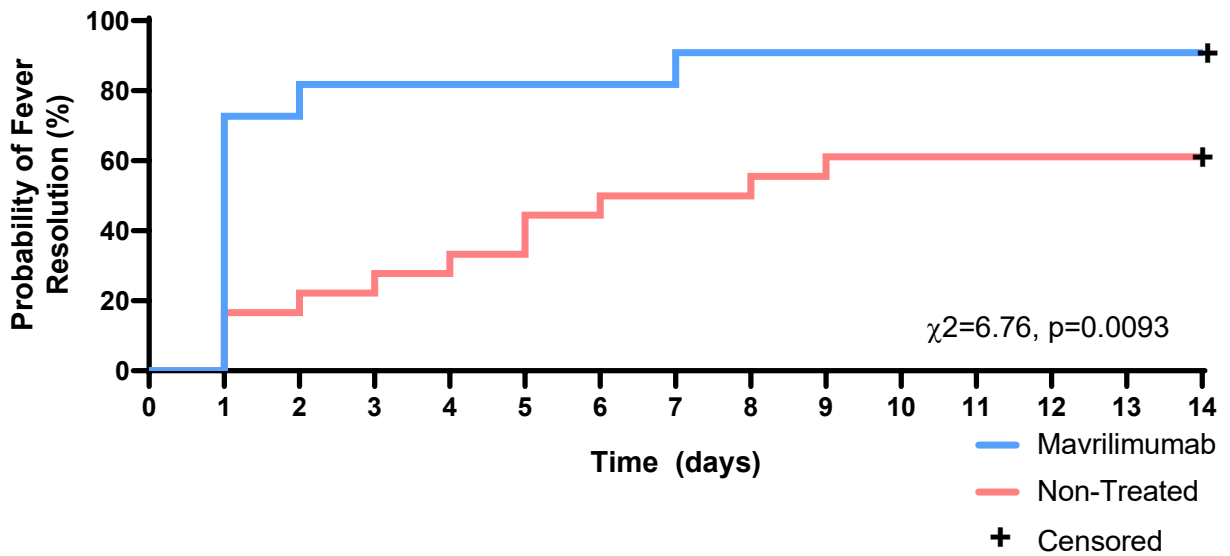


Mavrilimumab Treatment Protocol in Patients with COVID-19 Pneumonia & Hyperinflammation Showed Improved Clinical Outcomes Compared to Matched Contemporaneous Controls¹



Patients at Risk	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
Mavrilimumab	13	13	13	13	13	11	9	9	7	5	5	4	3	3	3	2	2	1	1	1	1	1	1	1	1				
Comparison group	26	26	26	26	26	26	26	25	24	24	22	21	18	16	15	15	14	14	13	13	13	12	12	11	11	11	10	10	9

100% (n=13/13) of mavrilimumab-treated patients and 65% (n=17/26) of control-group patients attained the clinical improvement endpoint (defined as improvement of ≥ 2 categories on a 7-point scale for assessment of clinical status) by Day 28 (p=0.0001)



Patients at Risk	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Mavrilimumab	11	11	3	2	2	2	2	2	1	1	1	1	1	1	1
Comparison group	18	18	15	14	13	12	10	9	9	8	7	7	7	7	7

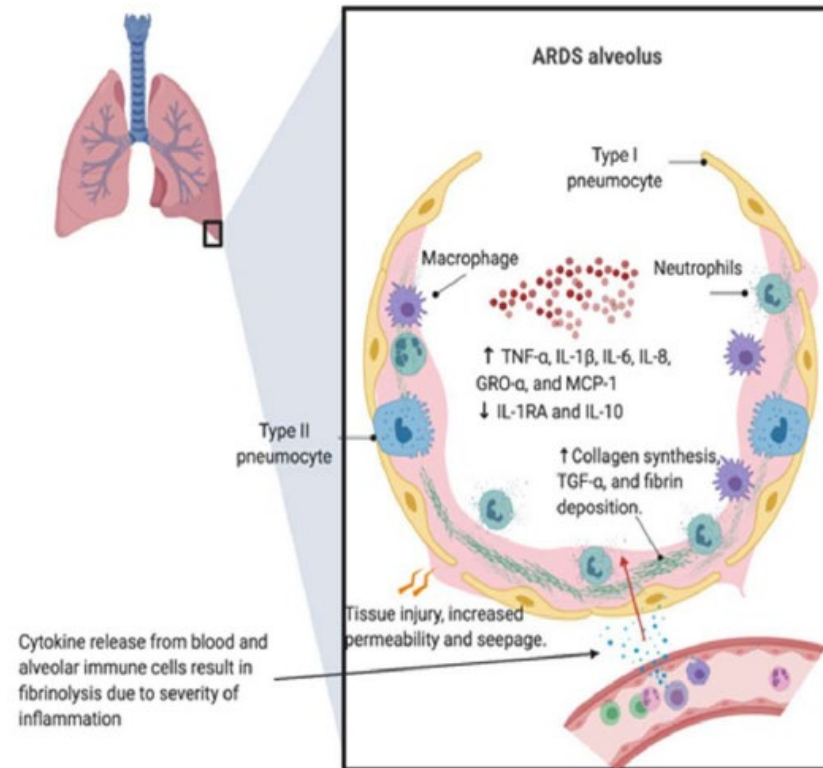
Fever resolved in 91% (n=10/11 febrile patients) of mavrilimumab-treated patients by Day 14, compared to 61% (n=11/18 febrile patients) of control-group patients (p=0.0093)

1) De Luca G. et al. GM-CSF blockade with mavrilimumab in severe COVID-19 pneumonia and systemic hyperinflammation: a single-centre, prospective cohort study. Lancet Rheumatol 2020 Published Online June 16, 2020 [https://doi.org/10.1016/S2665-9913\(20\)30170-3](https://doi.org/10.1016/S2665-9913(20)30170-3); The treatment protocol with the investigational drug mavrilimumab was conducted by Professor Lorenzo Dagna, MD, FACP, Head, Unit of Immunology, Rheumatology, Allergy and Rare Diseases IRCCS San Raffaele Scientific Institute and Vita-Salute San Raffaele University in Milan, Italy within a COVID-19 Program directed by Professor Alberto Zangrillo, Head of Department of Anesthesia and Intensive Care of the Scientific Institute San Raffaele Hospital and Professor in Anesthesiology and Intensive Care, Università Vita-Salute San Raffaele; p-values above are unadjusted for multiplicity.



Viral Infections Causing ARDS (i.e., influenza, H1N1, RSV, COVID-19, etc.) Have an *Inflammatory* Pathophysiology, Primarily Precipitated by Cytokine Storm

- Uncontrolled pro-inflammatory response, originating from the focal infected area, spreading through circulation and manifests as a **multiorgan failure** and **ARDS**
- Inflammation of the alveolar epithelial cells drives development of severe disease, destroying gas exchange and allowing **further viral exposure**
- Approach to treatment is **addressing host response** directly by targeting innate immune pathways that amplify inflammatory signals and contribute to epithelial damage

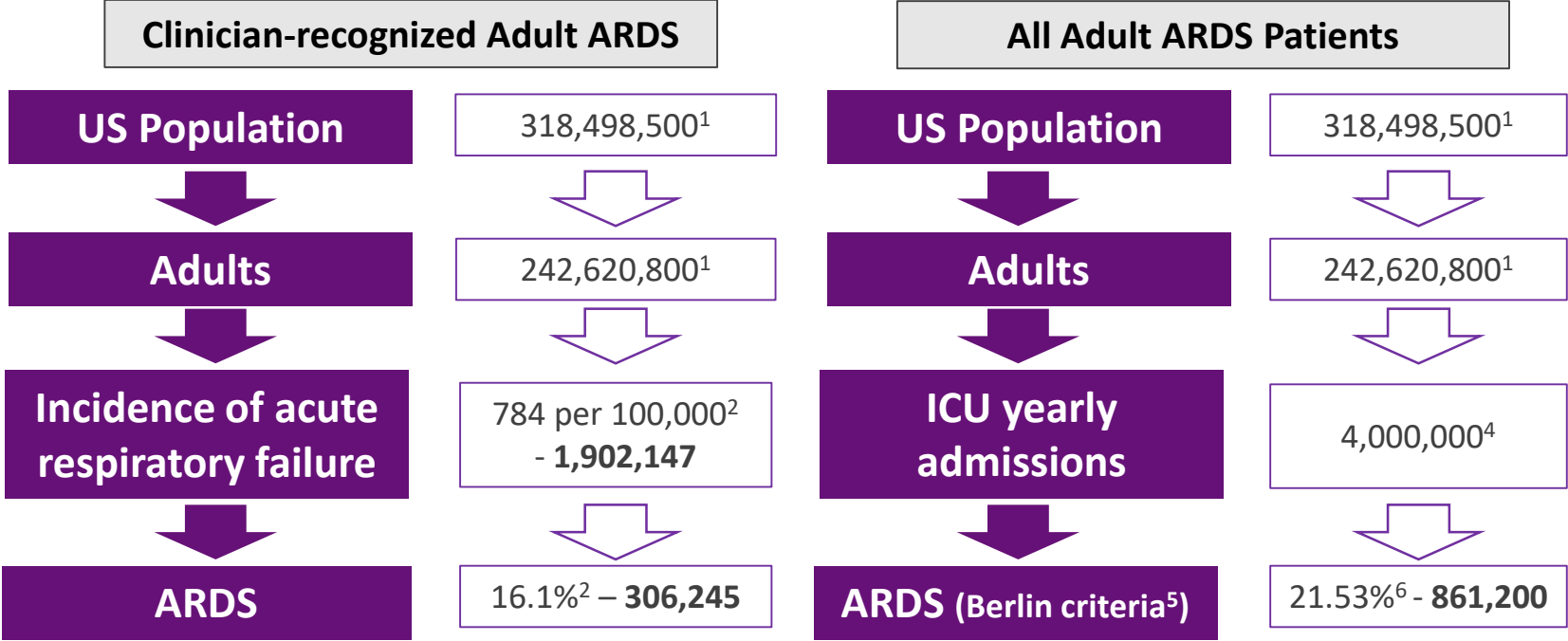


McGonagle, et al., Autoimmunity Reviews (2020), <https://doi.org/10.1016/j.autrev.2020.102537>

Under-diagnosis of viral infections causing ARDS

- Viral infection is sufficient to cause severe pneumonia and ARDS, but it can also act in conjunction with or be followed by bacterial agents, (most commonly by *S. aureus* and *S. pneumoniae*)
- Clinicians fail to clinically diagnose influenza in **up to two-thirds** of patients with confirmed influenza

There are between 300k and 860k Cases of Adult ARDS in the U.S. Every Year; Significant Unmet Need Remains in These Populations



- Excludes ARDS associated with COVID-19
- Pediatric ARDS occurs less often
- Most common causes of ARDS are pneumonia (59%) and sepsis (16%)³
- 84.5% of ARDS cases require mechanical ventilation⁷
- Considerable mortality (~40%⁸) with no effective treatments outside mechanical ventilation

~300,000 – 860,000 ARDS Cases Annually in US*

1) KFF's State Health Facts. Population Distribution by Age [Kaiser Family Foundation estimates based on the Census Bureau's American Community Survey, 2008-2018].
2) Stefan MS, Shieh MS, Pekow PS, et al. J Hosp Med. 2013;8(2):76–82. doi:10.1002/jhm.2004
3) Bellani G, Laffey JG, Pham T, et al JAMA. 2016;315(8):788–800. doi:10.1001/jama.2016.0291
4) Mullins PM, Goyal M, Pines JM. Acad Emerg Med. 2013;20(5):479–486. doi:10.1111/acem.12134
5) ARDS Definition Task Force. JAMA 2012;307(23):2526-2533.
6) Laffey JG, Madotto F, Bellani G, et al. Lancet Resp Med. 2017;5(8):627-638
7) Bellani G, Laffey JG, Pham T, et al Am J Respir Crit Care Med 2017;195(1):67–77
8) Calfee CS, Delucchi KL, Sinha P, et al. Lancet Respir Med. 2018;6(9):691–698. doi:10.1016/S2213-2600(18)30177-2

**There may be different ARDS phenotypes – some of which may not be ideal for GM-CSF inhibition. Further research is needed to understand which patient sub-types would best benefit from treatment with mavrilimumab*

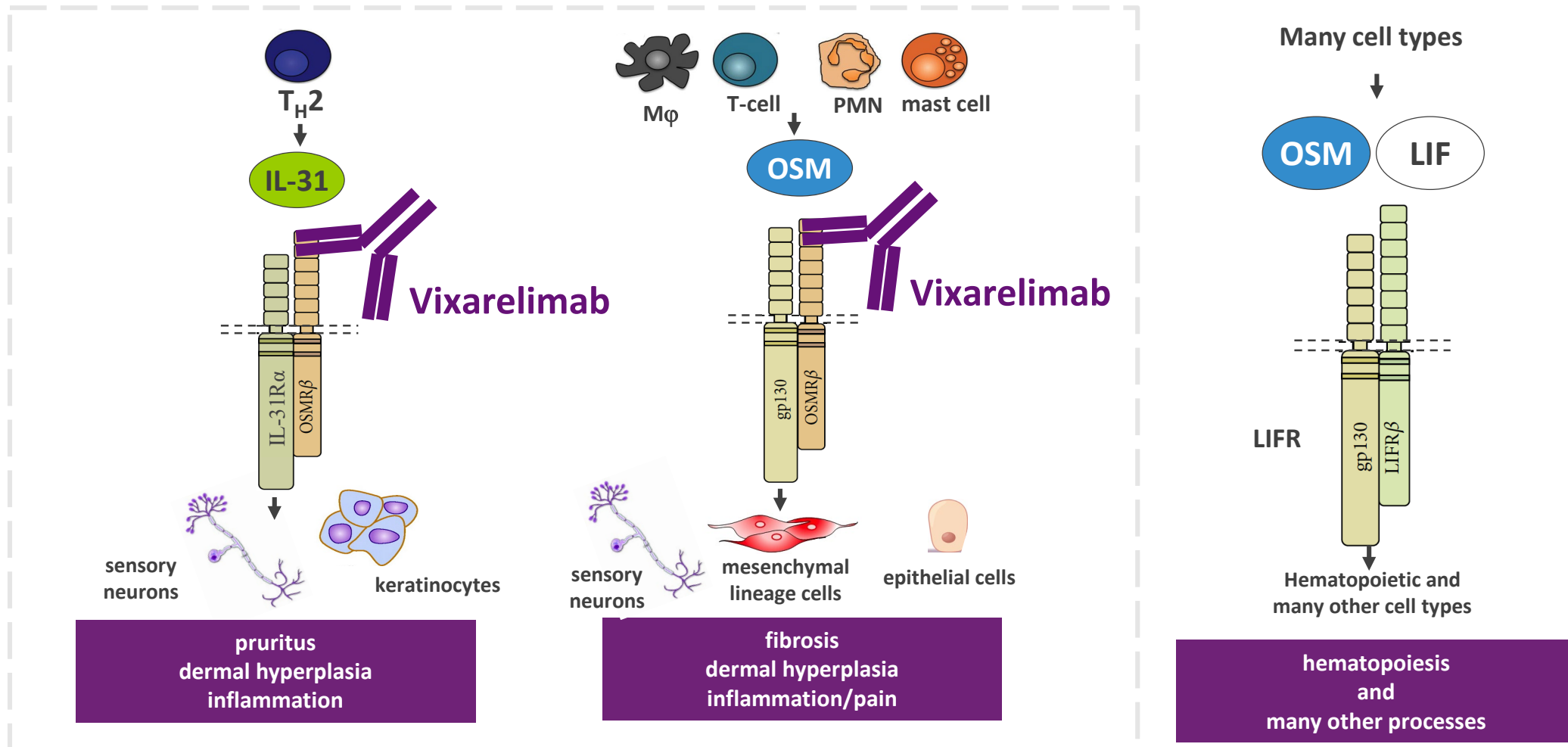




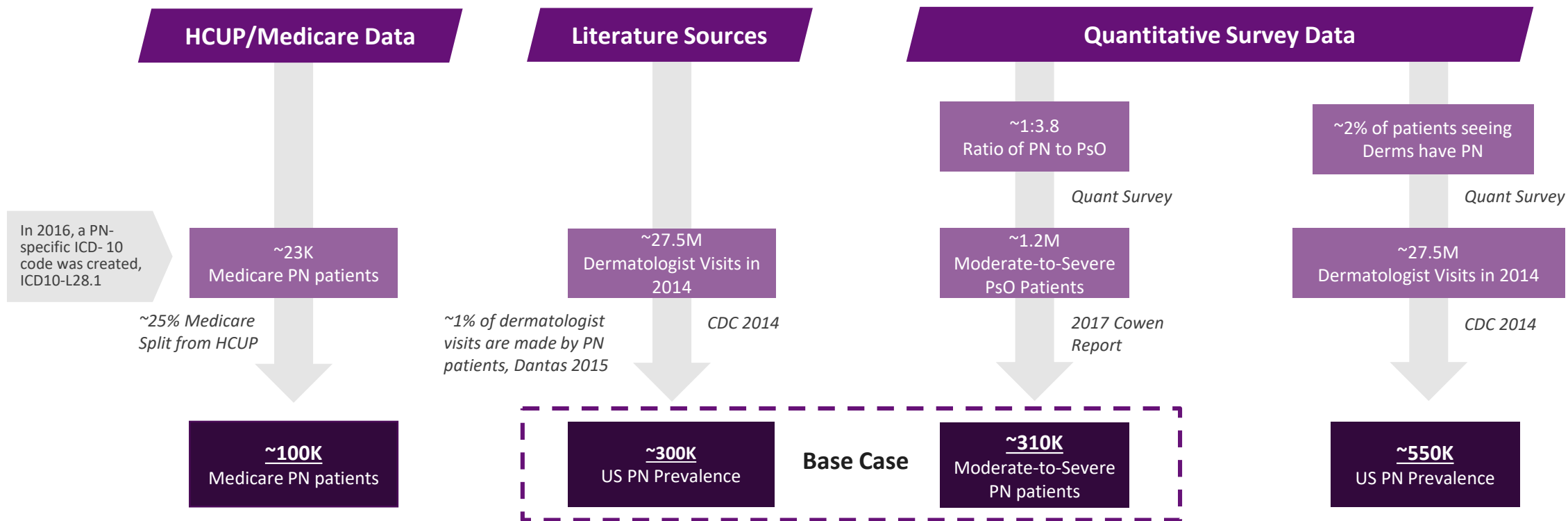
Every Second Counts!™

Appendix – Vixarelimab (KPL-716)

Vixarelimab Inhibits IL-31 & OSM Signaling Through OSMR β but Avoids Inhibiting Signaling Critical to Hematopoiesis Through OSM/LIFR *in vitro* Studies



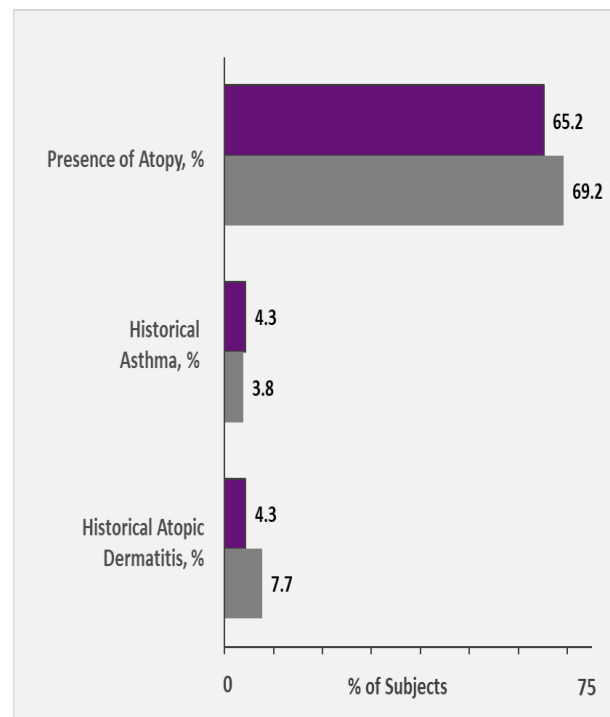
Prurigo Nodularis U.S. Prevalence Estimated to be ~300K Patients



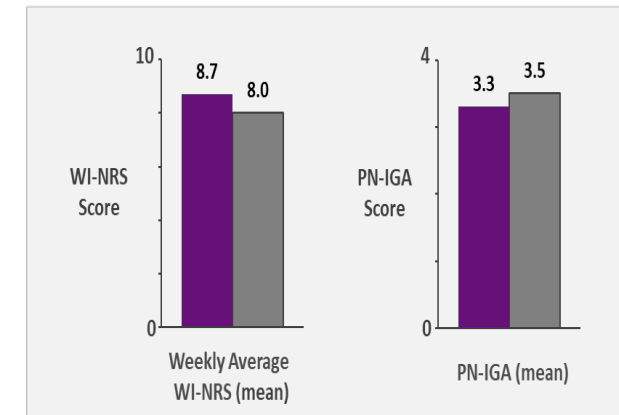
Vixarelimab Phase 2a Study in Prurigo Nodularis: Baseline Characteristics

General Characteristics*	Vixarelimab (n=23)	Placebo (n=26)	Total (n=49)
Age (Mean Years)	52	64	58
Sex (Male/Female)	10/13	10/16	20/29
Race			
White (n)	65.2% (15)	80.8% (21)	73.5% (36)
Black or African American (n)	21.7% (5)	11.5% (3)	16.3% (8)
Asian (n)	8.7% (2)	0	4.1% (2)
American Indian or Alaska Native (n)	0	3.8% (1)	2.0% (1)
Multiple (n)	4.3% (1)	0	2.0% (1)
Other (n)	0	3.8% (1)	2.0% (1)

Clinical Findings at Baseline: History of Atopy



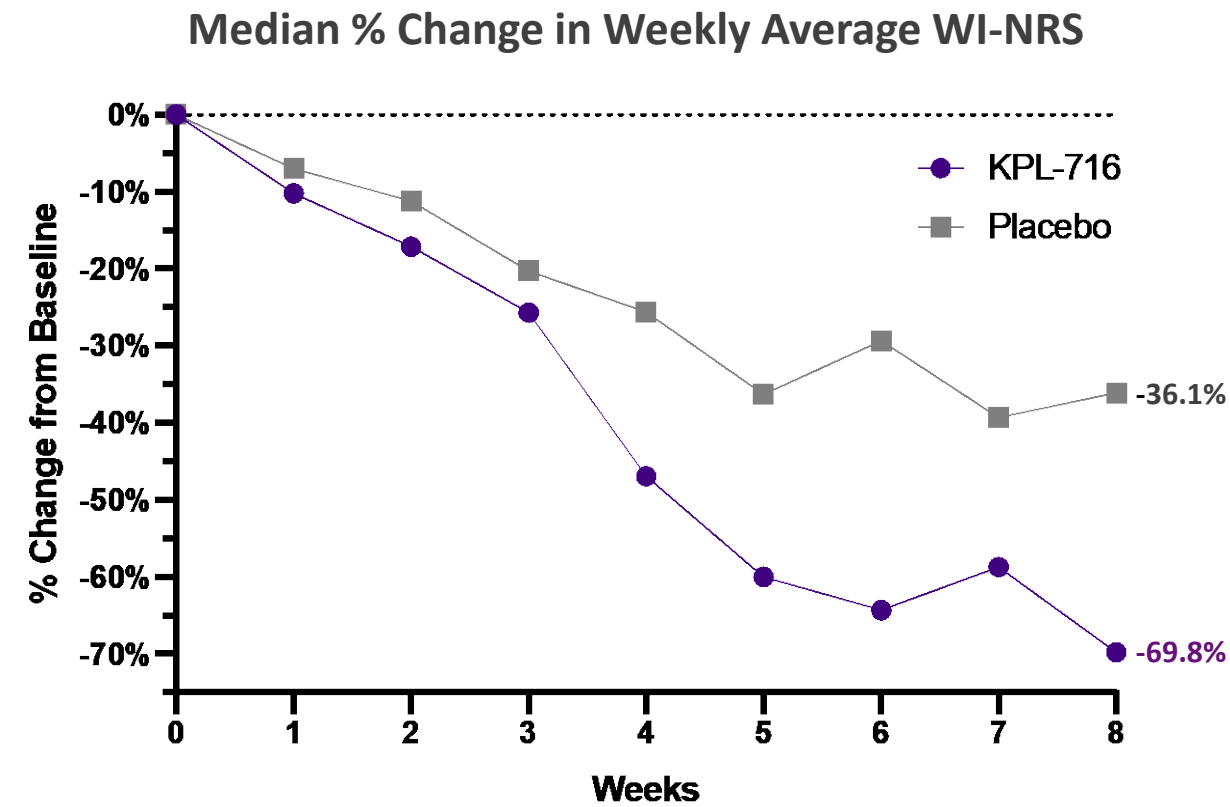
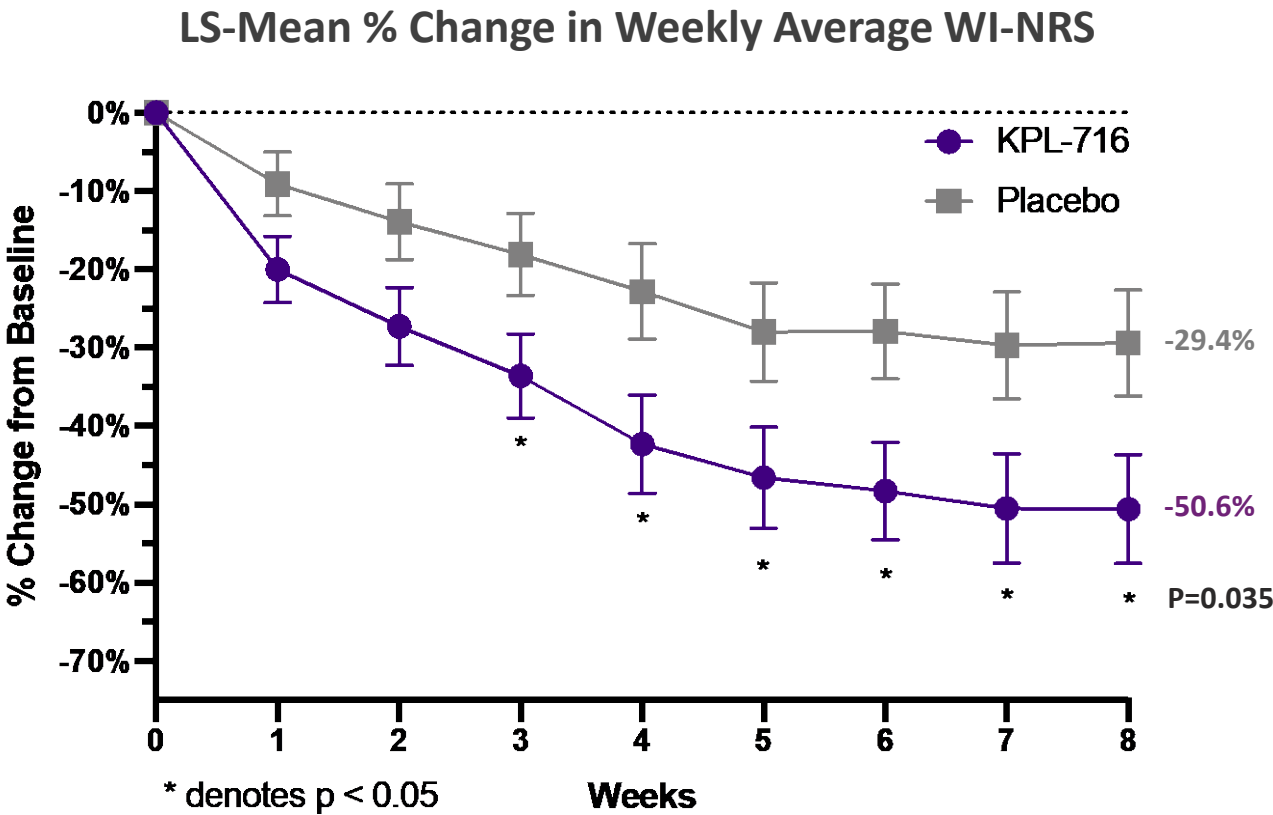
Clinical Findings at Baseline: WI-NRS & PN-IGA



■ Vixarelimab
■ Placebo

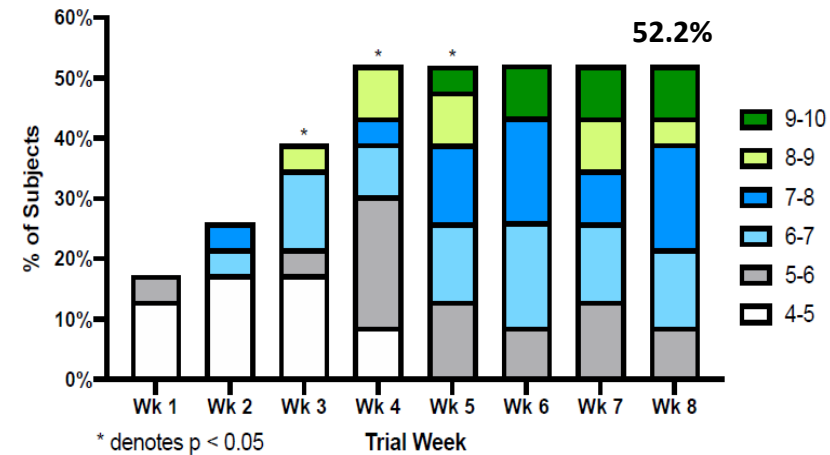
Vixarelimab Phase 2a Study in Prurigo Nodularis: Statistically Significant Primary Efficacy Endpoint of Reduction in Weekly-Average WI-NRS at Week 8

Median change from baseline in weekly-average WI-NRS at Week 8 was -69.8%

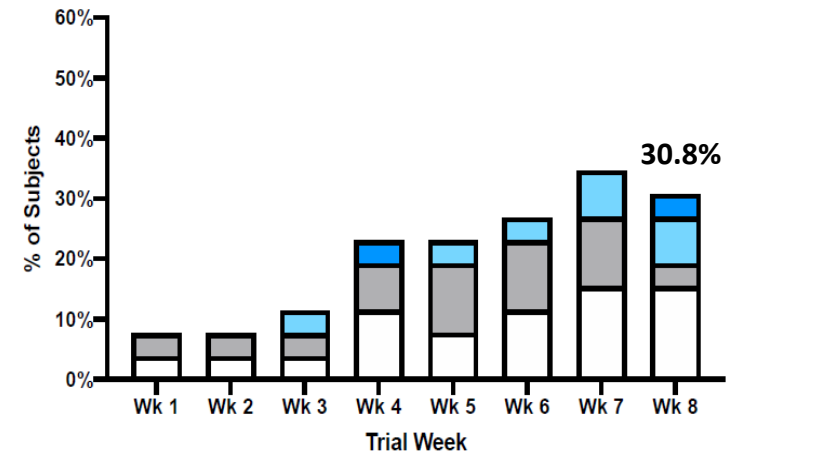


Vixarelimab Phase 2a Study in Prurigo Nodularis: Majority of Vixarelimab Recipients Showed a Clinically Meaningful ≥ 4 -Point Weekly-Average WI-NRS Reduction at Week 8

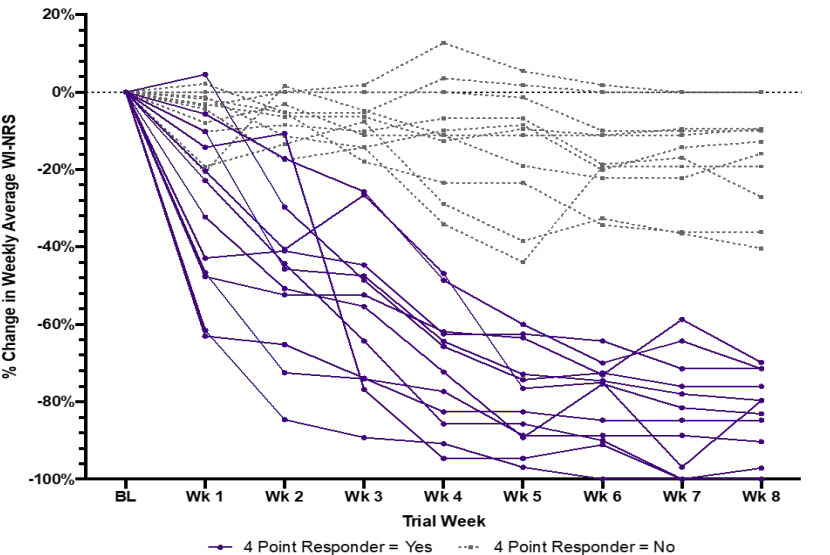
% of KPL-716 Subjects with a Clinically Meaningful Response in WI-NRS



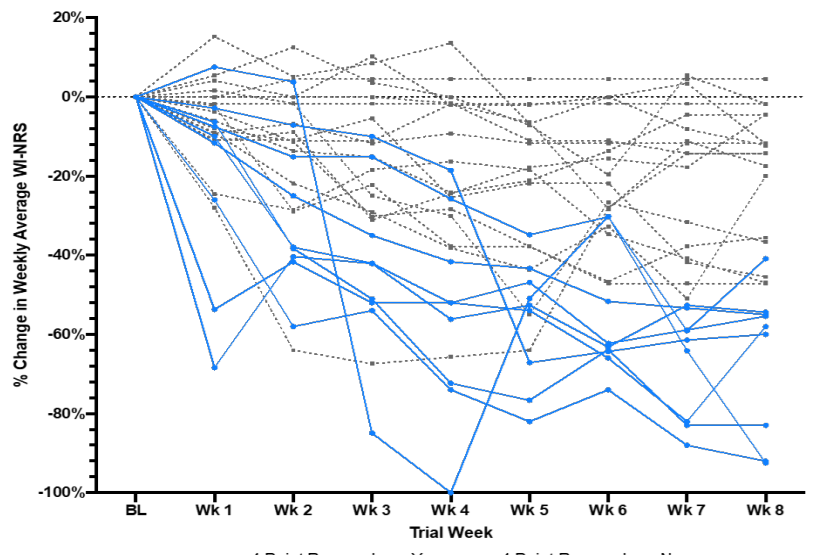
% of Placebo Subjects with a Clinically Meaningful Response in WI-NRS



KPL-716 Per Subject Plots

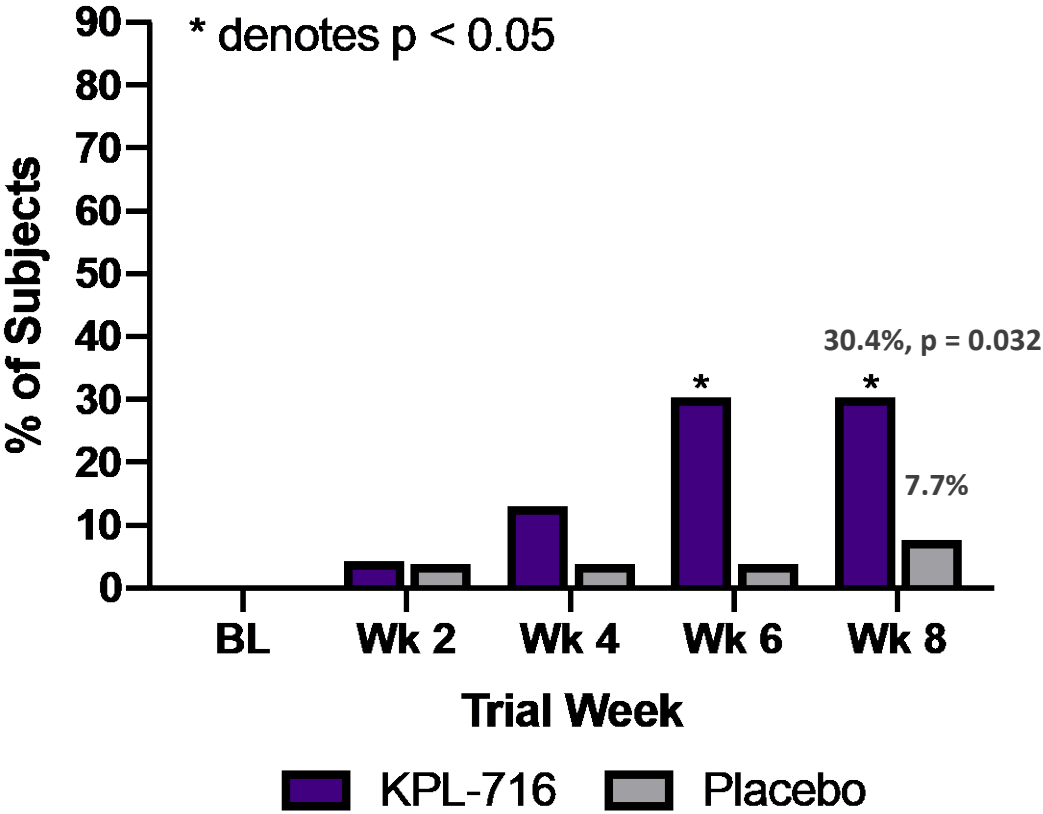


Placebo Per Subject Plots

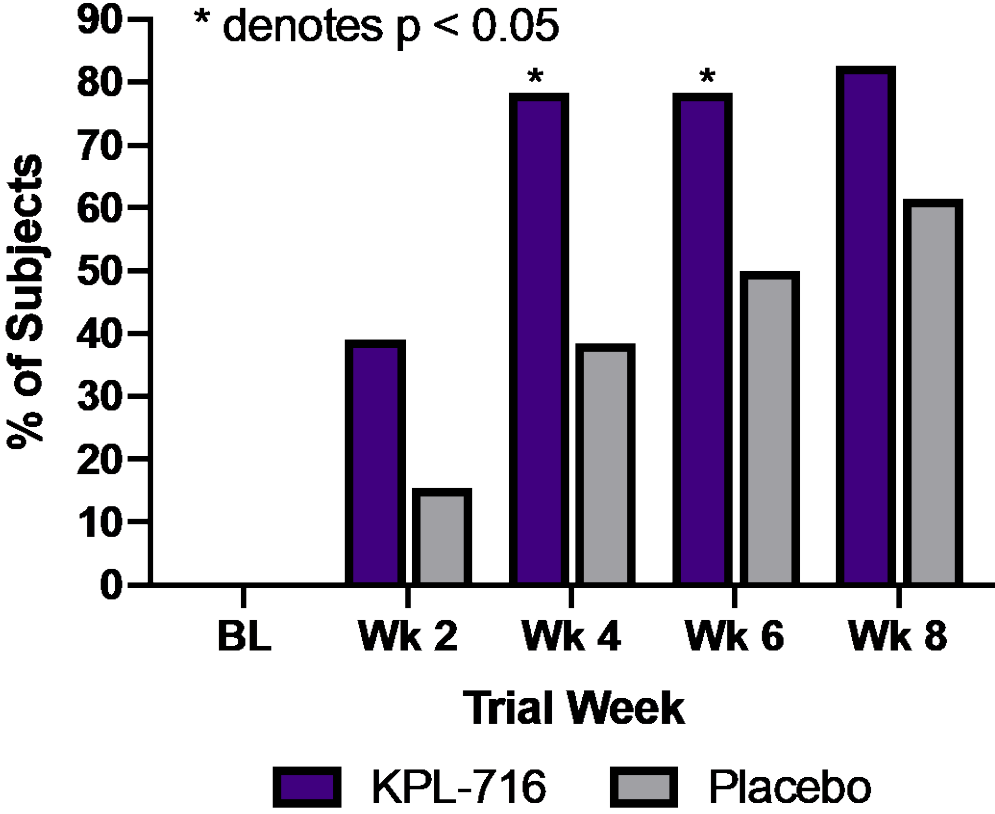


Vixarelimab Phase 2a Study in Prurigo Nodularis: Significantly More Vixarelimab Recipients Attained A Clear/Almost Clear Lesion Score by Week 8

PN-IGA Score of 0 or 1



≥1 Point Change in PN-IGA



Vixarelimab was Well-Tolerated in Prurigo Nodularis Phase 2a Study

Summary of Adverse Events	Vixarelimab (n=23)	Placebo (n=26)
Any AE (n)	82.6% (19)	65.4% (17)
TEAE (n)	82.6% (19)	65.4% (17)
Drug-Related TEAE (n)	39.1% (9)	30.8% (8)
Serious TEAE	0	0
Drug-Related Serious TEAE	0	0
TEAE Leading to Treatment Discontinuation	0	0
Drug-Related TEAE Leading to Treatment Discontinuation	0	0
Serious TEAE Leading to Treatment Discontinuation	0	0
Drug-Related Serious TEAE Leading to Treatment Discontinuation	0	0
TEAE Leading to Death	0	0

Vixarelimab was Well-Tolerated in Prurigo Nodularis Phase 2a Study

System Organ Class Preferred Term	Vixarelimab (n=23)	Placebo (n=26)
Infections and Infestations (n)	30.4% (7)	46.2% (12)
Upper Respiratory Tract Infection (n)	17.4% (4)	3.8% (1)
Nasopharyngitis (n)	4.3% (1)	7.7% (2)
Gastroenteritis Viral (n)	4.3% (1)	0
Influenza (n)	4.3% (1)	0
Postoperative Wound Infection (n)	4.3% (1)	0
Subcutaneous Abscess (n)	4.3% (1)	0
Urinary Tract Infection (n)	0	11.5% (3)
Bronchitis (n)	0	3.8% (1)
Cellulitis (n)	0	3.8% (1)
Eczema Impetiginous (n)	0	3.8% (1)
Herpes Simplex (n)	0	3.8% (1)
Otitis Media (n)	0	3.8% (1)
Skin Infection (n)	0	3.8% (1)
Tooth Abscess (n)	0	3.8% (1)

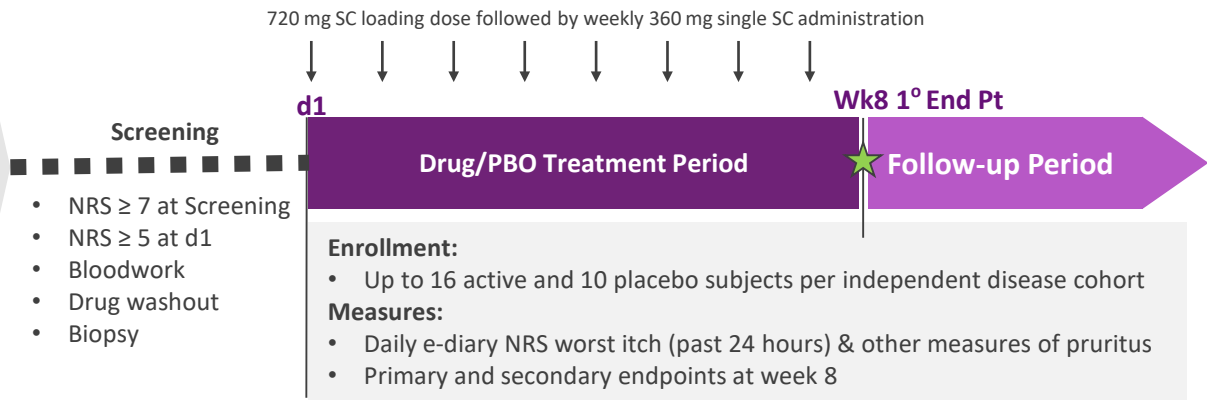
Vixarelimab Exploratory Phase 2 Study in Diseases Characterized by Chronic Pruritus

Pilot Study Rationale

- 1 Investigate presence of IL-31 & OSM signature in multiple diseases characterized by chronic pruritus
- 2 In diseases where IL-31 is present (based on post-hoc biopsy analysis) → link inhibition of IL-31 with vixarelimab to clinical response
- 3 Diseases where IL-31 is NOT present (based on post-hoc biopsy analysis) → Investigate whether blocking OSMRβ has any effect

Chronic Idiopathic Urticaria (CIU)	US Prevalence: ~2-3 M ^{1,2} Pruritus Burden: ~1-in-3 experience pruritus refractory to conventional therapies; ~15-20% treated with Xolair continue to experience pruritus ³
Chronic Idiopathic Pruritus (CIP)	US Prevalence: Treating physicians report ~1 CIP patient for every 3 atopic dermatitis patients ^{3,4} Pruritus Burden: ~50% experience symptoms lasting for >1-yr; ~1-in-3 treated patients experience refractory pruritus ³
Lichen Planus (LP)	US Prevalence: ~0.5 M ⁵ Pruritus Burden: ~1-in-3 treated patients experience refractory pruritus ³
Lichen Simplex Chronicus (LSC)	US Prevalence: Treating physicians report ~1 LSC patient for every PN patient ³ (~0.3 M addressable in the US) ^{6,7} Pruritus Burden: ~40% of treated patients experience refractory pruritus ³
Plaque Psoriasis	US Prevalence: ~12 M ^{8,9} Pruritus Burden: ~2-3 M patients in US with moderate-to-severe pruritus ⁹

Subject Experience in Each Disease Cohort



Note: US prevalence figures are estimates based on references which may include only a single EU country and/or based on primary market research where physicians were asked to relate the estimated number of patients they treat with the target disease in relation to another disease they treat where the prevalence estimates are more well known

1) Gaig et al., Epidemiology of urticaria in Spain, J Investig Allergol Clin Immunol. 2004 | 2) Saini, Chronic Spontaneous Urticaria, Immunology & Allergy Clinics, 2014 | 3) Kiniksa survey data (n=83 dermatologists, n=38 allergists) | 4) Weisshaar et al., European Guideline on Chronic Pruritus; Acta Derm Venereol 2012 | 5) Cleach & Chosidow, Lichen Planus, NEJM 2012 | 6) Dantas, 2015, Prevalence of dermatoses in dermatologic evaluation requests from patients admitted to a tertiary hospital for 10 years, An Bras Dermatol. 2015 | 7) HCUP/Medicare Data 2012/2013 | 8) Michalek et al., A systematic review of worldwide epidemiology of psoriasis, J Eur Acad Dermatol Venereol. 2017 | 9) Menlo Tx Company Presentation June 2018



Vixarelimab Exploratory Phase 2 Study in Diseases Characterized by Chronic Pruritus

Plaque psoriasis cohort achieved statistically significant reduction in weekly-average WI-NRS at Week 8

Enrolled patients experiencing moderate-to-severe pruritus and assigned them to one of the following cohorts based upon their diagnosis: plaque psoriasis, chronic idiopathic pruritus, lichen simplex chronicus, chronic idiopathic urticaria, or lichen planus

- Each cohort was evaluated as an independently randomized sub-study. Patients were randomized and received a loading dose of vixarelimab 720 mg or placebo subcutaneous (SC) followed by vixarelimab 360 mg or placebo SC weekly for 8 weeks.

Primary Efficacy Endpoint: percent change versus baseline in weekly-average WI-NRS at Week 8

Topline Observations:

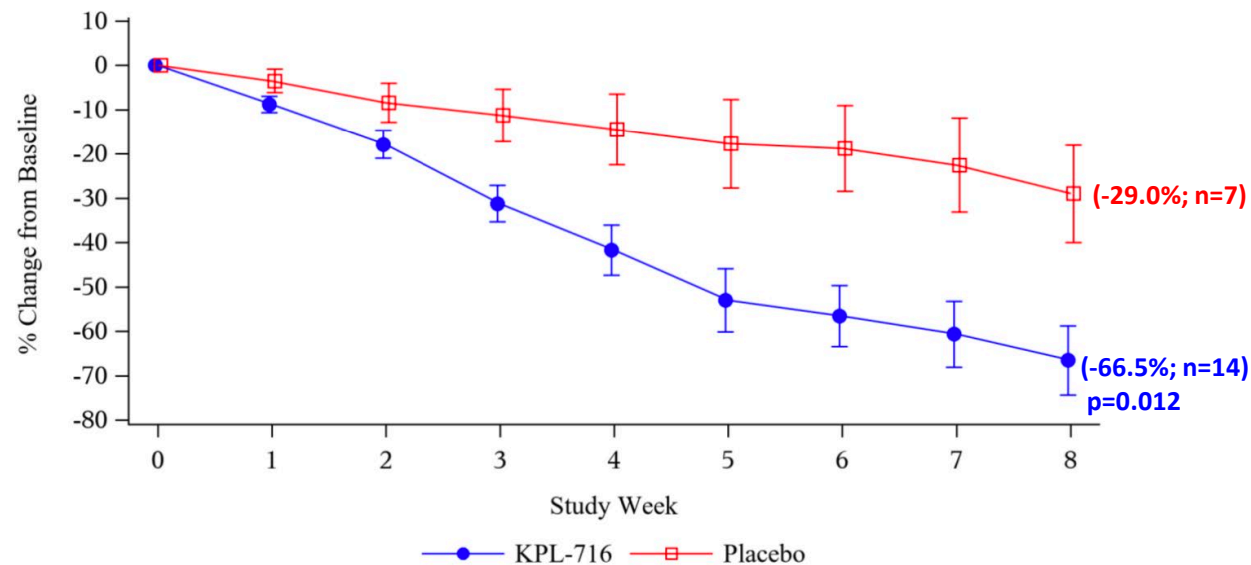
- The plaque psoriasis cohort achieved a statistically significant reduction in weekly-average WI-NRS at Week 8. Least squares (LS)-mean change from baseline (mean WI-NRS score of 8.4) in weekly-average WI-NRS at Week 8 was -66.5% (n=14) in vixarelimab recipients compared to -29.0% (n=7) in placebo recipients (LS-mean difference -37.5%; p=0.012).
- In the chronic idiopathic pruritus cohort, the LS-mean change from baseline (mean WI-NRS score of 8.1) in weekly-average WI-NRS at Week 8 was -52.4% (n=14) in vixarelimab recipients compared to -48.8% (n=9) in placebo recipients (LS-mean difference -3.6%; p=0.813).
- The lichen simplex chronicus (n=4), chronic idiopathic urticaria (n=4) and lichen planus (n=3) cohorts showed encouraging efficacy results as measured by percent change from baseline in weekly-average WI-NRS at Week 8. Comparative summary statistics were not performed due to the small number of patients enrolled in each cohort.
- Vixarelimab was well-tolerated, and no dose-limiting adverse events were recorded.

Vixarelimab Exploratory Phase 2 Study in Diseases Characterized by Chronic Pruritus: Reduction in Weekly-Average WI-NRS at Week 8

Plaque psoriasis cohort achieved statistically significant reduction in weekly-average WI-NRS at Week 8

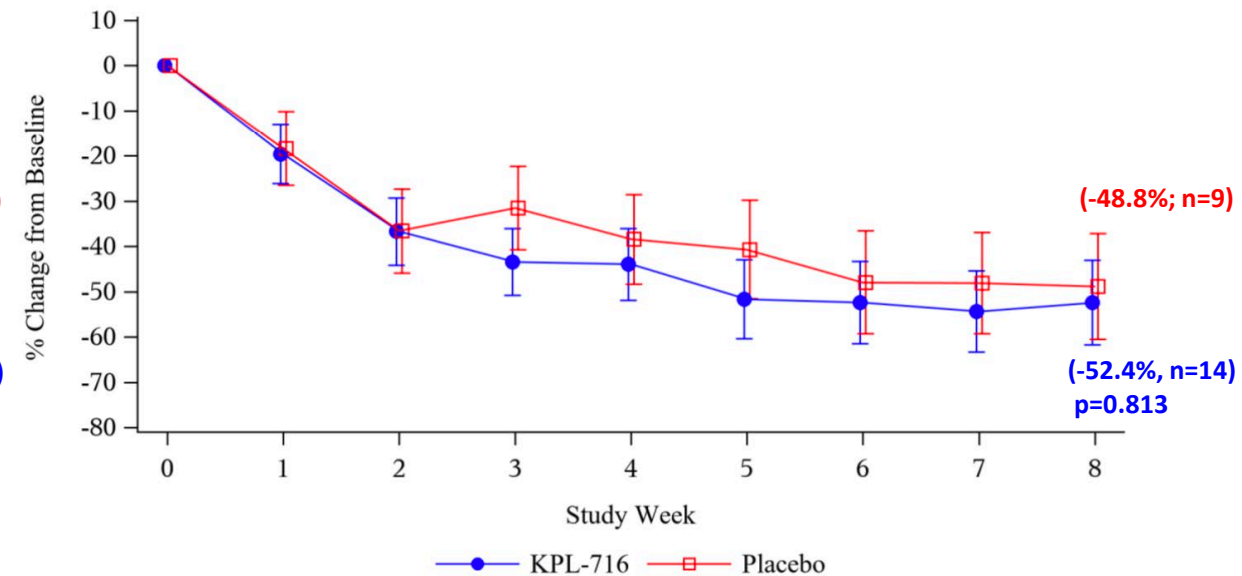
Plaque Psoriasis

LS-Mean % Change in Weekly Average WI-NRS



Chronic Idiopathic Pruritus

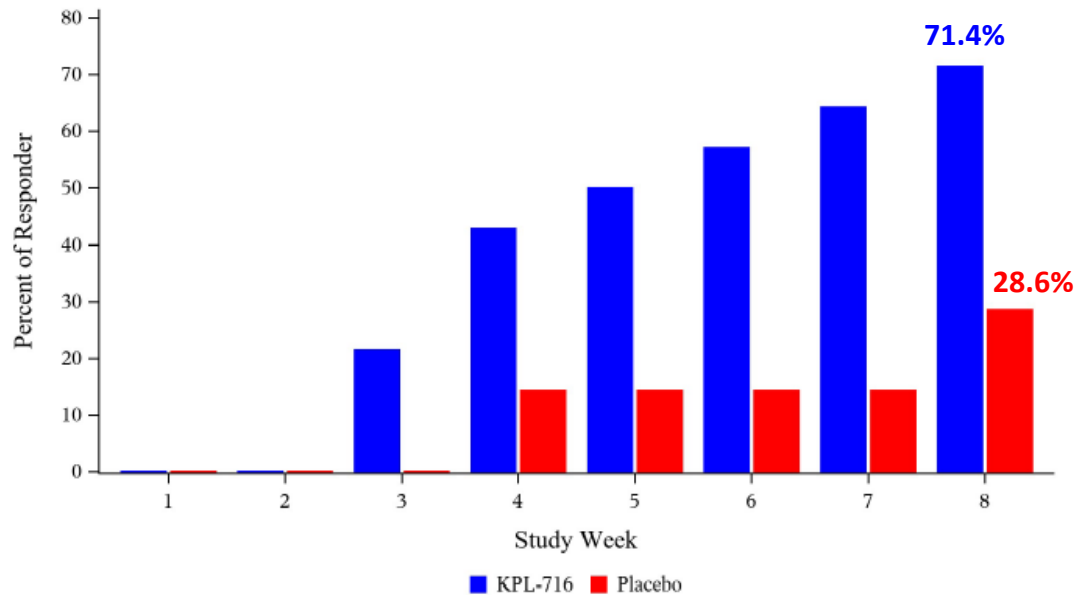
LS-Mean % Change in Weekly Average WI-NRS



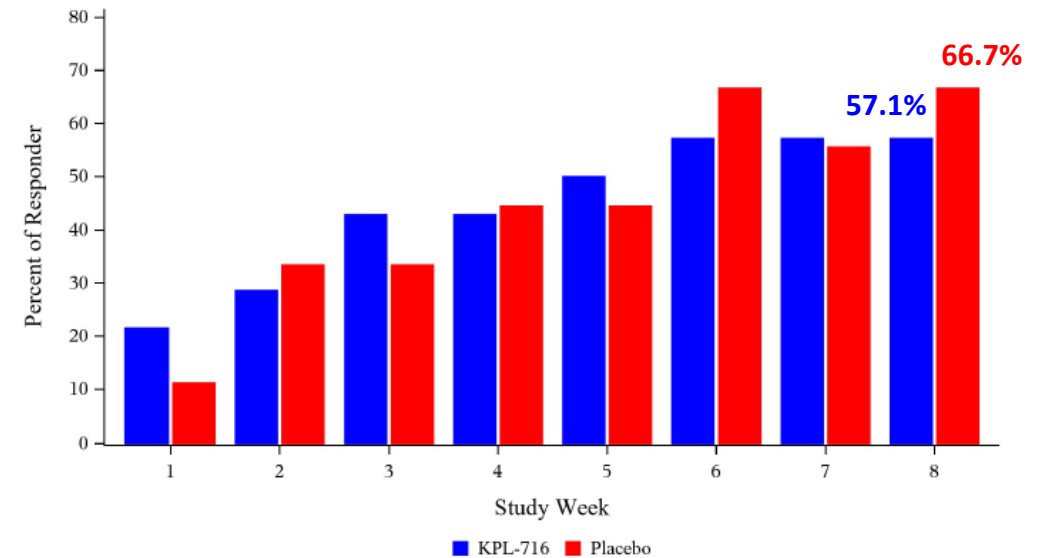
Vixarelimab Exploratory Phase 2 Study in Diseases Characterized by Chronic Pruritus: ≥ 4-Point Weekly-Average WI-NRS Reduction at Week 8

71.4% of vixarelimab recipients in plaque psoriasis cohort showed a clinically meaningful ≥ 4-point reduction

Plaque Psoriasis



Chronic Idiopathic Pruritus

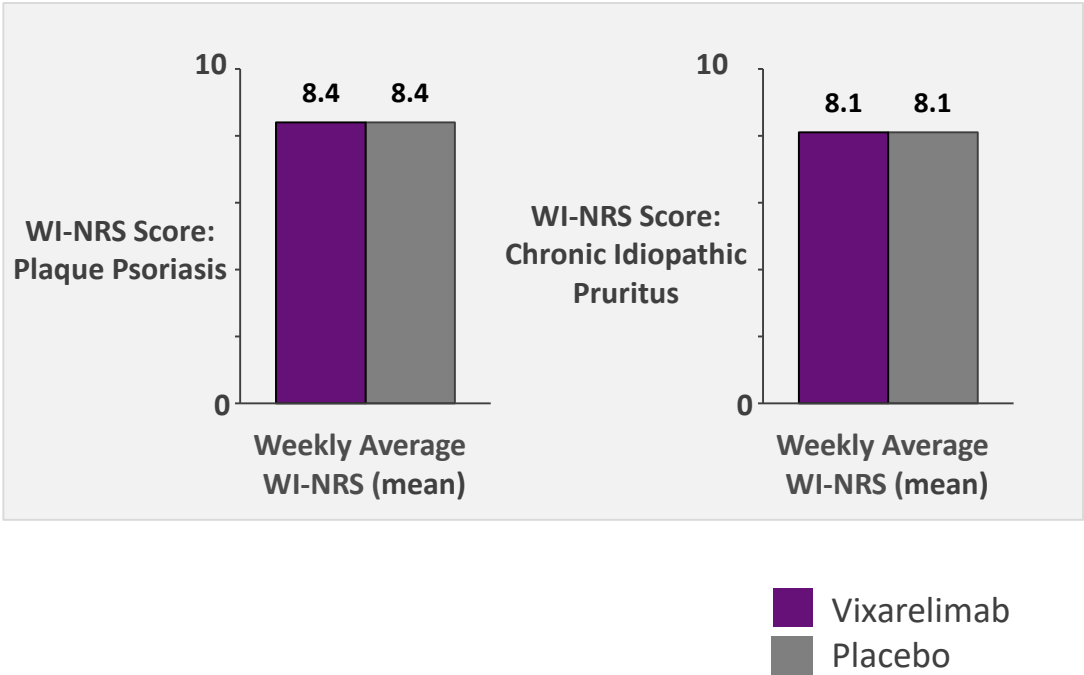


Vixarelimab Exploratory Phase 2 Study in Diseases Characterized by Chronic Pruritus: Baseline Characteristics

General Characteristics* Plaque Psoriasis	Vixarelimab (n=14)	Placebo (n=7)	Total (n=21)
Age (Mean Years)	49	53	50
Sex (Male/Female)	5/9	3/4	8/13
Race			
White (n)	92.9% (13)	85.7% (6)	90.5% (19)
Black or African American (n)	7.1% (1)	14.3% (1)	9.5% (2)

General Characteristics* Chronic Idiopathic Pruritus	Vixarelimab (n=14)	Placebo (n=9)	Total (n=23)
Age (Mean Years)	57	58	57
Sex (Male/Female)	4/10	1/8	5/18
Race			
White (n)	78.6% (11)	77.8% (7)	78.3% (18)
Black or African American (n)	14.3% (2)	22.2% (2)	17.4% (4)
Asian (n)	7.1% (1)	0	4.3% (1)

Clinical Findings at Baseline: WI-NRS



Vixarelimab was Well-Tolerated in Exploratory Phase 2 Trial

	Plaque Psoriasis Cohort		Chronic Idiopathic Pruritus Cohort	
Summary of Adverse Events	Vixarelimab (n=14)	Placebo (n=7)	Vixarelimab (n=14)	Placebo (n=9)
Any AE (n)	42.9% (6)	14.3% (1)	28.6% (4)	22.2% (2)
TEAE (n)	42.9% (6)	14.3% (1)	28.6% (4)	22.2% (2)
Drug-Related TEAE (n)	7.1% (1)	0	7.1% (1)	11.1% (1)
Serious TEAE	0	0	7.1% (1)	0
Drug-Related Serious TEAE	0	0	7.1% (1)	0
TEAE Leading to Treatment Discontinuation	0	0	7.1% (1)	0
Drug-Related TEAE Leading to Treatment Discontinuation	0	0	7.1% (1)	0
Serious TEAE Leading to Treatment Discontinuation	0	0	7.1% (1)	0
Drug-Related Serious TEAE Leading to Treatment Discontinuation	0	0	7.1% (1)	0
TEAE Leading to Death	0	0	0	0

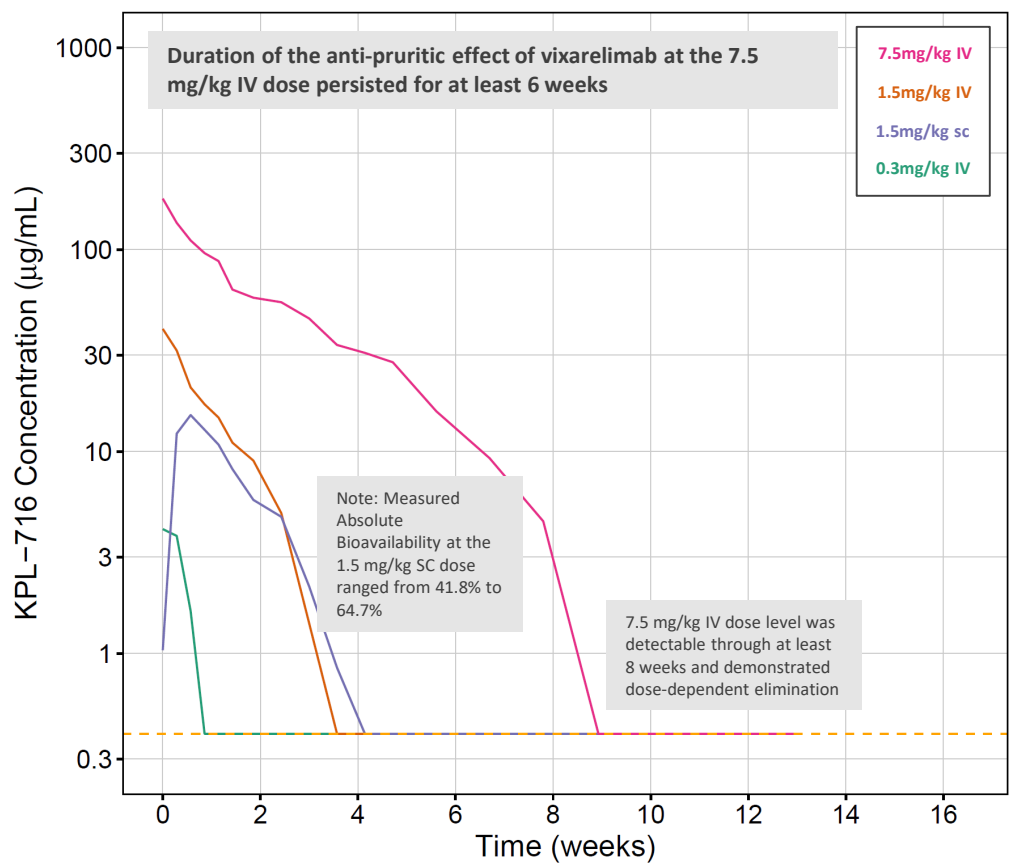


Vixarelimab was Well-Tolerated in Prurigo Nodularis Phase 2a Study

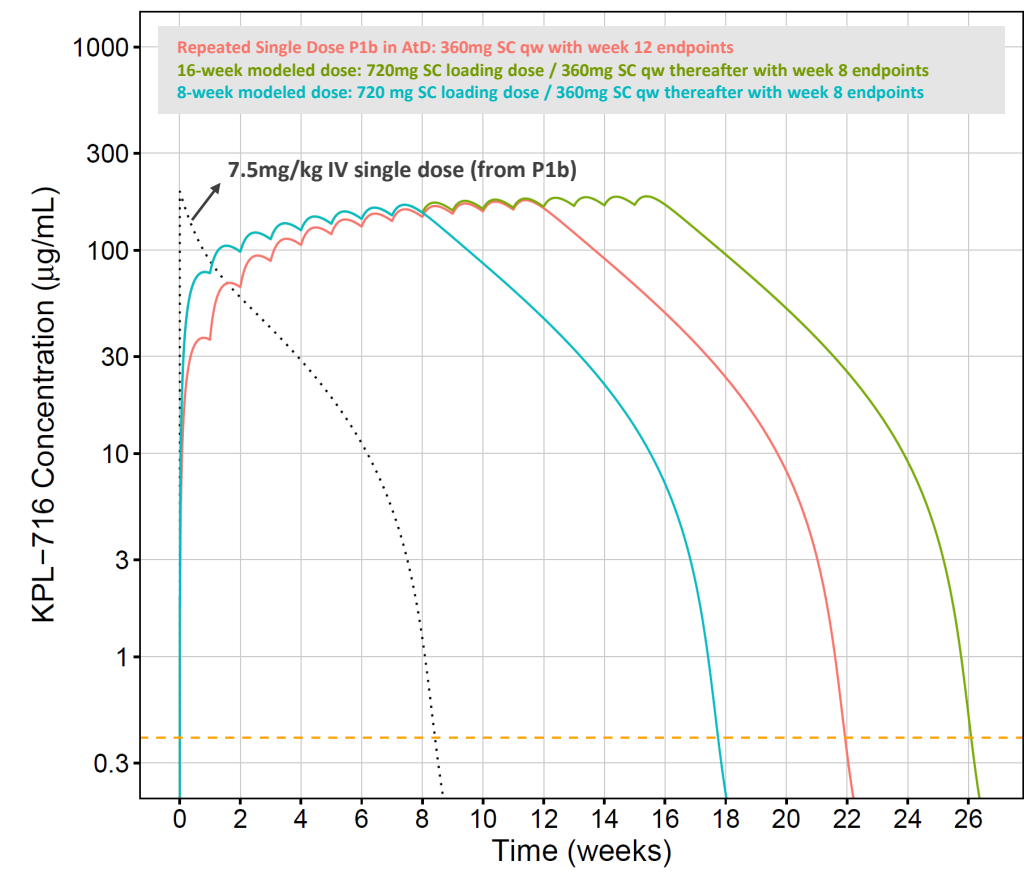
System Organ Class Preferred Term	Vixarelimab (n=23)	Placebo (n=26)
Skin and Subcutaneous Tissue Disorders	26.1% (6)	15.4% (4)
Eczema Nummular	4.3% (1)	3.8% (1)
Pruritus	4.3% (1)	3.8% (1)
Dermatitis Allergic	4.3% (1)	0
Idiopathic Angioedema	4.3% (1)	0
Night Sweats	4.3% (1)	0
Urticaria	4.3% (1)	0
Skin Burning Sensation	0	7.7% (2)
Neurodermatitis	0	3.8% (1)

PK/PD Model: Weekly SC Dosing Provided Sufficient/High Exposures for POC Studies and Alternate Dosing Regimens in Future Dose-Finding Studies (e.g., q2w and/or qm)

Measured Vixarelimab PK From P1b Single Dose



Phase 1b data used to build predictive PK/dosing model for multiple-dose studies (RSD, PN, Chronic Pruritic Diseases)



Note: Model based upon Absolute Bioavailability of 65% at the 360 mg SC dose





Every Second Counts!™