KINIKSA

Every Second Counts!™

Corporate Presentation

May 2021

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 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 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; our inability to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities; potential for applicable regulatory authorities to not accept our filings or to delay or deny approval of, or emergency use authorization for, any of our product candidates or to require additional data or trials to support any such approval or authorization; delays, difficulty or inability successfully execute on our commercial strategy for ARCALYST; 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 important factors discussed under the caption "Risk Factors" in our Annual Report on Form 10-K filed with the Securities and Exchange Commission (the "SEC") on February 25, 2021 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.

Building Patient-Centric Leadership in Immune-Modulating Therapies

Leveraging internal & external expertise to drive growth

1 FDA Approved Drug: ARCALYST®; 3 Clinical-Stage Assets

Validated Mechanisms or Strong Biologic Rationale

Targeting Debilitating Diseases with Unmet Medical Need

Pipeline-in-a-Molecule Potential Across the Portfolio

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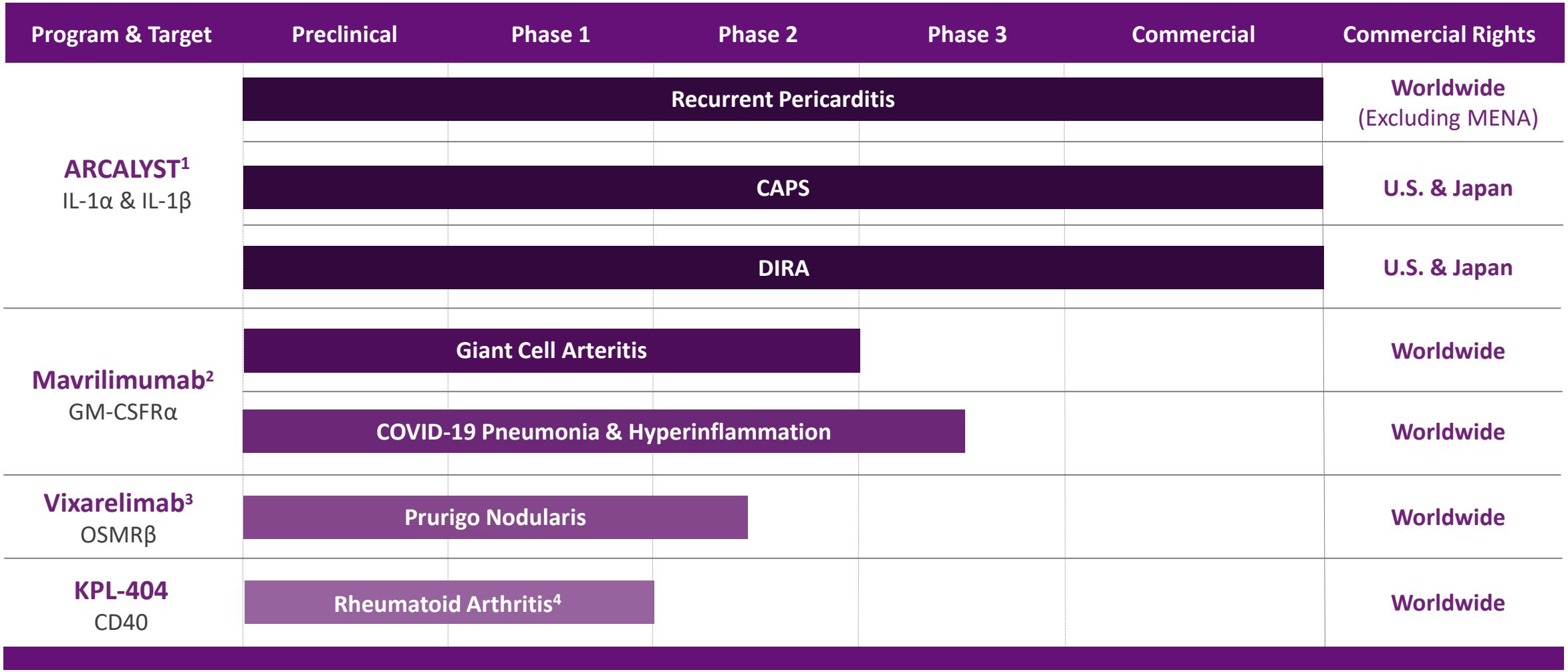
Portfolio of Four Immune-Modulating Assets



1) The FDA granted Breakthrough Therapy designation to ARCALYST for recurrent pericarditis in 2019 and Orphan Drug designation to ARCALYST for pericarditis in 2020; 2) The FDA granted Orphan Drug designation to mavrilimumab for giant cell arteritis in 2020; 3) The FDA granted Breakthrough Therapy designation to vixarelimab for the treatment of pruritus associated with prurigo nodularis in 2020; 4) Kiniksa plans to initiate a Phase 2 proof-of-concept trial in patients in the second half of 2021. The planned trial will provide safety and characterization of chronic administration as well as the potential to evaluate KPL-404 across a range of other autoimmune diseases ; IL-1α = interleukin-1α ; IL-1β = interleukin-1β; GM-CSFRα = granulocyte macrophage colony stimulating factor receptor alpha; OSMRβ = oncostatin M receptor beta; CAPS = Cryopyrin-Associated Periodic Syndromes; DIRA = deficiency of the interleukin-1 receptor antagonist; MENA = Middle East and North Africa

Lead Indications Based on Validated Mechanisms with Attractive Commercial Prospects

	Indication	Validated Mechanism	U.S. Current Prevalence	U.S. Current Addressable
ARCALYST	Recurrent Pericarditis	✓	~40k[1]	~14-17k[1]
Mavrilimumab	Giant Cell Arteritis	✓	~75-150k[2]	~45-65k[3]
Vixarelimab	Prurigo Nodularis	✓	~300k[4]	~75-105k[5]
KPL-404	Severe Autoimmune Diseases	✓	TBD	TBD

1) IQVIA PharMetrics Plus Claims Data 1/1/2013-3/31/2018; ClearView Analysis, UptoDate, Trinity Partners, Mayo Clin Proc. 2010 ;85 (6): 572-593; New Diagnostic Criteria for Acute Pericarditis: A Cardiac MRI Perspective, 2015 American College of Cardiology 2) Chandran AK, Udayakumar PD, Crowson CS, Warrington KJ, Matteson EL. The incidence of giant cell arteritis in Olmsted County, Minnesota, over a 60-year period 1950–2009. Scand J Rheumatol. 2015; 44(3):215–8. Labarca C, Koster MJ, Crowson CS, et al. Predictors of relapse and treatment outcomes in biopsy-proven giant cell arteritis: a retrospective cohort study. *Rheumatology (Oxford)*. 2016;55(2):347-356. Medcape; Trinity Lifesciences primary market research; Trinity Lifesciences analysis of Integrated 2016-2019 Medicare FFS & 2016-2019 IBM MarketScan Commercial & Medicare Supplemental data 3) Trinity Life Sciences –Trinity Life Sciences – EvidenceFirst Database Analysis, HCUP/Medicare Data, Quantitative Survey (n=102 rheumatologists) 4) Trinity Life Sciences – 2020 Analysis; Trinity Life Sciences - HCUP/Medicare Data; 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 5) Trinity Life Sciences Analysis; Moderate/Severe Patients inadequately controlled by topical corticosteroids

ARCALYST®

IL-1α and IL-1β cytokine trap

Disease Area: Recurrent pericarditis[1]; painful and debilitating auto-inflammatory cardiovascular disease

Competition[2]: First and only FDA-approved therapy for recurrent pericarditis

Regulatory: U.S. Orphan Drug designation in pericarditis; Breakthrough Therapy designation in recurrent pericarditis

Status: FDA-Approved

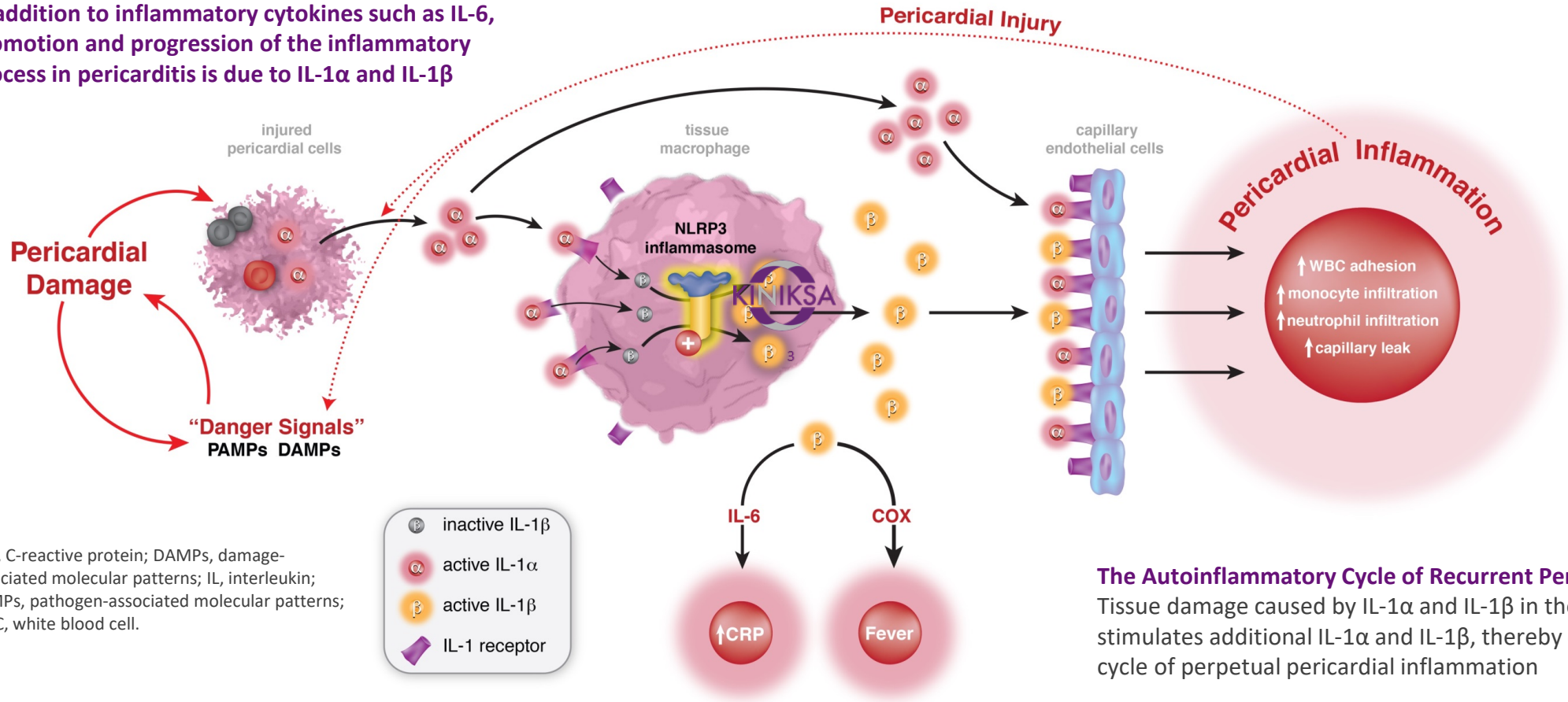
Economics: 50/50 profit split on the approved indications in the U.S.

Rights: Kiniksa has the rights to recurrent pericarditis worldwide (excluding MENA)

1) (ARCALYST®) is approved and marketed for cryopyrin-associated periodic syndrome (CAPS) and maintenance of remission of Deficiency of Interleukin-1 Receptor Antagonist (DIRA) in the United States c; 2) Drugs@FDA: Arcalyst Prescribing Information, Ilaris Prescribing Information, Kineret Prescribing Information; Kaiser et al. Rheumatol Int (2012) 32:295–299; Theodoropoulou et al. Pediatric Rheumatology 2015, 13(Suppl 1):P155 ; Fleischmann et al, 2017 ACR/ARHP Abstract 1196; Kosloski et al, J of Clin Pharm 2016, 56 (12) 1582-1590; Cohen et al. Arthritis Research & Therapy 2011, 13:R125; Cardiel et al. Arthritis Research & Therapy 2010, 12:R192; Hong et al. Lancet Oncol 2014, 15: 656-666; IL-1α = interleukin-1α; IL-1β = interleukin-1β;PDUFA = Prescription Drug User Fee Act; sBLA = supplemental Biologics License Application; MENA = Middle East North Africa

Role of IL-1α and IL-1β 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-1α and IL-1β



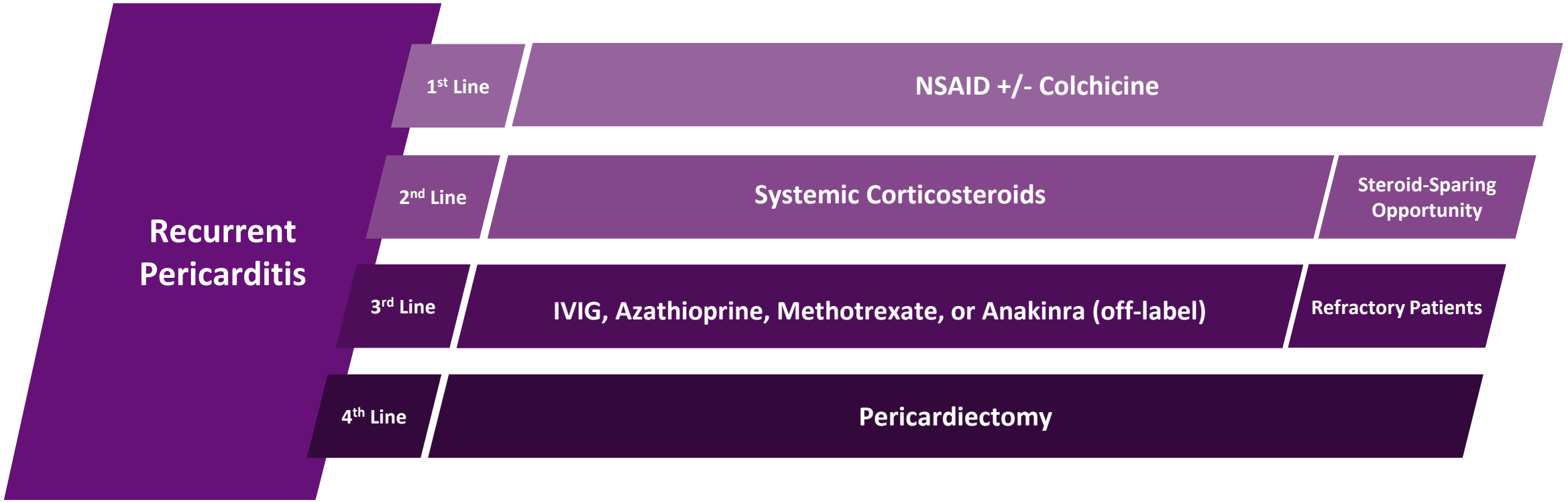
CRP, C-reactive protein; DAMPs, damage-associated molecular patterns; IL, interleukin; PAMPs, pathogen-associated molecular patterns; WBC, white blood cell.

The Autoinflammatory Cycle of Recurrent Pericarditis:
Tissue damage caused by IL-1α and IL-1β in the pericardium stimulates additional IL-1α and IL-1β, thereby creating a cycle of perpetual pericardial inflammation

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



Sources: 2015 ESC Guidelines for the Diagnosis and Management of Pericardial Diseases. Eur Heart J 2015; Aug 29; Trinity Partners, Kiniksa Analysis

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 Recurrences 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 cardiac 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 Acute Episode Resolves

- Testimonials reveal **negative impact on quality of life (QoL)** (anxiety, loss of sleep, lifestyle change, physical activity)[1,2,5]
- Between flares, 48% of patients 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 health[3]
- Increased **depression and anxiety** diagnoses seen in claims data following initial pericarditis event[4]
- 98% of patients express **need for additional therapies** that reduce the likelihood of another recurrence[1]

1) Patient ATU Research 2019 W1; 2) Patient & Physician Emotive Journey Qual 2019 Q2; 3) Ph2 Pilot study; 4) IQVIA PharMetrics Plus Claims Analyses; 5) Putnam Patient Journey Research 2018 Q1; 6) External Publications (Cremer, P "Complicated Pericarditis", ESC Guidelines), 7) HCP ATU Research 2019 W1; 8) ER ATU Research 2019 W1; 9) LeWinter (2020 ISPOR Abstract)

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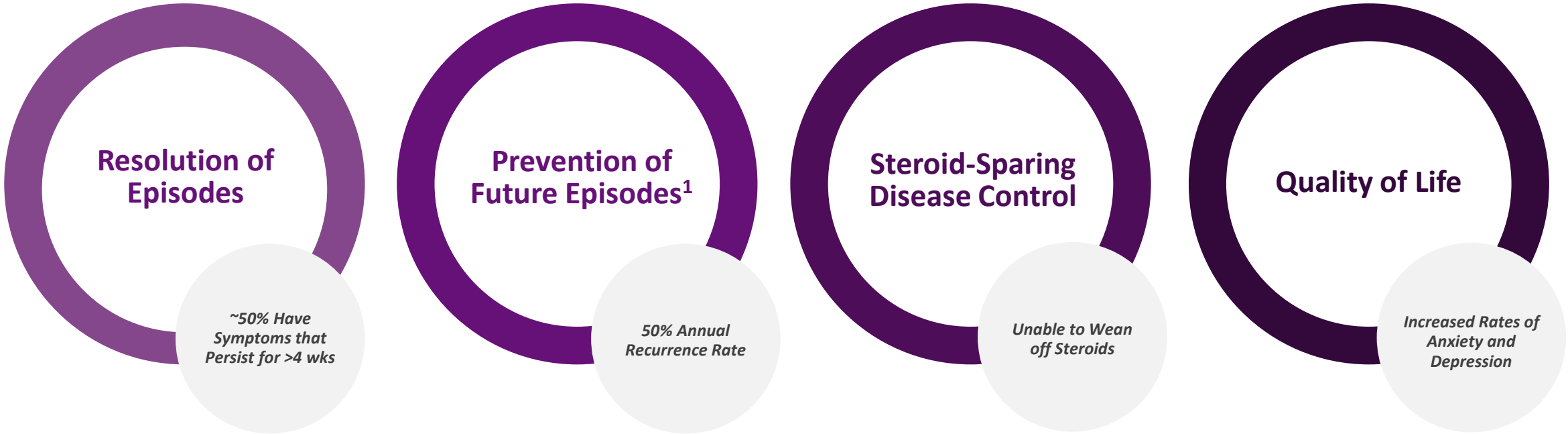
Key Areas of Unmet Need in Patients with Recurrent Pericarditis

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



Source: Kiniksa Pharmaceuticals data on file 2019; 1) Prevention of future episodes while on treatment

ARCALYST Label

ARCALYST is a patient-administered once-weekly subcutaneous therapy

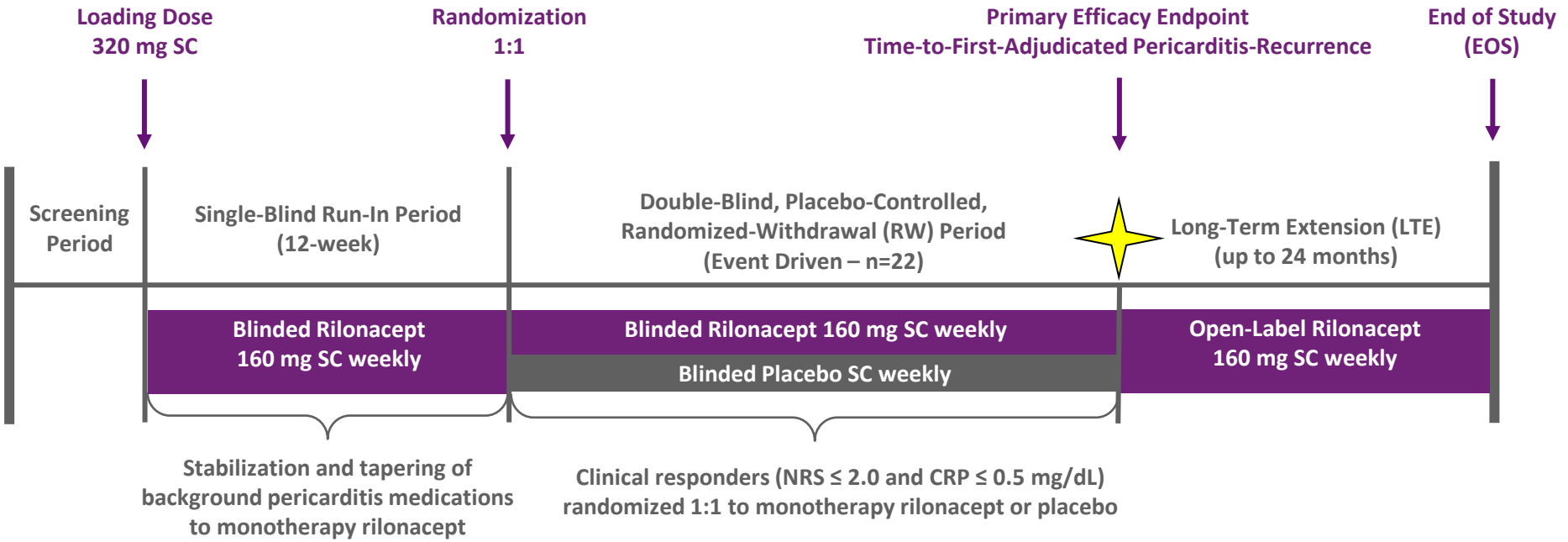
ADULTS (18 years and older)	**ADOLESCENTS** (12 to 17 years)
Loading dose: **320 mg** delivered as two 160 mg (2 mL) injections	**Loading dose:** **4.4 mg/kg** delivered up to a maximum of 320 mg, delivered as 1 or 2 injections (not to exceed 2 mL/injection)
Weekly maintenance dose: **160 mg** delivered once weekly as a 2 mL injection	**Weekly maintenance dose:** **2.2 mg/kg** delivered up to a maximum of 160 mg (2 mL) injection, once weekly

The first injection of ARCALYST should be performed under the supervision of a healthcare professional.

ARCALYST is supplied in sterile, single-use, 20-mL glass vials

- Each vial contains 220 mg ARCALYST, a sterile, white to off-white lyophilized powder
- Reconstitution with 2.3 mL of preservative-free Sterile Water for Injection is required prior to subcutaneous administration of the drug
- The reconstituted ARCALYST is a viscous, clear, colorless to pale yellow, free from particulates, 80-mg/mL preservative-free solution

Pivotal Phase 3 Trial of ARCALYST 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

CRP = C-reactive protein; NRS = Numerical Rating Scale; NSAIDs = nonsteroidal anti-inflammatory drugs; CEC = Clinical Endpoint Committee

Klein AL, Imazio M, Cremer P, et al. Phase 3 trial of interleukin-1 trap rilonacept in recurrent pericarditis. N Engl J Med. 2021;384(1):31-41.

ARCALYST Initiation Resulted in Rapid Resolution of Pericarditis Episodes

Pivotal Phase 3 RHAPSODY Data

RHAPSODY

Rapid and sustained reductions in both reported pain and inflammation as early as after the first dose of ARCALYST

Median time to pain response = 5.0 days; Median time to CRP normalization = 7.0 days

Secondary endpoints that were assessed during the run-in period

5 days

Time to treatment response (median; 95% CI: 4, 7)*

97%

Treatment response* rate

7.9 weeks

Time to ARCALYST monotherapy (median; 95% CI: 7, 8)

*Time to treatment response was defined as the time from the first dose to the first day when pericardial pain was NRS ≤2 and CRP ≤0.5 mg/dL (measured within 7 days before or after the pain response). During the 12-week run-in period, 77 of 79 patients demonstrated a treatment response.

Klein AL, Imazio M, Cremer P, et al. Phase 3 trial of interleukin-1 trap rilonacept in recurrent pericarditis. N Engl J Med. 2021;384(1):31-41.
ARCALYST (rilonacept) prescribing information 2021

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Patients treated with ARCALYST discontinued corticosteroids

In the run-in period of the Phase 3 trial RHAPSODY, patients receiving corticosteroids at baseline were transitioned to ARCALYST monotherapy in 7.9 weeks

Each patient treated with corticosteroids at baseline achieved clinical response with ARCALYST monotherapy

- 44.3% (27 of 61) of patients received corticosteroids at baseline
- None of the patients treated with corticosteroids at baseline and randomized to ARCALYST monotherapy experienced a recurrence while on therapy

Klein AL, Imazio M, Cremer P, et al. Phase 3 trial of interleukin-1 trap rilonacept in recurrent pericarditis. N Engl J Med. 2021;384(1):31-41.
ARCALYST (rilonacept) prescribing information 2021

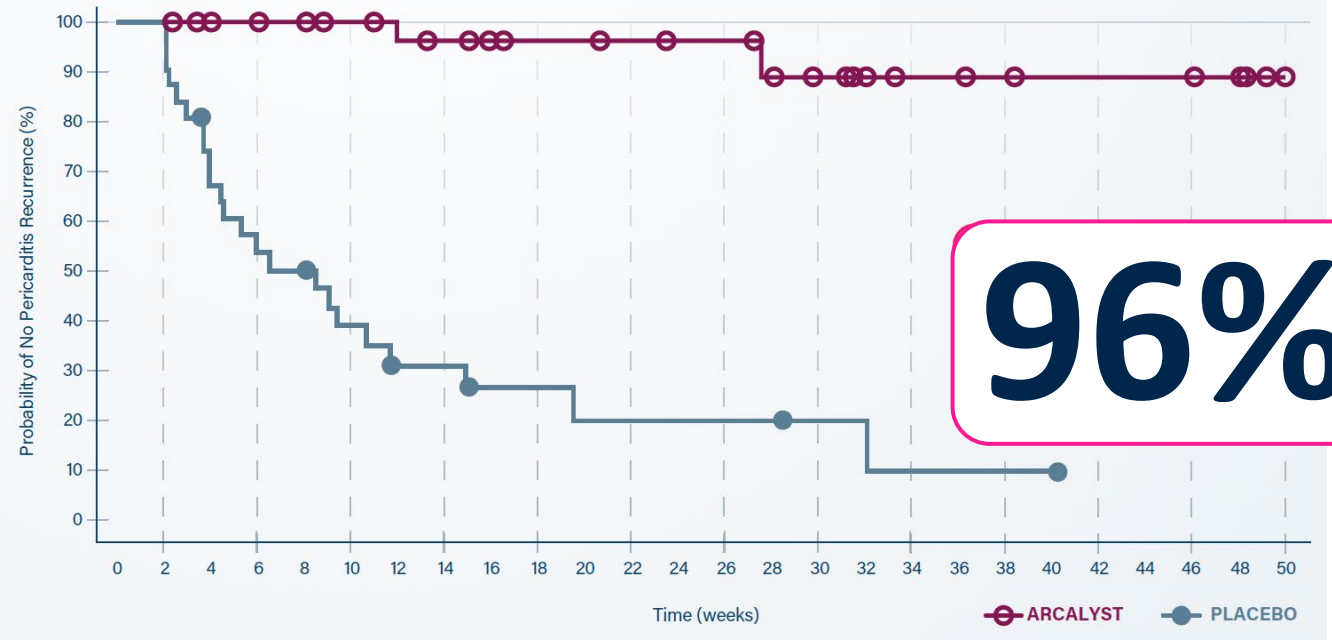
96% Reduction in Risk of Pericarditis Recurrence

Pivotal Phase 3 RHAPSODY Data

RHAPSODY

ARCALYST reduced the risk of pericarditis recurrence

The primary efficacy endpoint was time to first adjudicated pericarditis recurrence in the randomized withdrawal period.



The median time to recurrence on ARCALYST could not be estimated due to the low number of recurrences

- 2 of 30 of patients treated with ARCALYST had a recurrence
- The 2 pericarditis recurrences with ARCALYST occurred during temporary interruptions of 1 to 3 doses of ARCALYST

96% **reduction in the risk of recurrent pericarditis (hazard ratio: 0.04; *p*<0.0001)**

The median time to recurrence on placebo was 8.6 weeks (95% CI: 4.0, 11.7)

- 74% (23 of 31) of patients treated with placebo experienced a recurrence at the time that the event-driven portion of the trial was closed
- Consistent with the expected washout pharmacokinetics of once-weekly ARCALYST at steady state

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Klein AL, Imazio M, Cremer P, et al. Phase 3 trial of interleukin-1 trap rilonacept in recurrent pericarditis. N Engl J Med. 2021;384(1):31-41.
ARCALYST (rilonacept) prescribing information 2021

92% of Trial Days of No/Minimal Pain

Pivotal Phase 3 RHAPSODY Data

RHAPSODY

Patients on ARCALYST had significantly more trial days with no/minimal pain vs placebo

Secondary efficacy endpoint was assessed during the randomized withdrawal period

92% **of days**

Patients reported no/minimal (NRS≤2) pericarditis pain

Compared with 40% of trial days in patients on placebo ($p<0.0001$) at the secondary endpoint assessed at Week 16 of the randomized withdrawal period.

At Week 16 of the randomized withdrawal period:

- A majority (81%) of patients maintained a clinical response measured at Week 16 of the randomized withdrawal period compared with 20% of patients on placebo ($p=0.0002$)

Klein AL, Imazio M, Cremer P, et al. Phase 3 trial of interleukin-1 trap rilonacept in recurrent pericarditis. N Engl J Med. 2021;384(1):31-41.
ARCALYST (rilonacept) prescribing information 2021

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Most common ARCALYST adverse reactions: Injection-site reactions and upper respiratory tract infections

RHAPSODY

Adverse experiences in RHAPSODY

	RUN-IN PERIOD	RANDOMIZED-WITHDRAWAL PERIOD				TOTAL (N=86)
EVENT	Rilonacept (N=86)	Rilonacept, Including Bailout (N=30)	Placebo, Including Bailout (N=31)	Rilonacept, Before Bailout (N=30)	Placebo, Before Bailout (N=31)	
			number of patients with event (percent)			
Any adverse event	69 (80)	24 (80)	22 (71)	24 (80)	13 (42)	74 (86)
Adverse events according to maximum severity†						
Mild	52 (60)	16 (53)	17 (55)	16 (53)	9 (29)	47 (55)
Moderate	15 (17)	8 (27)	5 (16)	8 (27)	4 (13)	25 (29)
Severe	2 (2)	0	0	0	0	2 (2)
Serious adverse event	1 (1)	1 (3)	3 (10)	1 (3)	1 (3)	5 (6)
Adverse event leading to death	0	0	0	0	0	0
Adverse event leading to dose interruption	0	1 (3)	0	1 (3)	0	1 (1)
Adverse event leading to discontinuation of rilonacept or placebo	4 (5)	0	0	0	0	4 (5)
Cancer‡	0	1 (3)	0	1 (3)	0	1 (1)
Injection-site reaction	28 (33)	6 (20)	2 (6)	5 (17)	0	29 (34)
Infection or infestation	14 (16)	12 (40)	7 (23)	12 (40)	3 (10)	29 (34)
Upper respiratory tract infection	12 (14)	7 (23)	2 (6)	7 (23)	0	19 (22)

*Patients with multiple events were counted once in each appropriate category

†Counted once, according to the maximum severity of the adverse event.

‡Cancer was an event of special interest.

Klein AL, Imazio M, Cremer P, et al. Phase 3 trial of interleukin-1 trap rilonacept in recurrent pericarditis. N Engl J Med. 2021;384(1):31-41.

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ARCALYST Use in Clinical Practice

Average Duration of Recurrent Pericarditis is 2 Years[1]

- The presence of certain baseline characteristics may identify patients who may benefit from longer-term treatment
- The mean duration of disease in RHAPSODY in patients prior to enrollment was 2.4 years

Median treatment duration in RHAPSODY was 9 months, with a range up to 14 months, at the close of the randomized period

- ARCALYST treatment was associated with a 96% reduction in risk for pericarditis recurrence
- Patients on ARCALYST experienced none/minimal pericarditis pain for 92% of trial days[2]
- 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 treatment duration tailored to duration of autoinflammation

- Registry data indicate patients treated for 6 months have worse outcomes compared to patients treated for 9 months[3]
- The only events in the ARCALYST arm in the randomized period of RHAPSODY took place in the setting of temporary drug interruptions of 1-3 doses
- Continued ARCALYST treatment resulted in continued treatment response.

Additional data anticipated from LTE, in which patients are assessed at 18 months (including imaging) for possible treatment cessation under observation[4]

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) Compared to 40% of trial days in patients treated with placebo; 3) 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; 4) A. Klein, et al.; 2020 AHJ Reference for Phase 3 design; LTE = long-term extension

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ARCALYST: First and Only FDA-Approved Therapy for Recurrent Pericarditis

Third indication for ARCALYST underscores utility in IL-1 mediated diseases

Arcalyst® (rilonacept) Injection for Subcutaneous Use

Arcalyst® (rilonacept) For Injection

2008	2020	2021
CAPS FDA Approved	DIRA FDA Approved	Recurrent Pericarditis FDA Approved

KINIKSA oneconnect™ support made simple.

CAPS = cryopyrin-associated periodic syndromes ; DIRA = deficiency of IL-1 receptor antagonist

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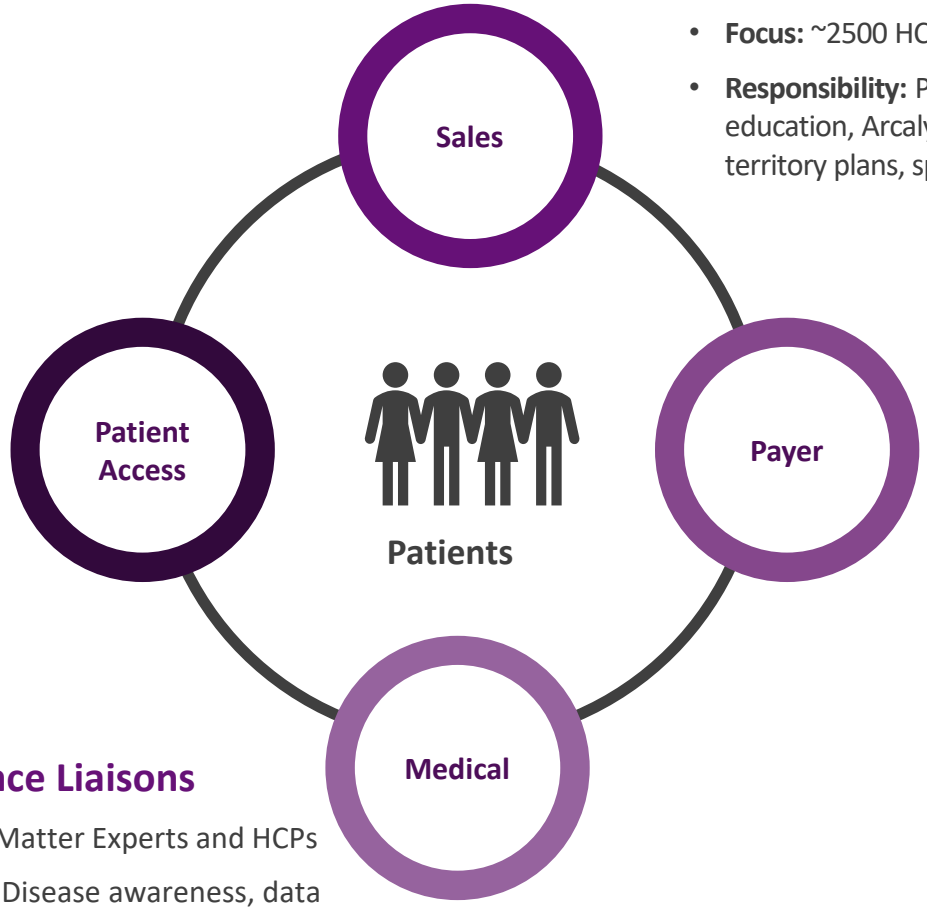
Collaborative Field Force to Drive Awareness, Overcome Access Barriers and Help Ensure Positive Patient and Physician Experience

Clinical Sales Specialists

- **Focus:** ~2500 HCPs across ~800 accounts
- **Responsibility:** Physician accounts, disease education, Arcalyst promotion, account and territory plans, speaker program planning

Patient Access Leads

- **Focus**: Patients and caregivers, HCPs seeking reimbursement support for their patients
- **Responsibility:** Optimize patient and customer experience with Arcalyst and Kiniksa, provide seamless initiation, reimbursement, and adherence support



Strategic Accounts

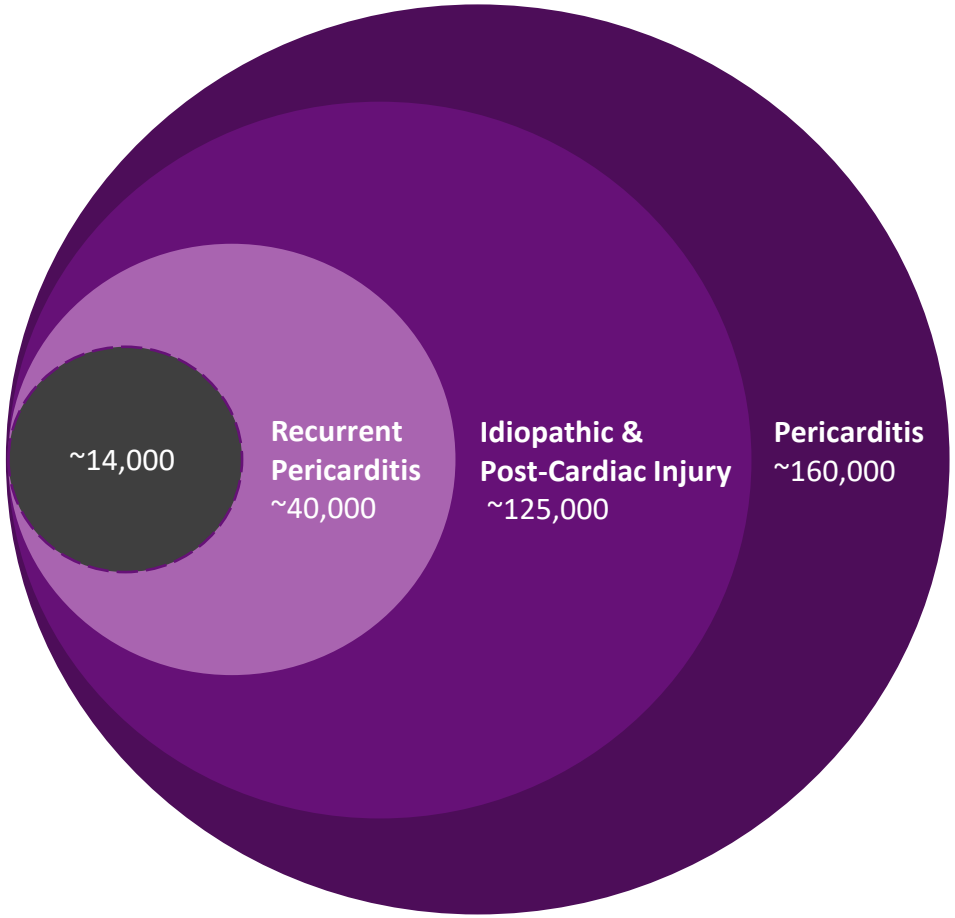
- **Focus:** ~350 payers and 5 Specialty Pharmacies
- **Responsibility:** Payer/specialty pharmacy relationship, strategic account planning, support sales team

Medical Science Liaisons

- **Focus:** Subject Matter Experts and HCPs
- **Responsibility:** Disease awareness, data dissemination, advocacy development, account and payer support, speaker management

HCP = health care provider

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 therapy[1]

- **~ 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 injury[3-5]
- **~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 year[8]

1) Cremer et al. American Journal of Cardiology. 2016;2311-2328; 2) DOF, Kiniksa Pharmaceuticals, Ltd.; 3) Brucato A, Maestroni S, Cumetti D, et al. Autoimmun Rev. 2008; 8:44-47; 4) Lange R, Hills L. N Engl J Med. 2004; 351: 2195-2202; 5) Imazio M, Cecchi E, Demichelis B, et al. Circulation. 2007; 115: 2739-2744; 6) Imazio et al. Circulation. 2005;112:2012-2016; 7) Adler et al. Circulation. 1998;97:2183-2185; 8) DOF, Kiniksa Pharmaceuticals, Ltd.

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

~8K	~5K	~1K
Refractory[1,2]	Multiple Relapsing[1,2]	Steroid-Dependent[1,2]

Potential to Broaden Utilization Over Time

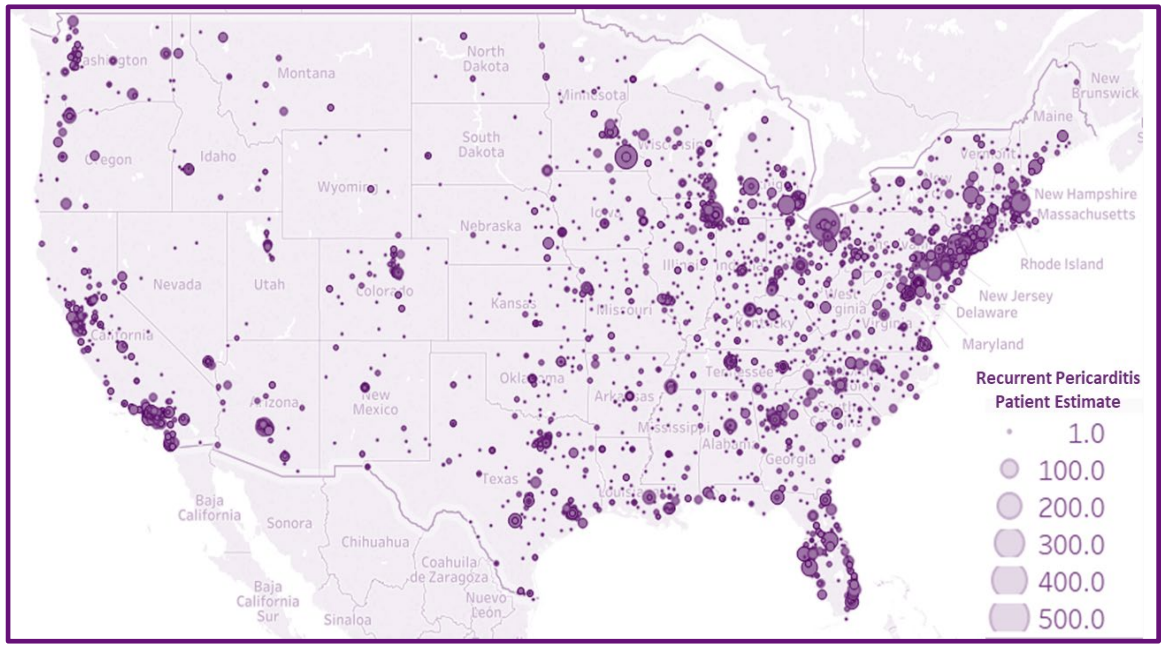
~3K
First Recurrence, High Risk[1,2]

1) Klein A, Cremer P, Kontzias A, Furqan M, Tubman R, Roy M, Magestro M. Annals of Epidemiology. 2019;36:71; 2) Lin D, Majeski C, DerSarkissian M, Magestro M, Cavanaugh C, Laliberte F, Lejune D, Mahendran M, Duh M, Klein A, Cremer P, Kontzias A, Furqan M, Tubman R, Roy M, Mage. (Nov, 2019). *Real-World Clinical Characteristics and Recurrence Burden of Patients Diagnosed with Recurrent Pericarditis in the United States.* Poster session presented at the American Heart Association, Philadelphia, PA.; 3) ClearView Forecasting Analysis 2019 Q1

Specialty Cardiology Salesforce Expected to Reach ~70% of U.S. Recurrent Pericarditis Patients

Estimated Recurrent Pericarditis Patients by Account

Strategy Targeting



Focused & Targeted Sales Execution

National	Territory Level	
Initial launch focus on top tier accounts **~45%** of RP patients nationally **~350** accounts nationally	**First 3 months**	**Within the First Year**
Following adoption, moving into next deciles to **~70%** of RP patients nationally **~800** accounts nationally (20% of total accounts)	**10-15** accounts **~60** high value HCPs	**30** accounts **~100** high value HCPs

Specialty cardiology sales force of ~30 reps

HCP = health care physicians

COVID-19: Strategic Response and Tools to Help Ensure a Successful Launch

Enabled Tools to Support Effective Remote Detailing

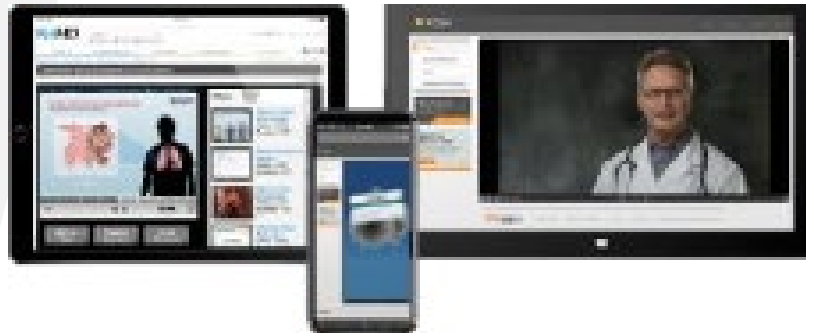
- Support convenient, impactful and compliant virtual content sharing
- Mitigate COVID-19 risk of physical access restriction

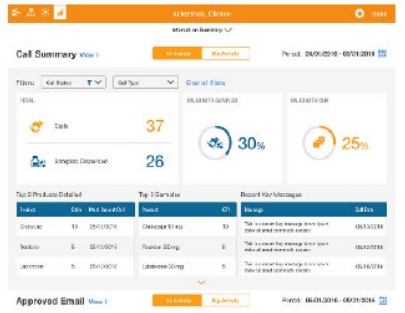
Representative-Triggered Approved Emails

- Improve quality of email reach with more tailored messages
- Drive engagement rates due to a known cardiovascular sales representative

Field Force Build

- Extensive Cardiology, Biologic and Rare Disease experience
- Previous experience with multiple drug launches and familiarity with virtual selling





Building to and Supporting a Successful Launch

Disease Educational Programs

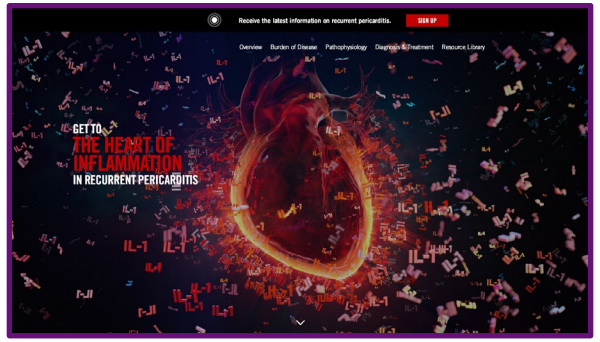
- Whatispericarditis.com; co-created with patients to provide support and self-advocacy including doctor discussion guides
- Heartofinflammation.com; targeted for healthcare professional disease knowledge
- Webcast series focused on recurrent pericarditis disease understanding

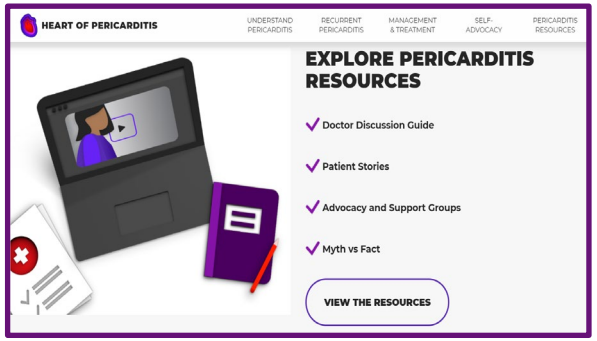
Promotional Engagements

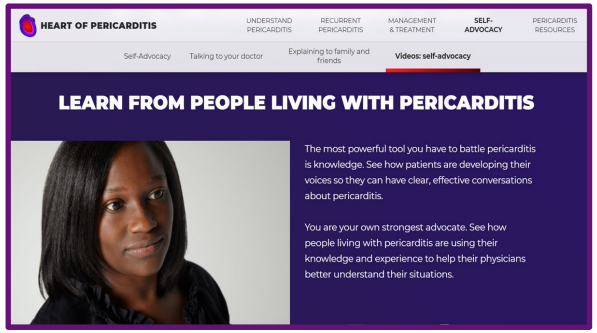
- Launch meetings in top accounts during early weeks of launch
- Treatment focused patient webcasts
- Peer-to-Peer speaker programs
- Key congresses in 2021

Continued Patient Advocacy

- Pericarditis Alliance
- Myocarditis Foundation
- Autoinflammatory Alliance







PERICARDITIS ALLIANCE

MYOCARDITIS FOUNDATION

American Heart Association.

AUTOINFLAMMATORY ALLIANCE formerly known as The NOMID Alliance

AMERICAN COLLEGE of CARDIOLOGY

>1,000 Patients & Caregivers Registered with Kiniksa

KINIKSA

Pricing, Access and Distribution Considerations

Pricing

- Kiniksa maintains the already established list price for ARCALYST **of $20,000 per month**

  Based on first and only FDA-approved therapy for recurrent pericarditis, in-line with specialty biologics with Breakthrough Therapy and Orphan Drug designation.

- Helping to ensure patient affordability and access to treatment is one of our core principles and to this end, we offer a suite of programs to support affordability to eligible patients who are prescribed ARCALYST.

Access

- Kiniksa's goal is to enable rapid and broad access to ARCALYST for patients with Recurrent Pericarditis, CAPS, and DIRA.
- Payer mix for ARCALYST is largely **commercial (60%) and Medicare (25%)**.
- Early payer engagement has increased awareness of recurrent pericarditis and the differentiated value of ARCALYST (145 meetings and 24 clinical presentations)*
- **Kiniksa One Connect** is a personalized treatment support program for patients prescribed ARCALYST

Distribution

- ARCALYST is distributed through a closed network of **5 specialty pharmacies and the Veterans Affairs**.
- The distribution network for ARCALYST was developed to provide a high and consistent level of patient support with broad access. Network pharmacies provide customized services to support patients.

**Estimated through end of March*
CAPS = cryopyrin-associated periodic syndromes ; DIRA = deficiency of IL-1 receptor antagonist

Comprehensive Support for Patients Through Kiniksa One Connect

KINIKSA oneconnect™
support made simple.

The Patient Access Lead provides one-on-one support, including:

- ✓ Insurance coverage determination
- ✓ Explanation of benefits verification
- ✓ Assistance with prior authorizations and appeals
- ✓ Virtual or hybrid model injection training support and education with ARCALYST Nurse Educators
- ✓ Identification of possible sources of financial assistance
- ✓ Help with ARCALYST shipment and delivery

KINIKSA

Summary of ARCALYST Profit Share Arrangement with Regeneron[1]

ARCALYST Net Sales (CAPS + DIRA + Recurrent Pericarditis)[2]

Minus 100% of Cost of Goods Sold[3]

Minus 100% of Field Force Expenses

Minus Marketing & Commercial Expenses (Subject to Specified Limits)

Minus 100% of Regulatory & Certain Other Expenses

Calculated ARCALYST Operating Profit to be Shared

Minus 50% of Shared ARCALYST Operating Profit (Booked as a separate line item within Opex)

Minus R&D Expenses for Additional Indications or Other Studies Required for Approval

Minus Marketing & Commercial Expenses that Exceeded Specified Limits (if any)

Kiniksa Operating Income from ARCALYST

- Upfront payment: $5 million
- 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 CAPS[4], DIRA[5], oncology, and local application for eye and inner ear
- Kiniksa has rights to develop and commercialize ARCALYST in our field worldwide, with the exception of MENA[6]
- The BLA[7] for ARCALYST in CAPS transferred to Kiniksa following highly statistically significant Phase 3 clinical data
- The scope of the license expanded to include CAPS and DIRA in the U.S. and Japan upon the approval for recurrent pericarditis. Kiniksa is responsible for the sales and distribution of ARCALYST across all approved indications
- Profits on sales of ARCALYST will be equally split after deducting certain commercialization expenses subject to specified limits

1) Subject to description contained in definitive agreement; 2) Global net sales for CAPS, DIRA and recurrent pericarditis recognized as revenue on Kiniksa's income statement; 3) Including cost of product purchased from Regeneron as well as relevant Kiniksa overhead; 4) CAPS = Cryopyrin-Associated Periodic Syndromes; 5) DIRA = deficiency of the interleukin-1 receptor antagonist; 6) MENA = Middle East and North Africa; 7) BLA = Biologics License Application

KINIKSA

Mavrilimumab

Monoclonal antibody inhibitor targeting GM-CSFRα

Disease Areas: Giant Cell Arteritis (GCA): chronic inflammatory disease of medium-to-large arteries; COVID-19 Pneumonia and Hyperinflammation

Competition[1]: Only one FDA-approved therapy for GCA, but unmet needs remain

Regulatory: U.S. Orphan Drug designation in GCA

Status: Positive Phase 2 data in GCA reported in Q4 2020; Phase 2 data from Phase 2/3 in severe COVID-19 pneumonia and hyperinflammation reported in 1H 2021

Economics: Clinical, regulatory and sales milestones; tiered royalty on annual net sales

Rights: Worldwide

1) Cortellis,;UpToDate; Correspondence, Trial of Tocilizumab in Giant-Cell Arteritis, NEJM, 2017; GM-CSFRα = granulocyte macrophage colony stimulating factor receptor alpha

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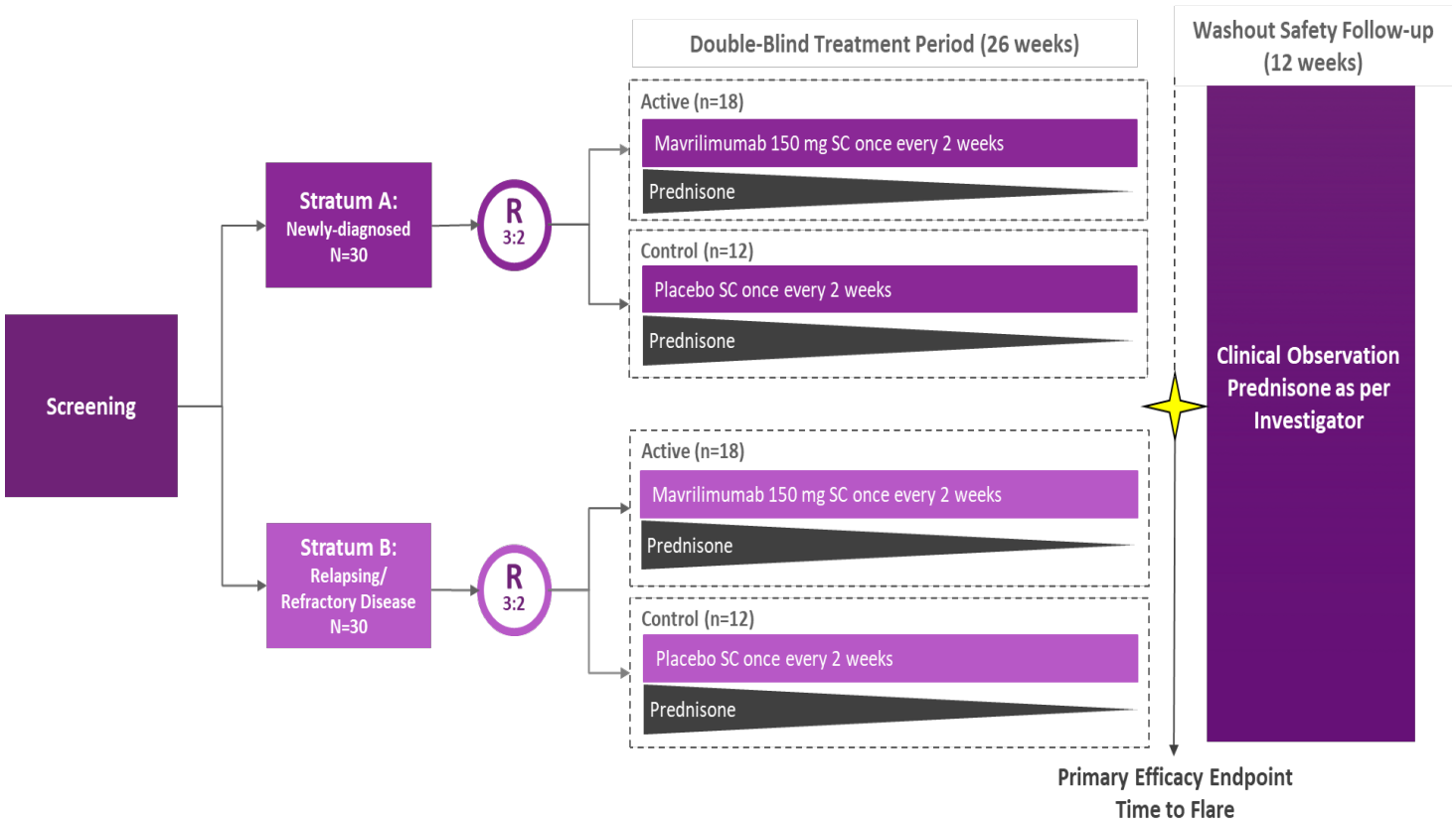
Phase 2 Clinical Trial of Mavrilimumab in GCA

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)



Treatment Period:
- Randomization 3:2 to mavrilimumab (150 mg) vs PBO SC q2wk)
- Prednisone (20-60 mg/day at Randomization) tapered over 26 weeks according to protocol-defined schedule

Efficacy Endpoints:
- Primary: Time to adjudicated GCA flare by Week 26
- Secondary: Sustained remission rate at Week 26

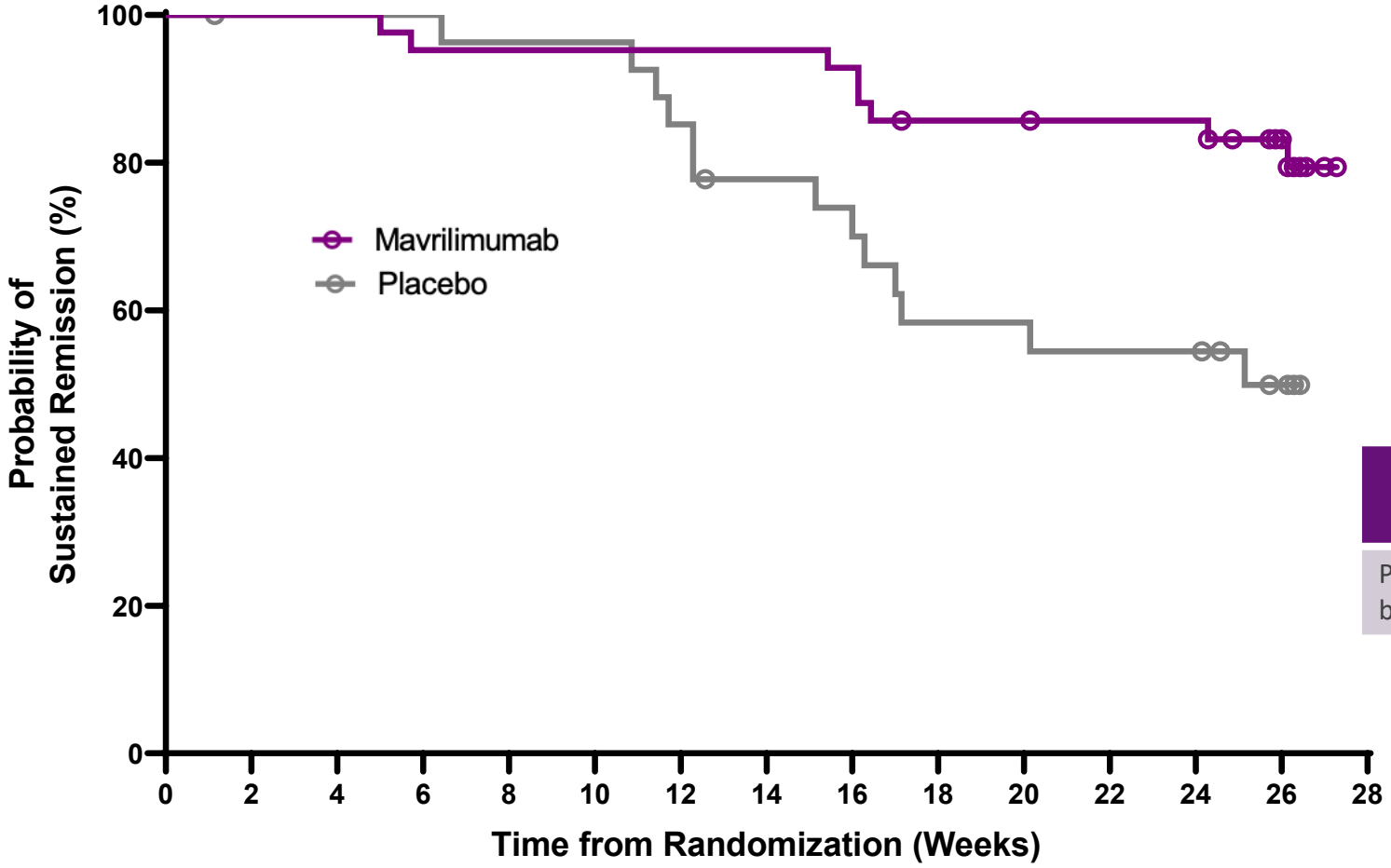
GCA Flare Definition (Adjudicated):
- Re-increase of CRP from normal to ≥1mg/dL and/or of ESR from <20 mm to ≥30 mm

-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

Primary Efficacy Endpoint: Time-to-First Adjudicated GCA Flare by Week 26

Mavrilimumab Phase 2 Giant Cell Arteritis Data



HR = 0.38
Risk Reduction = 62%
p=0.0263

	Mavrilimumab (N=42)	Placebo (N=28)
Patients with Flare by Week 26, n (%)	8 (19)	13 (46.4)

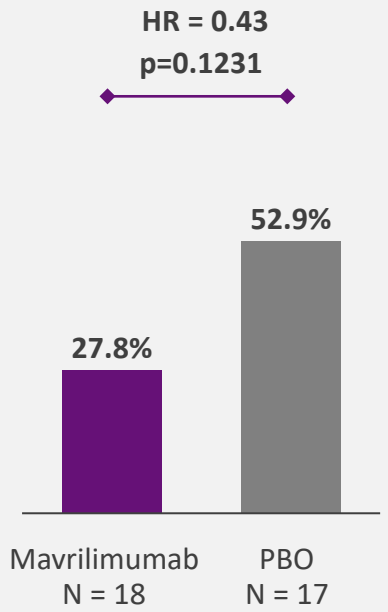
Median time-to-flare by Week 26 could not be estimated in mavrilimumab recipients due to the low number of flares in the mavrilimumab treatment arm. The median time-to-flare for placebo recipients was 25.1 weeks. There was a 62% lower risk of flare in mavrilimumab recipients compared to placebo recipients.

Unmet Need and Commercial Opportunity for Safe and Effective GCA Therapies

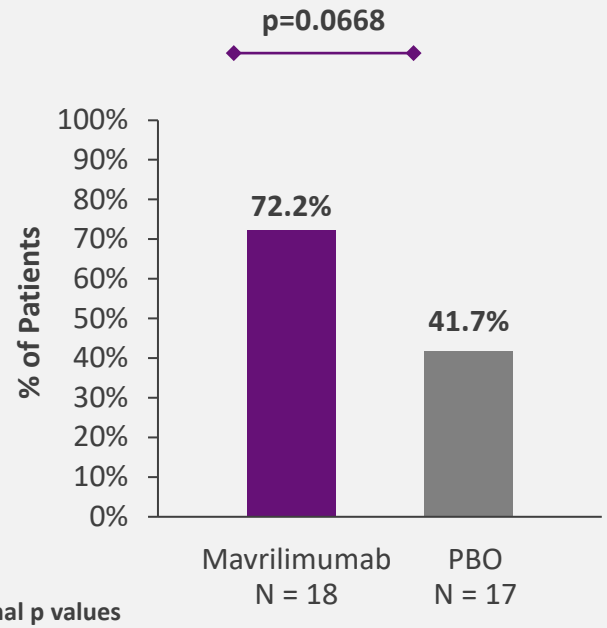
Mavrilimumab Phase 2 giant cell arteritis data[1]

Relapsing/Refractory Cohort

Patients With Flare by Week 26



Sustained Remission at Week 26



*Nominal p values

Remaining Unmet Need

- Cumulative U.S. GCA prevalence expected to grow 50% by 2035[2]
- ~50% of relapse / refractory patients are unable to achieve sustained remission within 1-year of starting treatment with approved biologics[3]
- Mechanistic (GM-CSFRα vs. IL-6) and administrative (Q2WK vs QWK) differentiation
- Well-tolerated safety profile particularly important given large elderly patient population

1) Statistically significant primary (p=0.0263) and secondary endpoint (p=0.0038); consistent trend of efficacy in relapsing/refractory cohort; 2) Chandran AK, Udayakumar PD, Crowson CS, Warrington KJ, Matteson EL. The incidence of giant cell arteritis in Olmsted County, Minnesota, over a 60-year period 1950–2009. Scand J Rheumatol. 2015; 44(3):215–8.; Labarca C, Koster MJ, Crowson CS, et al. Predictors of relapse and treatment outcomes in biopsy-proven giant cell arteritis: a retrospective cohort study. *Rheumatology (Oxford)*. 2016;55(2):347-356.; Medcape; Trinity Lifesciences primary market research; Trinity Lifesciences analysis of Integrated 2016-2019 Medicare FFS & 2016-2019 IBM MarketScan Commercial & Medicare Supplemental data; 3) Trinity Partners Primary Market Research; Stone et al., NEJM 2017

Mavrilimumab: Potential Treatment of COVID-19 Pneumonia and Hyperinflammation

Mechanism	• GM-CSF is a key growth factor and cytokine in autoinflammation and autoimmunity[1] • Mavrilimumab is a monoclonal antibody inhibitor targeting GM-CSFRα
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-19[2] • 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 hyperinflammation[4] • In U.S. IIS data showed an early signal of efficacy, with trends toward clinical improvement as well as lower mortality and shorter duration of mechanical ventilation in patients treated with mavrilimumab on top of corticosteroids • Phase 2 portion of the Phase 2/3 trial in non-mechanically-ventilated patients (Cohort 1) with severe COVID-19 pneumonia and hyperinflammation achieved its primary efficacy endpoint of the proportion of patients alive and free of mechanical ventilation at Day 29
Differentiation	• Mavrilimumab is believed to be the only GM-CSF receptor blocker; other anti-GM-CSF therapeutic approaches inhibit the ligand • GM-CSFRα blockade potentially prevents pathogenic cells from infiltrating into the target tissue, and suppresses multiple markers of inflammation (e.g., IL-2Rα, IL-6, CRP)[5,6,7] • Once hyperinflammation and CRS have begun, anti-virals may be less effective[8] • Vaccines likely to provide incomplete population immunity + limited supply/access; vaccine does not help once virus occurs[9]
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 • Enrollment in the Phase 3 Portion of an adaptive design Phase 2/3 clinical trial of mavrilimumab in severe COVID-19 pneumonia and hyperinflammation is ongoing

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

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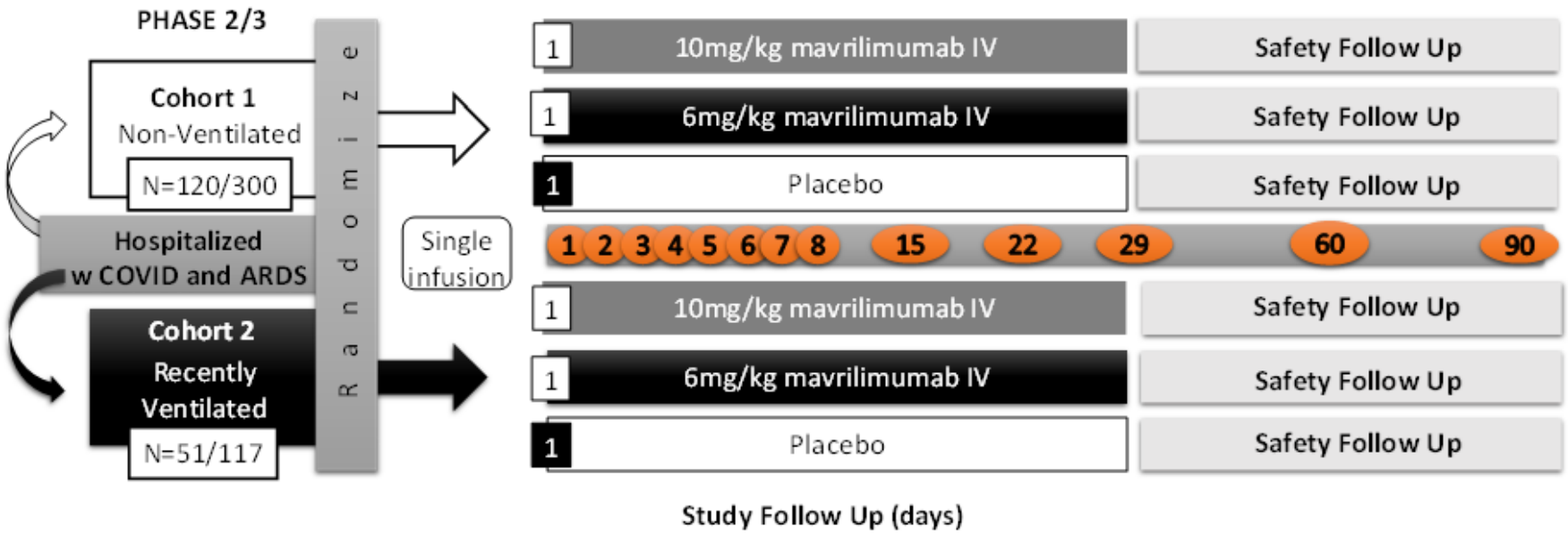
Phase 2/3 Clinical Trial of Mavrilimumab in Severe COVID-19 Pneumonia and Hyperinflammation

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



Cohort 1:

Primary Efficacy Endpoint:

- Proportion of patients alive and without mechanical ventilation at Day 29.

Secondary Efficacy Endpoints:

- Time to 2-point improvement by Day 29
- Time to return to Room Air or Discharge by Day 29
- Mortality rate at Day 29

Prespecified evidentiary standard for Phase 2 endpoints was a 2-sided p value of 0.2, without adjustment for multiplicity

Data from Phase 2 Portion of the Phase 2/3 trial of Mavrilimumab in Severe COVID-19 Pneumonia and Hyperinflammation

The Phase 2/3 trial is a global, randomized, double-blind, placebo-controlled study designed to evaluate the efficacy and safety of mavrilimumab treatment in adults hospitalized with severe COVID-19 pneumonia and hyperinflammation.

- In the non-mechanically ventilated cohort (Cohort 1), 116 patients with hypoxia and severe COVID-19 pneumonia/hyperinflammation were enrolled across sites in the United States, Brazil, Chile, Peru, and South Africa. Patients were randomized in a 1:1:1 ratio to receive a single intravenous (IV) dose of mavrilimumab 10 mg/kg, 6 mg/kg, or placebo.
- Baseline demographics were balanced across treatment arms: the population was ethnically/racially diverse (43% non-white), 49% were obese (body mass index ≥ 30), and 29% were older than 65 years.
- Local standard of care therapy: 96% received corticosteroids/dexamethasone and 29% received antivirals/remdesivir.

Primary Efficacy Endpoint: The proportion of patients alive and free of mechanical ventilation at Day 29.
Key Secondary Efficacy Endpoints: Time to two-point clinical improvement on the NIAID[1] scale, time to return to room air, and mortality at Day 29.
The prespecified evidentiary standard for Phase 2 endpoints was a 2-sided alpha value of 0.2, without adjustment for multiplicity.

Non-mechanically ventilated patients (Cohort 1) treated with mavrilimumab demonstrated a reduction in mechanical ventilation and death at Day 29 pooled across dose levels:

- The proportion of patients alive and free of mechanical ventilation at Day 29 was 12.3 percentage points higher in mavrilimumab recipients (86.7%) compared to placebo recipients (74.4%) (Primary efficacy endpoint; p=0.1224).
  - Mavrilimumab recipients experienced a 65% reduction in the risk of mechanical ventilation or death (Hazard Ratio (HR) = 0.35; p=0.0175).
- Day 29 mortality was 12.5 percentage points lower in mavrilimumab recipients (8%) compared to placebo recipients (20.5%) (p=0.0718).
  - Mavrilimumab recipients experienced a 61% reduction in the risk of death (HR= 0.39; p=0.0726).
- No apparent differences were observed between the 10 mg/kg and 6mg/kg IV treatment arms.

Mavrilimumab was well-tolerated and exhibited a favorable safety profile:

- One treatment-emergent serious adverse event related to study drug was reported on placebo, and there were no notable dose-related adverse events.
- Infections were noted in all groups including placebo recipients. All thrombotic events occurred in placebo recipients.

1) National Institute of Allergy and Infectious Diseases

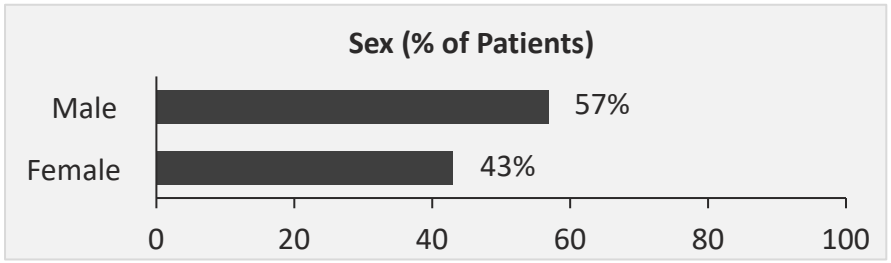
Baseline Demographics and Baseline Characteristics

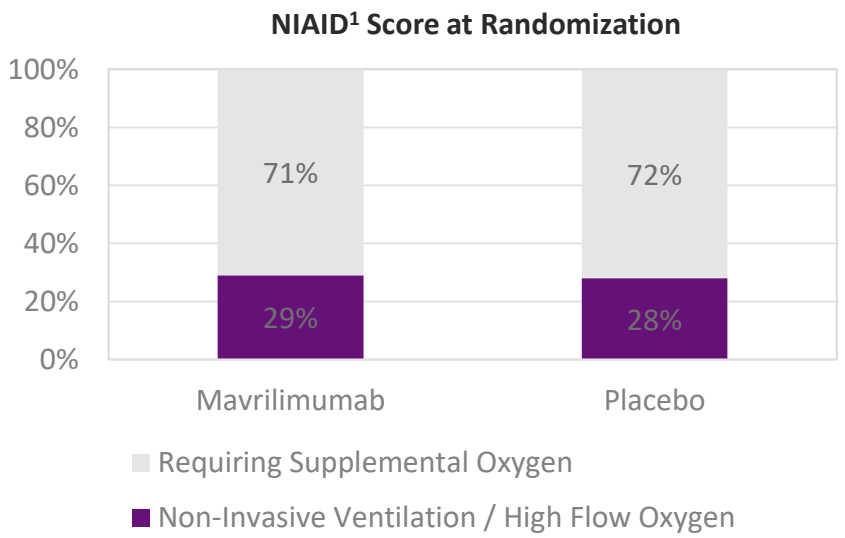
Phase 2 Portion of Phase 2/3 trial of Mavrilimumab in Severe COVID-19 Pneumonia and Hyperinflammation

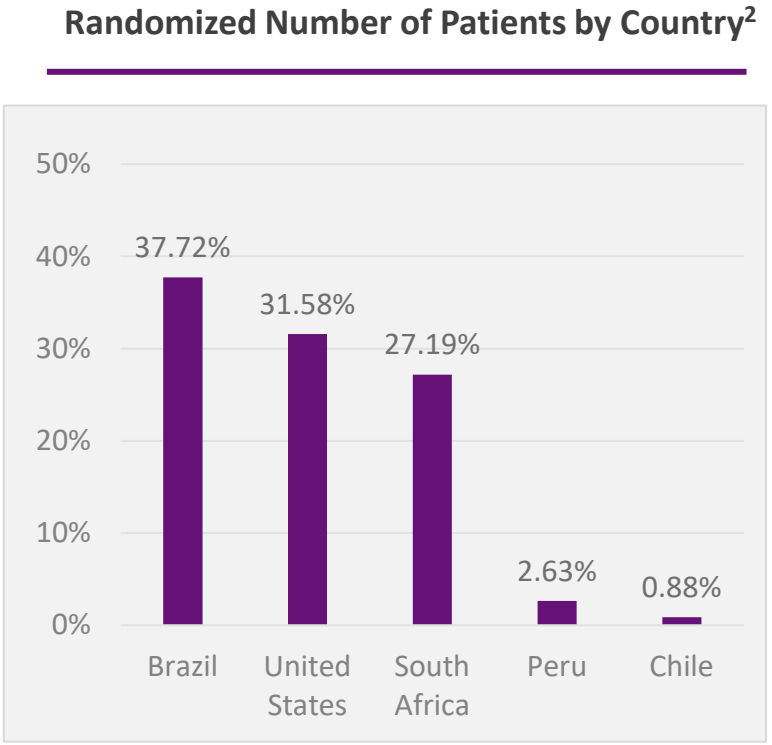
Median time to randomization from diagnosis was 7 days

Baseline Demographics were Balanced Across Treatment Arms	
Mean Age (years)	57.1
Age Range (years)	29-86
> 65 years old	29%
Non-white	43%
Body mass index ≥ 30	49%

Local Standard of Care During 29-Day Treatment Period	
Received Corticosteroids/Dexamethasone	96%
Received Antivirals/Remdesivir	29%





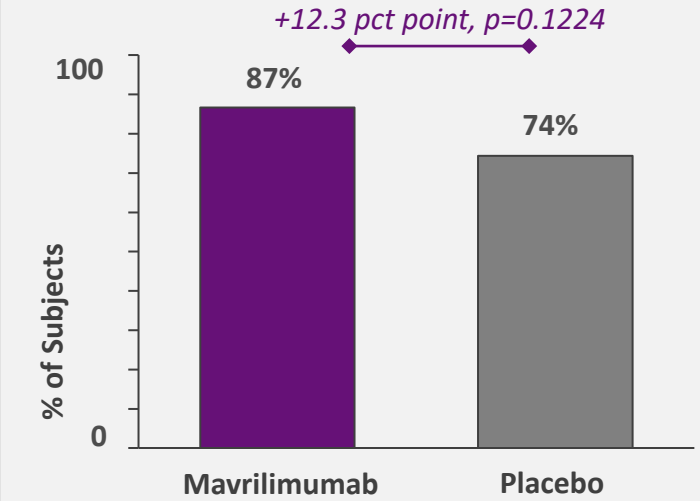


1) National Institute of Allergy and Infectious Diseases; 2) One patient randomized to Cohort 2 but analyzed as part of Cohort 1

Non-Mechanically Ventilated Patients Treated with Mavrilimumab Demonstrated a Reduction in Mechanical Ventilation and Death at Day 29 Pooled Across Dose Levels

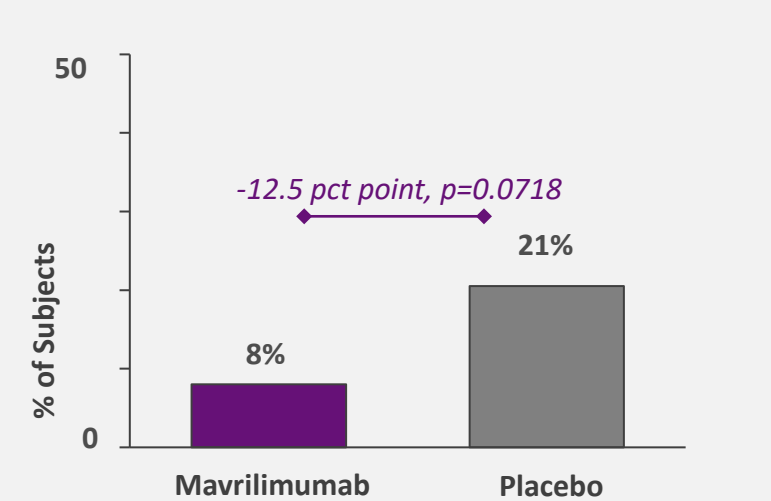
Phase 2 Portion of Phase 2/3 trial of Mavrilimumab in Severe COVID-19 Pneumonia and Hyperinflammation

Primary Endpoint: Proportion of Patients Alive and Free of Mechanical Ventilation at Day 29



Mavrilimumab recipients experienced a 65% reduction in the risk of mechanical ventilation or death (Hazard Ratio (HR) = 0.35; p=0.0175).

Key Secondary Endpoint: Mortality at Day 29

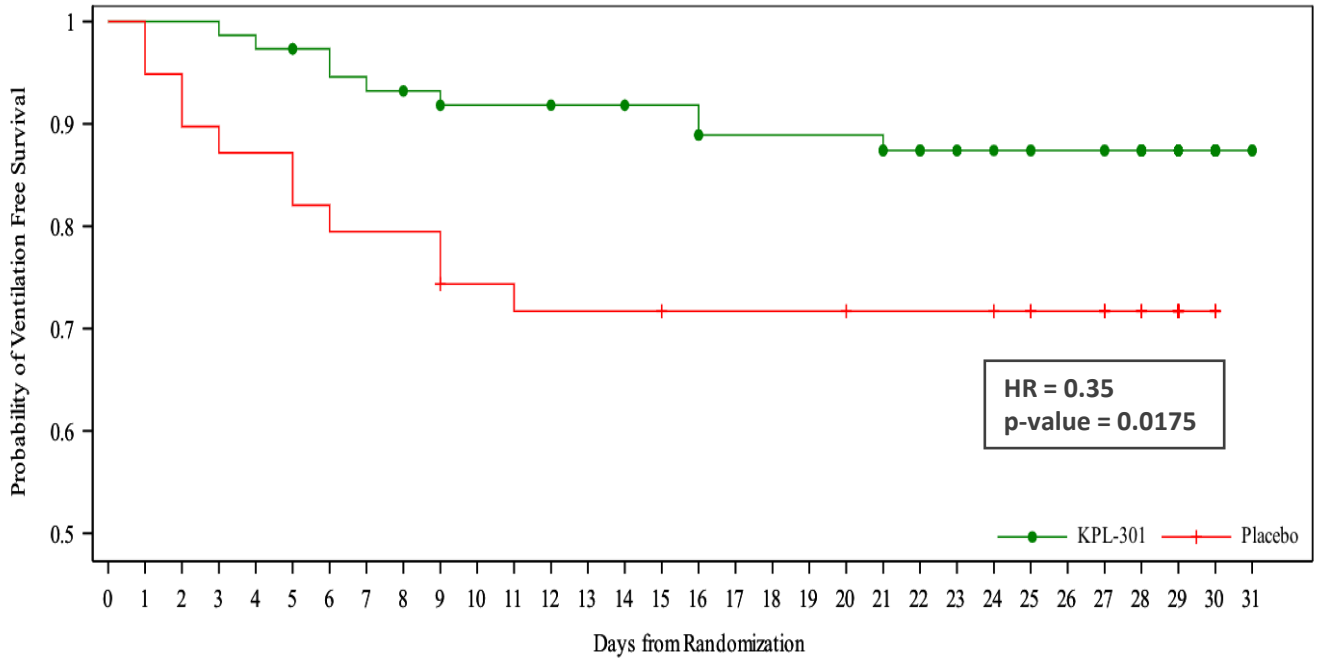


Mavrilimumab recipients experienced a 61% reduction in the risk of death (HR= 0.39; p=0.0726).

The prespecified evidentiary standard for Phase 2 endpoints was a 2-sided alpha value of 0.2, without adjustment for multiplicity.

Mavrilimumab Reduced the Risk of Mechanical Ventilation or Death by 65% Versus Placebo

Phase 2 Portion of Phase 2/3 trial of Mavrilimumab in Severe COVID-19 Pneumonia and Hyperinflammation



KPL-301	75	75	75	75	74	73	71	69	68	67	65	65	65	64	64	63	63	59	59	59	59	59	55	52	50	49	47	47	45	38	18	3
Placebo	39	39	37	35	34	34	32	31	31	31	28	28	27	27	27	27	26	26	26	26	26	25	25	25	25	24	22	22	17	14	4	

Note: Time to ventilation or death by Day 29 is defined as time (in days) from randomization to the date of death or start date of using mechanical ventilation (NIAID <= 2) by Day 29. All subjects who never had NIAID <= 2 by Day 29 will be censored at last assessment date of NIAID 8-point ordinal scale.

Mavrilimumab was Well-Tolerated and Exhibited a Favorable Safety Profile

Phase 2 Portion of Phase 2/3 trial of Mavrilimumab in Severe COVID-19 Pneumonia and Hyperinflammation

Category	KPL-301 10mg/kg (N=35) n (%)	KPL-301 6mg/kg (N=41) n (%)	Placebo (N=40) n (%)
Treatment Emergent Adverse Events (TEAEs)	19 (54.3)	19 (46.3)	26 (65.0)
TEAEs by Maximum Severity [1]			
Mild	10 (28.6)	8 (19.5)	6 (15.0)
Moderate	5 (14.3)	5 (12.2)	6 (15.0)
Severe	4 (11.4)	6 (14.6)	14 (35.0)
TEAEs related to KPL-301 or Placebo [2]	2 (5.7)	3 (7.3)	4 (10.0)
Serious TEAEs (SAE)	4 (11.4)	5 (12.2)	13 (32.5)
SAEs related to KPL-301 or Placebo [2]	0	0	1 (2.5)
TEAEs Leading to Death	3 (8.6)	4 (9.8)	9 (22.5)
TEAEs Leading to Dose Interruption	0	0	1 (2.5)
TEAEs of Special Interest [1]	3 (8.6)	2 (4.9)	6 (15.0)

1) AESIs include: Hepatic Function Abnormality / induced Liver Injury, Acute and Delayed, Hypersensitivity Reactions, Neutropenia, Serious Infection, Worsening of Cytokine Release Syndrome

KINIKSA

Potential Broad Utility

Next steps for development of mavrilimumab expected in 1H 2021

Mavrilimumab Data Across 3 Indications:

Giant Cell Arteritis

Phase 2 trial of mavrilimumab in giant cell arteritis achieved both the primary and secondary efficacy endpoints with statistical significance

Severe COVID-19 Pneumonia and Hyperinflammation

Encouraging and similar trends in mortality shown in 28-day clinical outcomes data from the open-label treatment protocol in Italy and U.S. IIS

Rheumatoid Arthritis

Mavrilimumab was dosed in over 550 patients with rheumatoid arthritis through Phase 2b clinical studies in Europe and achieved prospectively-defined primary and secondary efficacy endpoints

Mavrilimumab has been shown to be well-tolerated in giant cell arteritis, severe COVID-19 pneumonia and hyperinflammation, and rheumatoid arthritis clinical trials

Vixarelimab

Monoclonal antibody inhibitor targeting OSMRβ

Disease Area: Prurigo Nodularis (PN); chronic inflammatory skin disease with pruritic nodules

Competition[1]: No FDA-approved therapies for PN

Regulatory: U.S. Breakthrough Therapy designation for the treatment of pruritus associated with prurigo nodularis

Status: Enrolling and dosing in a Phase 2b clinical trial, evaluating a range of once-monthly dose regimens

Economics: Clinical, regulatory and sales milestones; tiered royalty on annual net sales

Rights: Worldwide

1) 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 ; OSMRβ = oncostatin M receptor beta

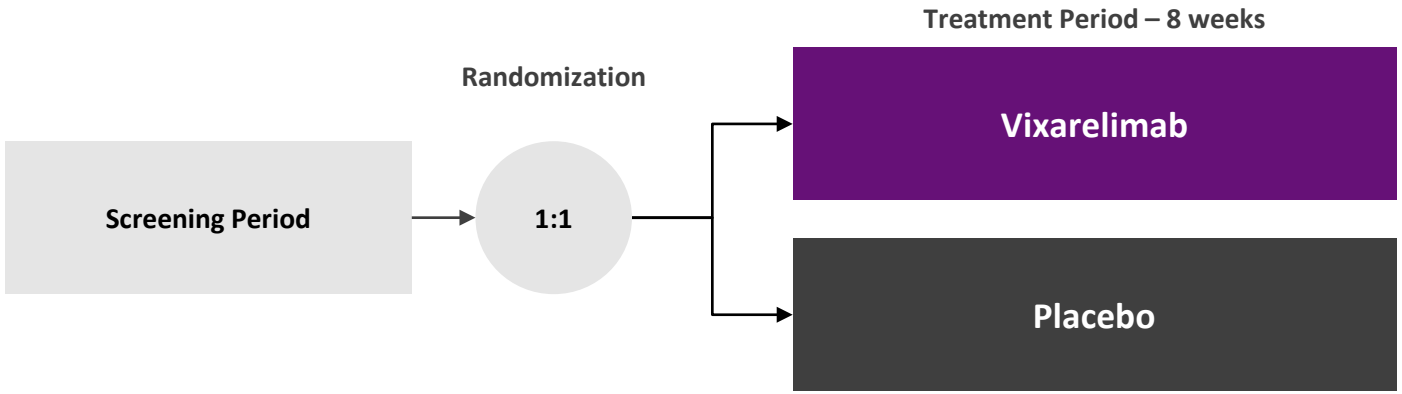
Vixarelimab Phase 2a Study in Prurigo Nodularis

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

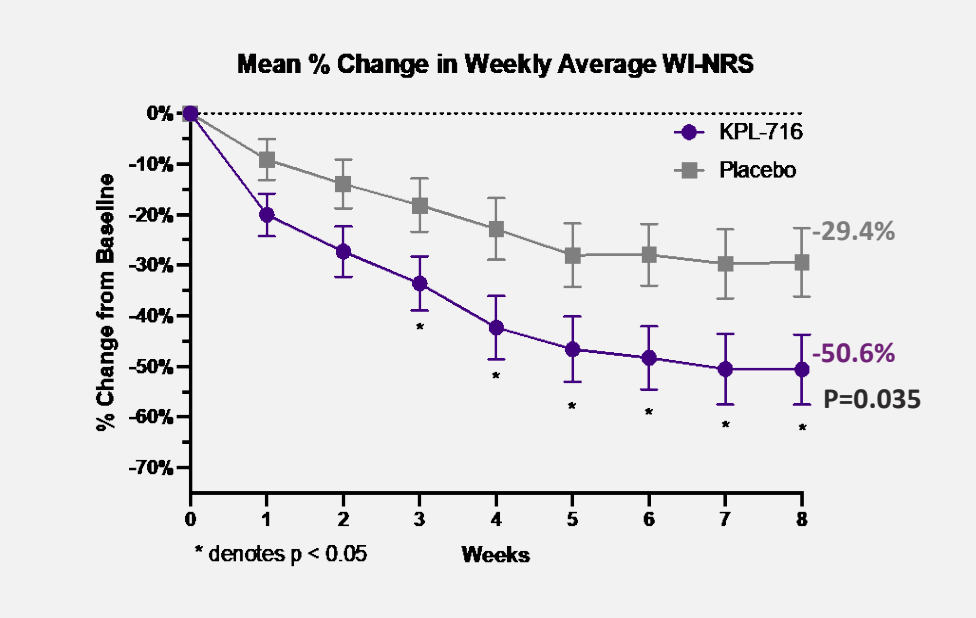
Dual Mechanism Offers Potential Pruritus Relief and Nodule Improvement

Vixarelimab Phase 2a prurigo nodularis data

Vixarelimab is the only mAb targeting OSMRβ, which mediates signaling of key cytokines (IL-31 & OSM)

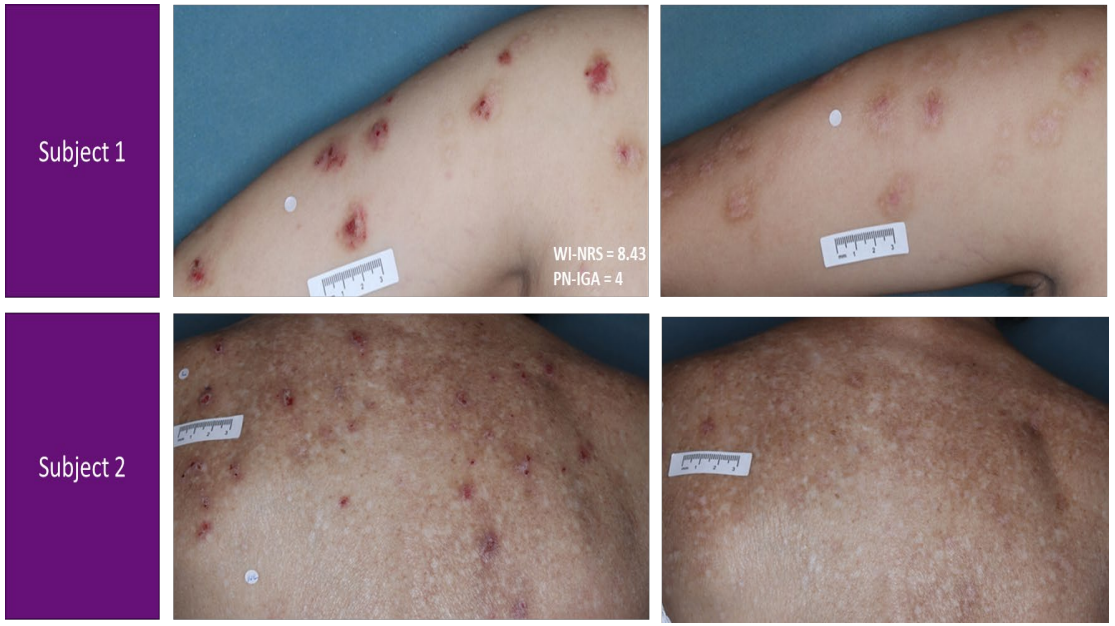
Primary Efficacy Endpoint

Mean change in weekly-average WI-NRS at Week 8 was -50.6% in vixarelimab recipients compared to -29.4% in placebo recipients (p=0.035).



Secondary Efficacy Endpoint

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).



Representative Treatment Response

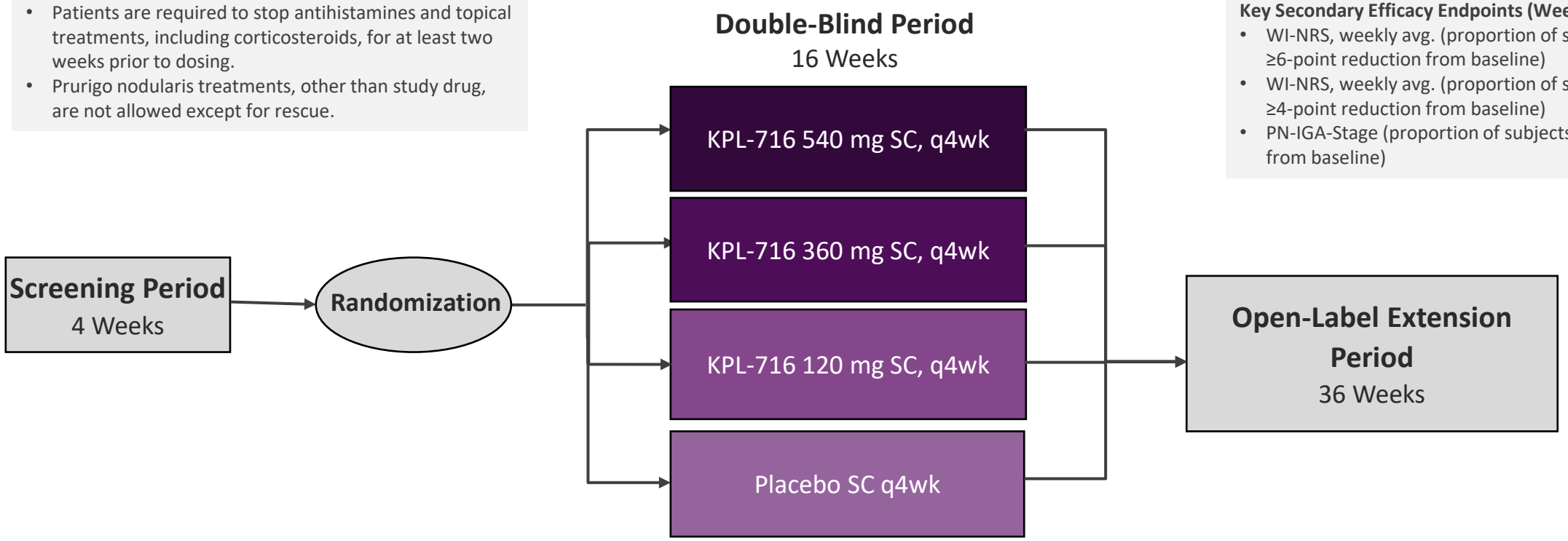
mAb = monoclonal antibody; OSMRβ = oncostatin M receptor beta; IL-31 = interleukin-31; OSM = oncostatin M; WI-NRS = Worst-Itch Numeric Rating Scale; PN-IGA = prurigo nodularis-investigator's global assessment

Vixarelimab Phase 2b Dose-Ranging Study in Prurigo Nodularis

Enrollment and dosing of patients commenced in Q4 2020

Expected to enroll approximately 180 patients

- Moderate-to-severe prurigo nodularis experiencing severe pruritus.
- Patients are required to stop antihistamines and topical treatments, including corticosteroids, for at least two weeks prior to dosing.
- Prurigo nodularis treatments, other than study drug, are not allowed except for rescue.



Primary Efficacy Endpoint (Week 16):

- WI-NRS (% change from baseline in weekly average)

Key Secondary Efficacy Endpoints (Week 16):

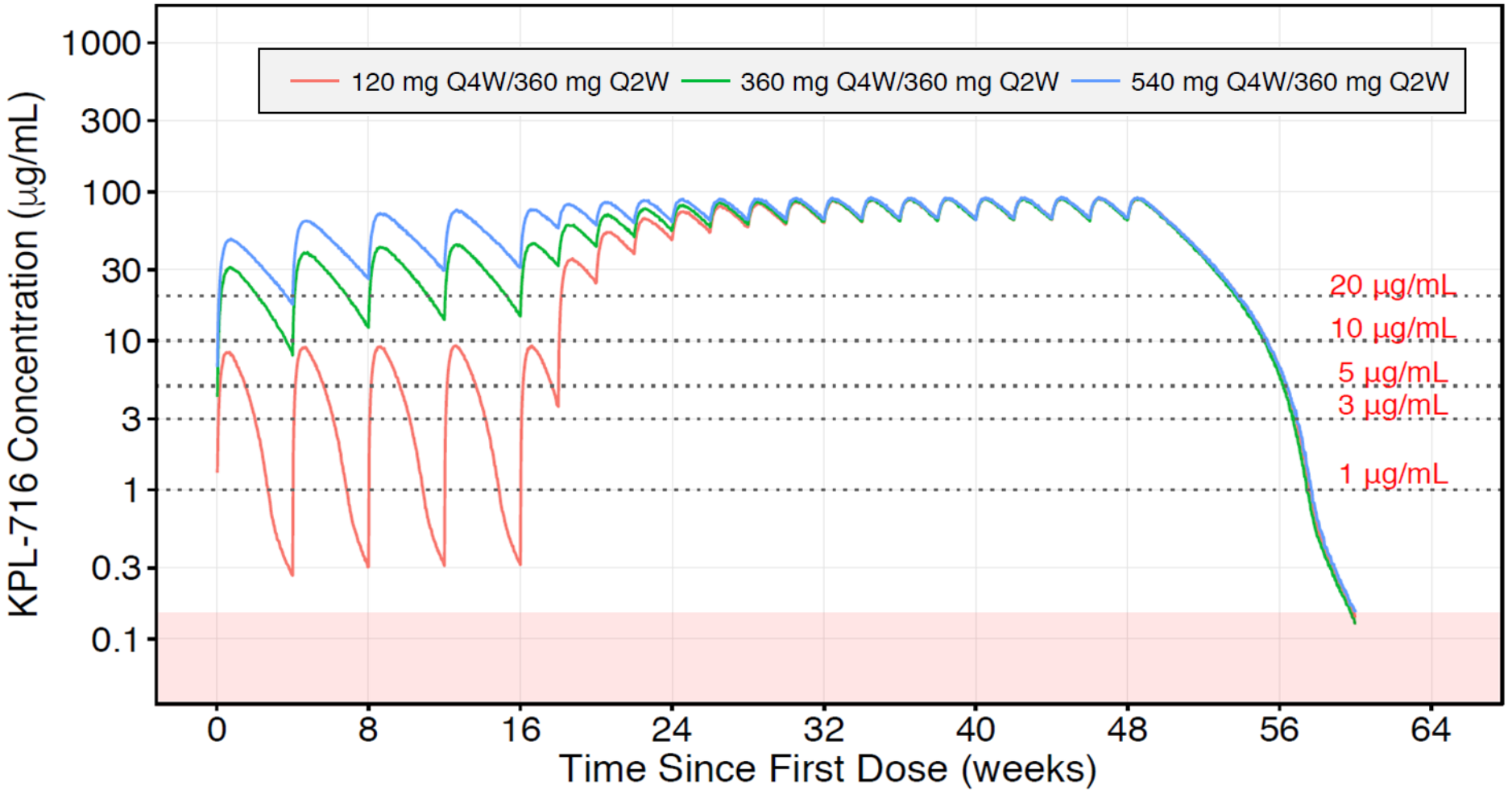
- WI-NRS, weekly avg. (proportion of subjects achieving ≥6-point reduction from baseline)
- WI-NRS, weekly avg. (proportion of subjects achieving ≥4-point reduction from baseline)
- PN-IGA-Stage (proportion of subjects achieving 0 or 1 from baseline)

WI-NRS = Worst-Itch Numeric Rating Scale; PN-IGA = prurigo nodularis-investigator's global assessment

Vixarelimab Dose-Ranging Phase 2b Study in Prurigo Nodularis

Pharmacokinetic Simulation

Supraphysiologic doses of IL-31 in a non-human primate IL-31 challenge model suggest a C_{eff} of 5-8ug/ml
Data from studies of vixarelimab in prurigo nodularis and chronic pruritic diseases support a potential C_{eff} of approximately 5-8ug/ml



KPL-404

Monoclonal antibody inhibitor interaction between CD40 and CD40L

Disease Area: 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]

Scientific Rationale[2,3]: Attractive target for blocking T-cell dependent, B-cell–mediated autoimmunity

Status: Phase 1 single-ascending-dose study in healthy volunteers completed and supports further development in patients with optionality for testing SC and/or IV dosing; Expect to initiate Phase 2 proof-of concept trial in patients in 2H 2021

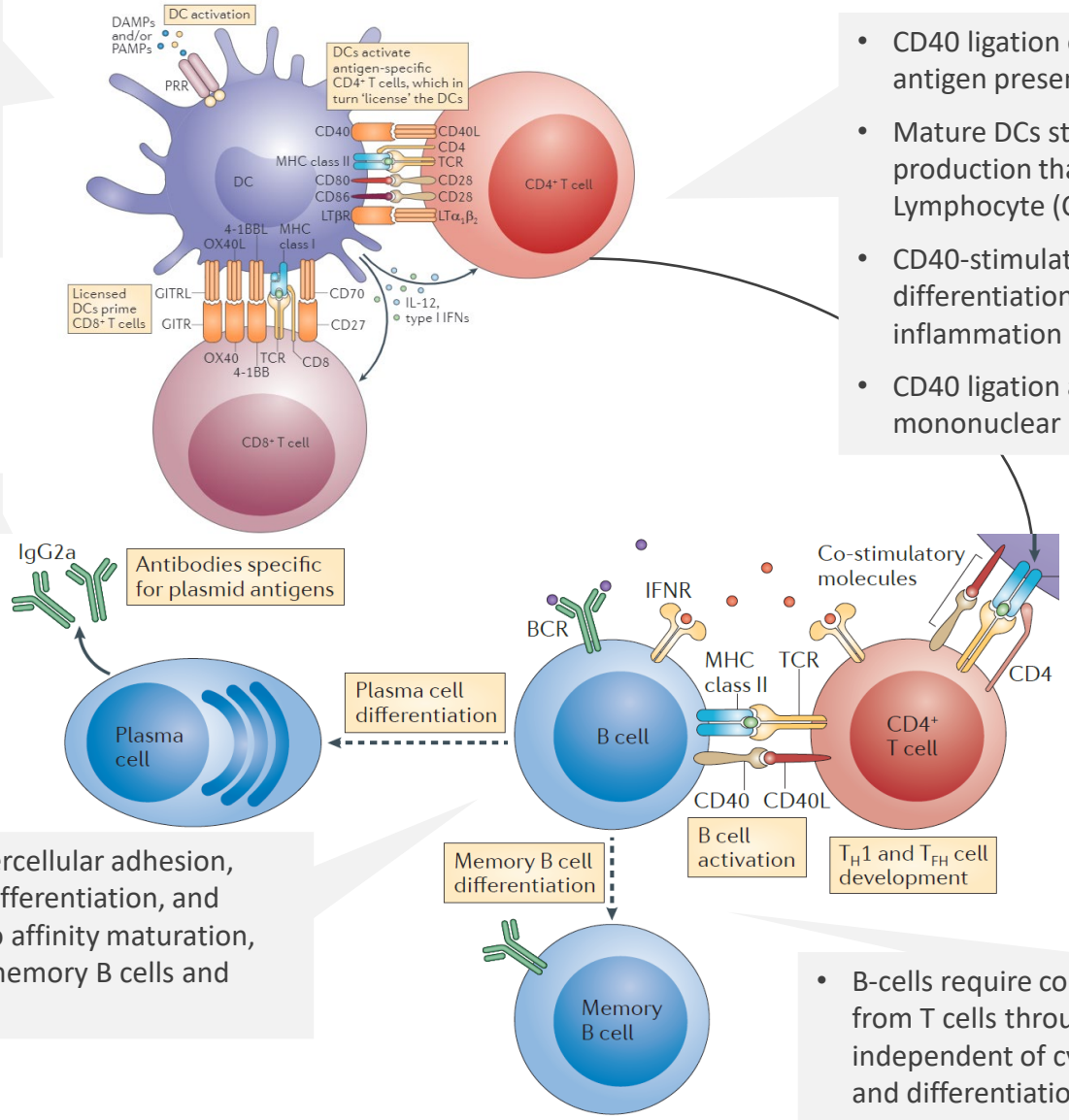
Economics: Clinical and regulatory milestones and royalty on annual net sales

Rights: Worldwide

1) Poster presentation at the Keystone Symposia: Antibodies as Drugs: New Horizons in the Therapeutic Use of Engineered Antibodies: KPL-404, a CD40 antagonist, blocked antigen-specific antibody responses in an in vivo NHP model and demonstrated strong PK/PD correlation; 2) Elgueta, et al. Immunol Rev 2009, 229 (1), 152-172; 3) Peters, et al. Semin Immunol 2009, 21 (5) 293-300; CD40L = CD40 ligand; RO = receptor occupancy; TDAR = T-cell Dependent Antibody Response

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

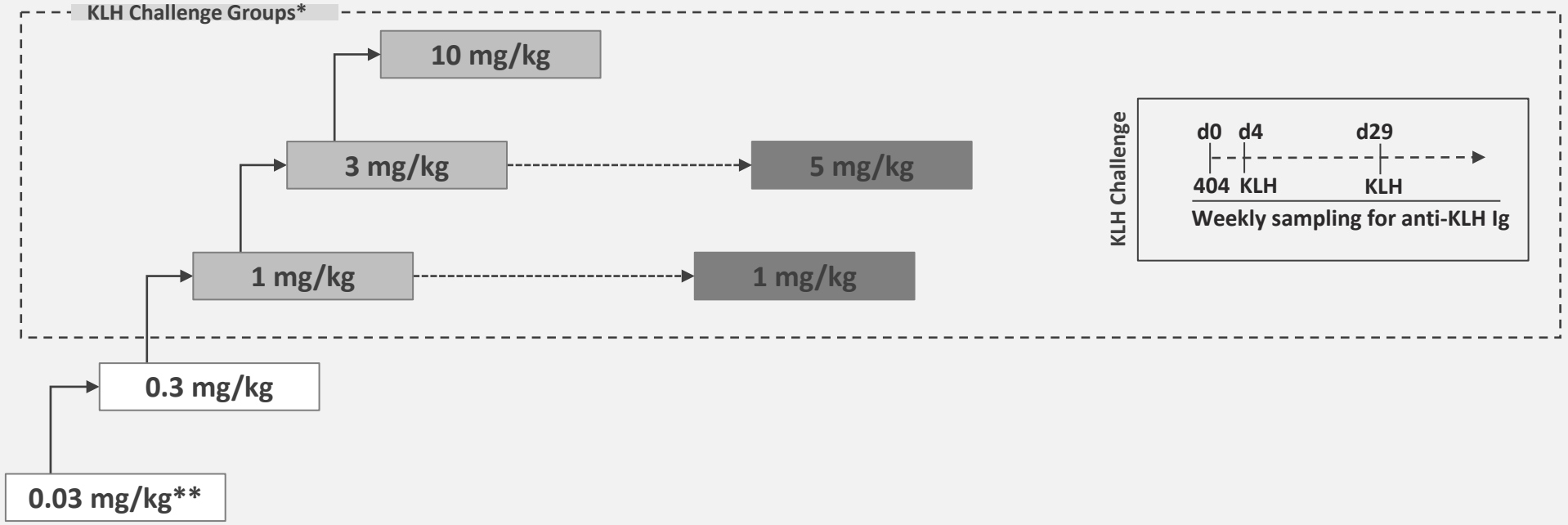
- B-cells require contact-dependent stimulus from T cells through CD40/CD40L interaction independent of cytokines to trigger growth and differentiation

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 Single-Ascending-Dose Phase 1 Study

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

Part A (Single IV dose) | Part B (Single SC Dose)



- **Primary endpoints:** Safety and Tolerability
- **Secondary endpoints:** PK and ADA / CD40 RO in blood / Serum anti-KLH Ig levels
- **Exploratory endpoints:** Serum CXCL13 levels

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

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

Final Data from KPL-404 Single-Ascending-Dose Phase 1 Study

The randomized, double-blind, placebo-controlled first-in-human (FIH) study is designed to investigate the safety, tolerability, PK and PD properties of single-ascending intravenous (IV) and subcutaneous (SC) doses of KPL-404 in healthy subjects.

- 2 single-ascending-dose arms (SAD):
  - Single-dose KPL-404 0.03 mg/kg, 0.3 mg/kg, 1 mg/kg, 3 mg/kg or 10 mg/kg IV and
  - Single-dose KPL-404 1 mg/kg or 5 mg/kg SC

Primary Endpoint: Safety and tolerability of single ascending intravenous (IV) and subcutaneous (SC) doses of KPL-404 in healthy subjects.

- KLH challenge in 1 mg/kg, 3 mg/kg, and 10 mg/kg IV and 1 mg/kg and 5 mg/kg SC cohort

Secondary Endpoints: Pharmacokinetics and anti-drug antibody response following single IV and SC doses of KPL-404 in healthy subjects, serum anti- keyhole limpet hemocyanin (KLH) IgG levels

Exploratory Endpoint: Receptor occupancy of KPL-404 on CD40 in healthy subjects

Preliminary Data:

- All dose escalations occurred as per protocol with no dose limiting safety findings. All 6 subjects dosed with KPL-404 3 mg/kg IV showed full receptor occupancy through Day 29, which corresponded with complete suppression of the T-cell Dependent Antibody Response (TDAR) to KLH through Day 29. Consistent dose relatedness was shown in the lower dose level cohorts, including 0.03 mg/kg, 0.3 mg/kg, 1 mg/kg IV and 1 mg/kg SC. Data collection for the higher dose level cohorts, 10 mg/kg IV and 5 mg/kg SC, is ongoing.
- The data to-date support subsequent study in patients, including potential IV or SC monthly administration. Kiniksa expects final data and safety follow-up from all cohorts in the first half of 2021.

Final Data:

- KPL-404 showed dose-dependent increases in concentration across cohorts. All dose escalations occurred as per protocol with no dose-limiting safety findings.
- KPL-404 was well-tolerated, and there were no serious adverse events.
- Subjects dosed with KPL-404 10 mg/kg IV showed full RO through at least Day 71 and complete suppression of TDAR after KLH challenge and re-challenge through at least Day 57.
- Subjects dosed with KPL-404 5 mg/kg SC showed full RO through Day 43 and suppression of TDAR after KLH challenge through at least Day 29. These data confirm and extend previously-reported 3 mg/kg IV cohort data, in which RO and suppression of TDAR after KLH challenge were demonstrated through Day 29.
- The 3 mg/kg IV dose level had previously demonstrated complete suppression of memory TDAR response to a re-challenge on Day 29.
- Anti-drug antibodies to KPL-404 were suppressed for at least 57 days at 10 mg/kg IV; the suppression of antibody responses to the drug itself is an independent indicator of target engagement and pharmacodynamic effect.

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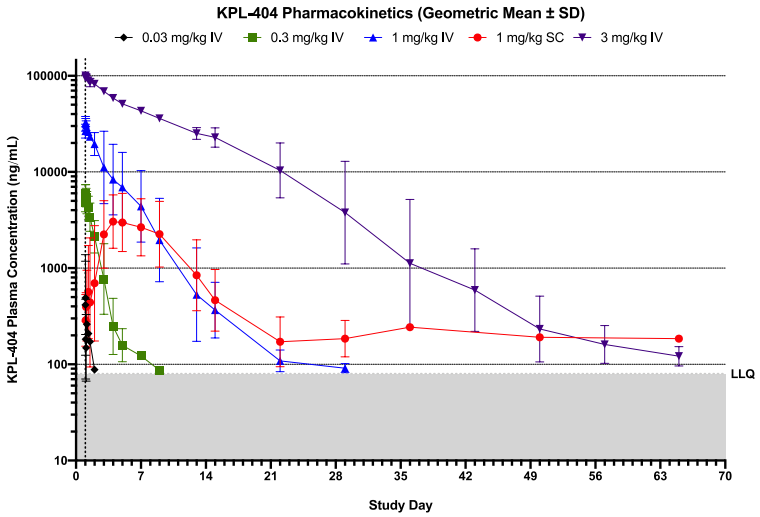
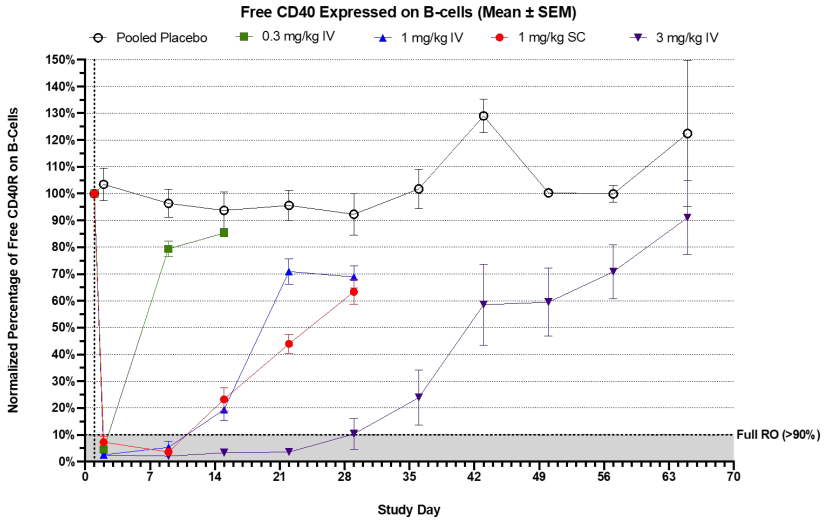
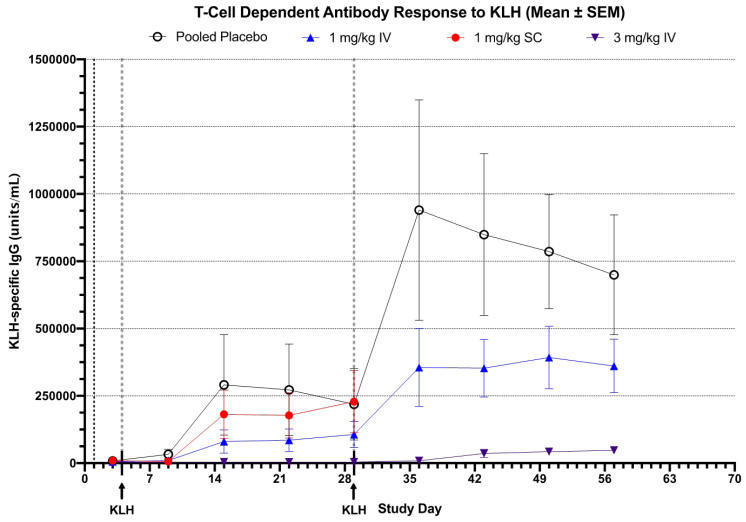
RO and TDAR Suppression Shown Through Day 29 at 3mg/kg IV

Preliminary KPL-404 Phase 1 data







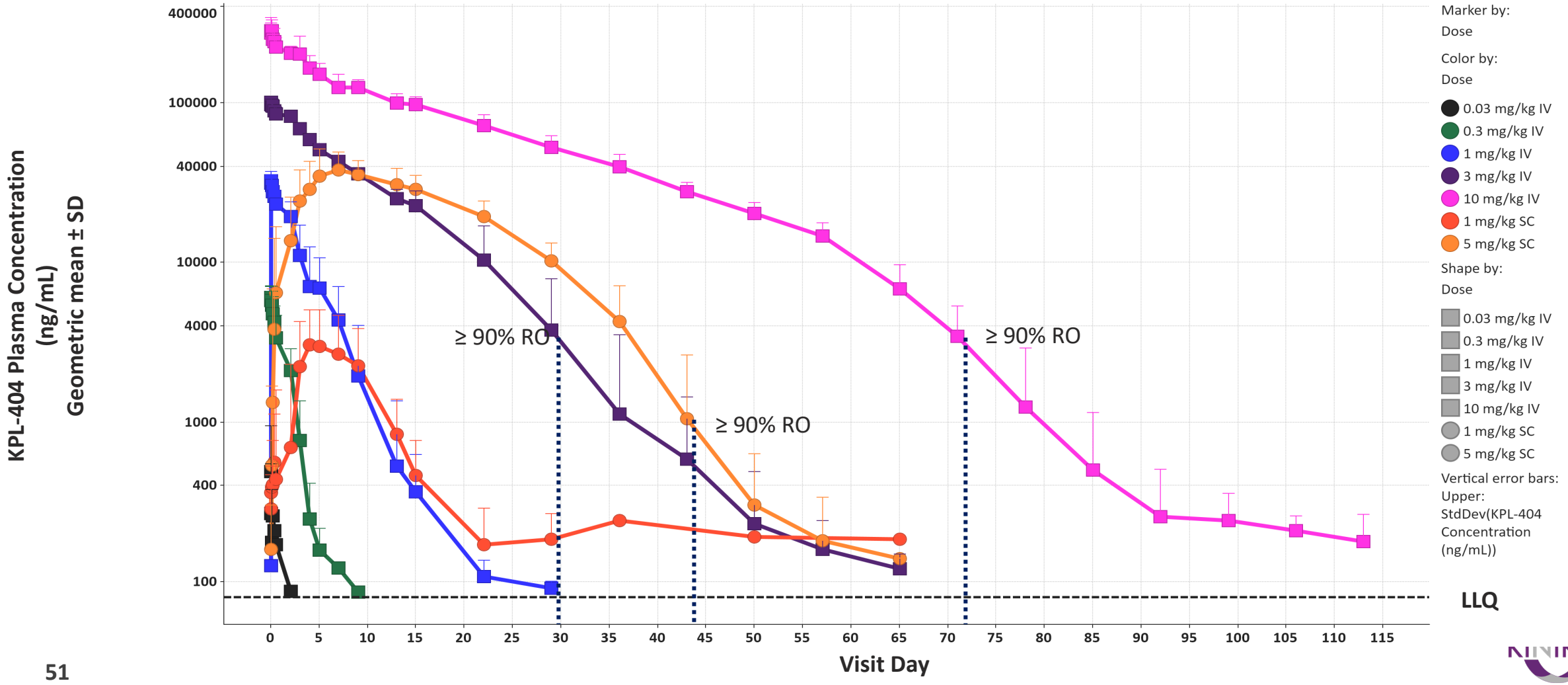
Preliminary data support subsequent study in patients, including potential monthly intravenous or subcutaneous administration

Final data from all cohorts expected in 1H 2021

1) Free CD40R = inverse of receptor occupancy; RO = receptor occupancy; KLH = keyhole limpet hemocyanin; TDAR = T-cell dependent antibody response ; IV = intravenous

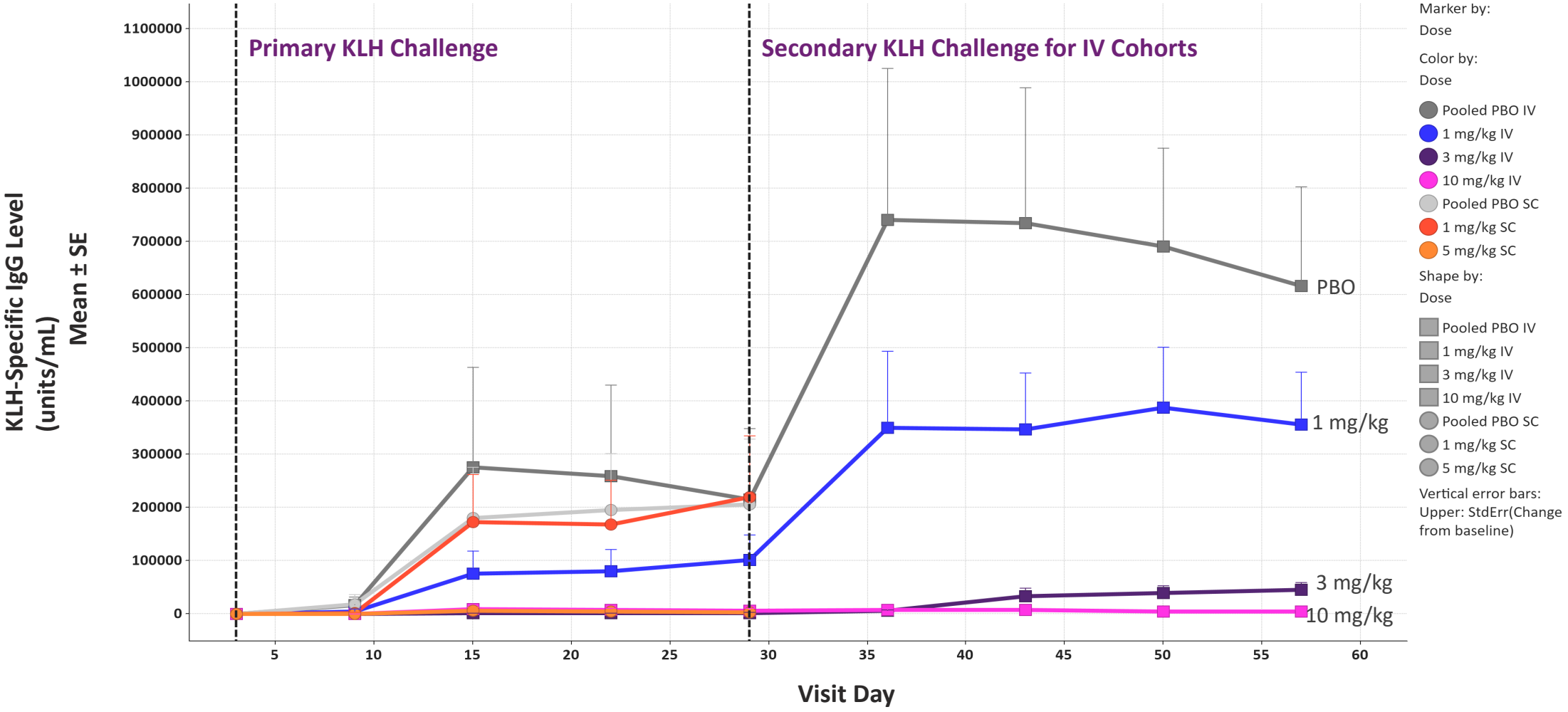
Final Data from KPL-404 Single-Ascending-Dose Phase 1 Study

Pharmacokinetic profiles for KPL-404



Final Data from KPL-404 Single-Ascending-Dose Phase 1 Study

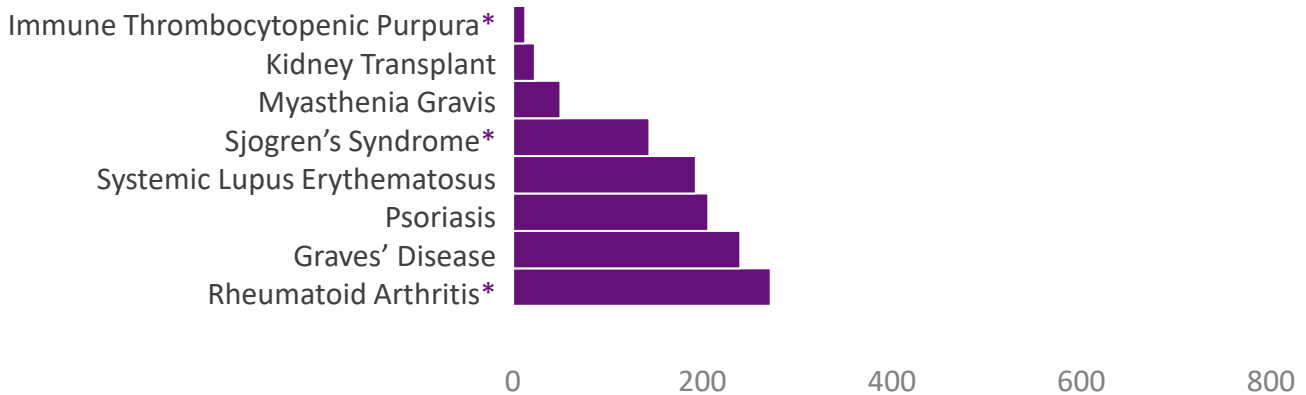
T-Cell Dependent Antibody Response (TDAR) for KLH antigen challenge



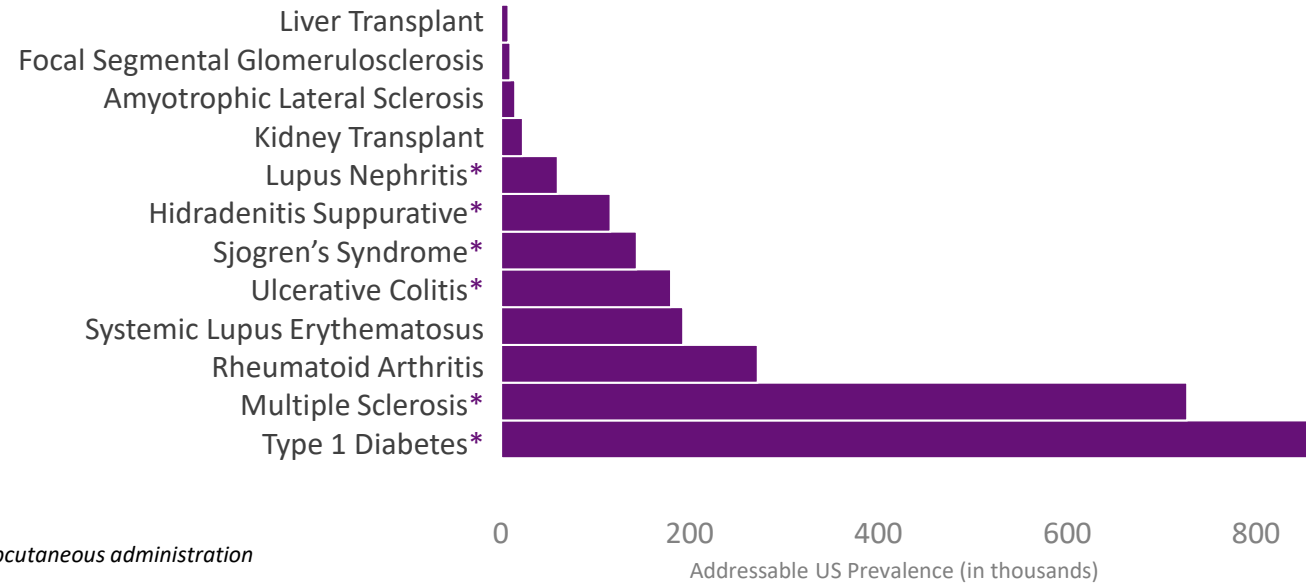
KLH = keyhole limpet hemocyanin

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

Indications with Published Data[1]



Indications with Pending Data & Trials Ongoing[1]



Indication Selection Criteria

- **Robust Data or proof-of-concept supporting mechanism**
- **Differentiation vs. Competitors**
- **Commercial Attractiveness**

**Indications evaluated with subcutaneous administration*

1) With the CD40 mechanism

Sources: 2019 numbers: https://unos.org/data/transplant-trends/; Hunter et al. Prevalence of rheumatoid arthritis in the United States adult population in healthcare claims databases, 2004-2014; Rheumatol Int. 2017 Sep;37(9):1551-1557; Overall Prevalence: Maciel et al, Arthritis Care Res (Hoboken) 2017; Qin et al, Ann Rheum Dis 2015; UpToDate; Baldini et al. Prevalence of Severe Extra-Glandular Manifestations in a Large Cohort of Patients with Primary Sjögren's Syndrome; 2012 ACR/ARHP Annual Meeting, ABSTRACT NUMBER: 2185; Wallin et al. The prevalence of MS in the United States A population-based estimate using health claims data, Neurology, March 5, 2019; Somers et al.; Prevalence of Systemic Lupus Erythematosus in the United States: Preliminary Estimates from a Meta-Analysis of the Centers for Disease Control and Prevention Lupus Registries; 2019 ACR/ARP Annual Meeting ABSTRACT NUMBER: 2886; Garg et al. JAMA Dermatol. 2017;153(8):760-764. doi:10.1001/jamadermatol.2017.0201 Sex- and Age-Adjusted Population Analysis of Prevalence Estimates for Hidradenitis Suppurativa in the United States; MayoClinic.org; Yale J Biol Med. 2013 Jun; 86(2): 255–260. N Engl J Med 2016;375:2570-81; https://www.diabetesresearch.org/diabetes-statistics; Nephcure.org; Kitiyakara C, Eggers P, Kopp JB. Twenty-one-year trend in ESRD due to focal segmental glomerulosclerosis in the United States. Am J Kidney Dis. 2004 Nov;44(5):815-25; Rachakonda et al. J Am Acad Dermatol . 2014 Mar;70(3):512-6. doi: 10.1016/j.jaad.2013.11.013. Epub 2014 Jan 2. Psoriasis prevalence among adults in the United States; Yeung et al. Psoriasis severity and the prevalence of major medical co-morbidities: a population-based study; JAMA Dermatol. 2013 Oct 1; 149(10): 1173–1179; Hoover etal. Kidney Int. 2016 Sep; 90(3): 487–492. Insights into the Epidemiology and Management of Lupus Nephritis from the U.S. Rheumatologist's Perspective.

Building Value at Kiniksa

2021 Corporate Priorities

ARCALYST	*Commercial launch in recurrent pericarditis (April 2021)*
Mavrilimumab	*COVID-19 data (April 2021) and next steps for program (expected Q2 2021)*
Vixarelimab	*Phase 2b study in PN evaluating a range of once-monthly dose regimens*
KPL-404	*Final Phase 1 data (May 2021); plan to initiate Phase 2 proof-of-concept trial in rheumatoid arthritis in 2H 2021*

Q1 2021 ~$264M Cash Reserves Expected to Fund Current Operating Plan into 2023[1]

1) As used herein the term, "Cash Reserves" means our cash, cash equivalents and short-term investments (unaudited) as of March 31, 2021; COVID-19 = Severe COVID-19 pneumonia and hyperinflammation; PN = prurigo nodularis

KINIKSA

Every Second Counts!™

Appendix

Every Second Counts!™

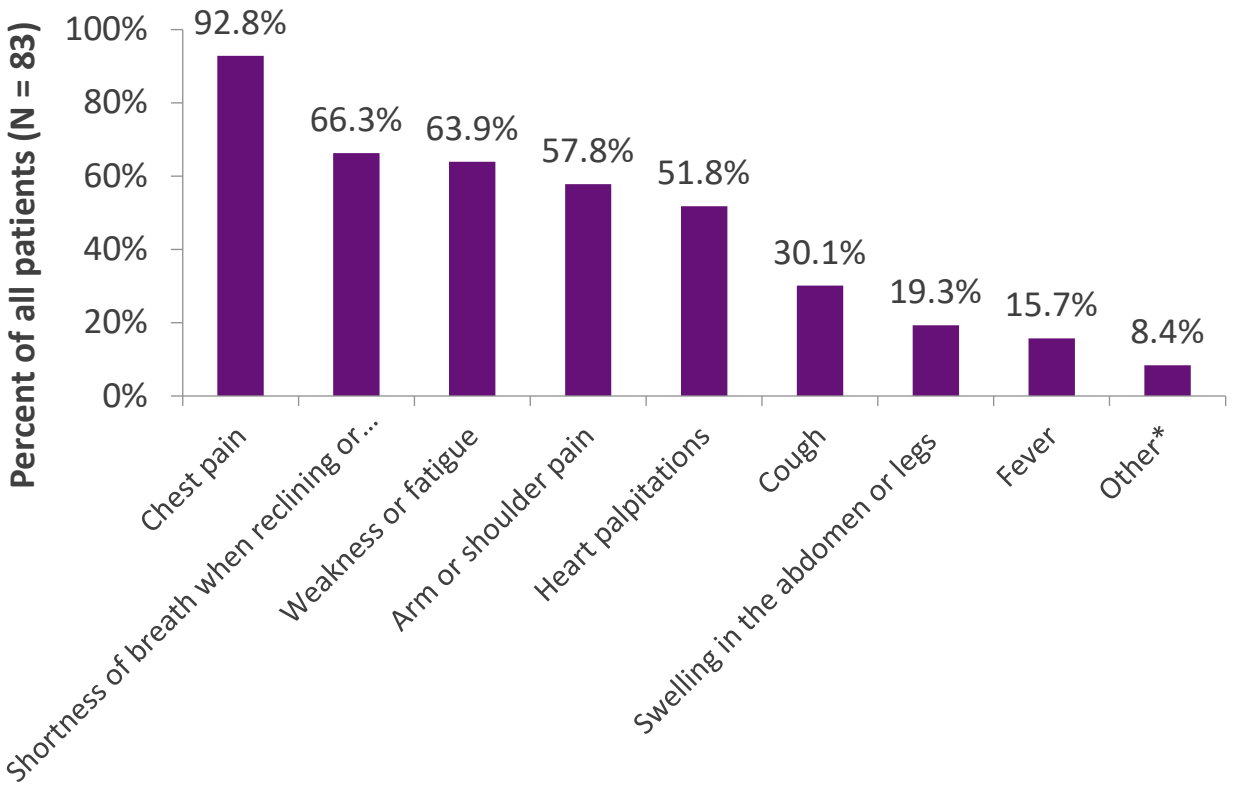
Appendix – ARCALYST (rilonacept)

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 health[3]
- 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).

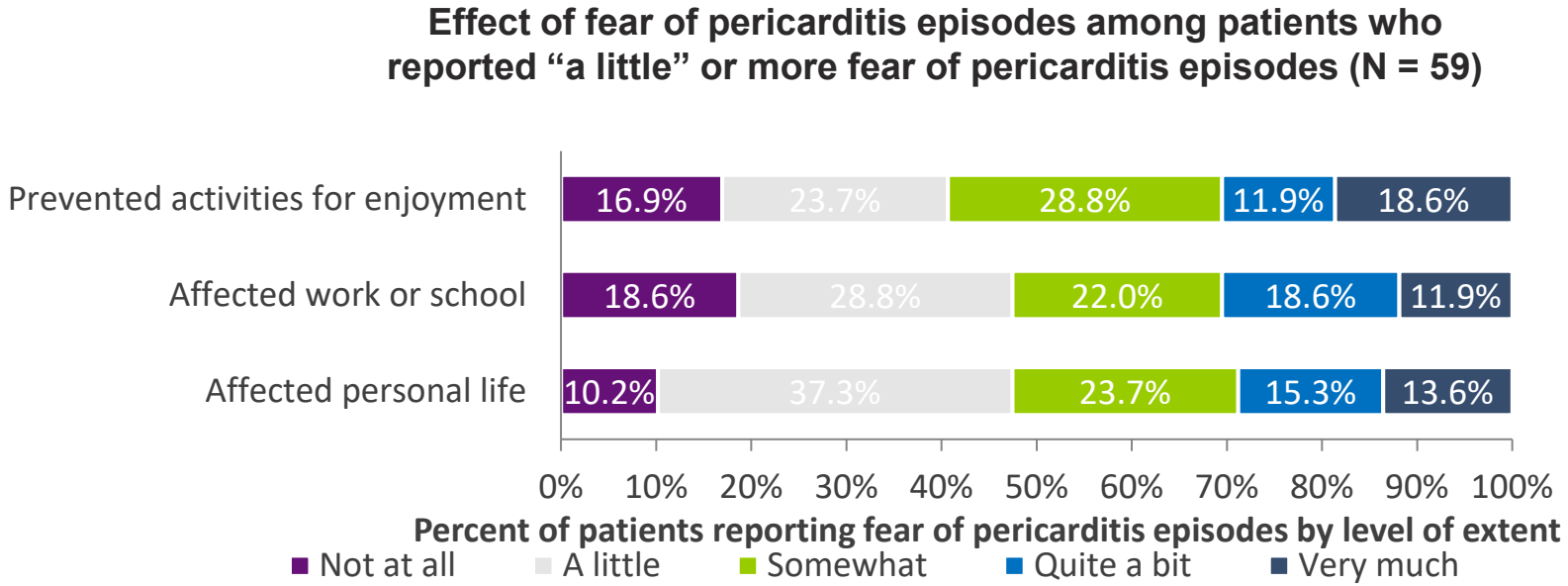
1. Results from an IRB-approved cross-sectional survey study of 80 respondents with a confirmed diagnosis of RP

1) Patient ATU Research 2019 W1; 2) Patient & Physician Emotive Journey Qual 2019 Q2; 3) Ph2 Pilot study; 4) IQVIA PharMetrics Plus Claims Analyses; 5) Putnam Patient Journey Research 2018 Q1; 6) External Publications (Cremer, P "Complicated Pericarditis", ESC Guidelines), 7) HCP ATU Research 2019 W1; 8) ER ATU Research 2019 W1; 9) LeWinter (2020 ISPOR Abstract)

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

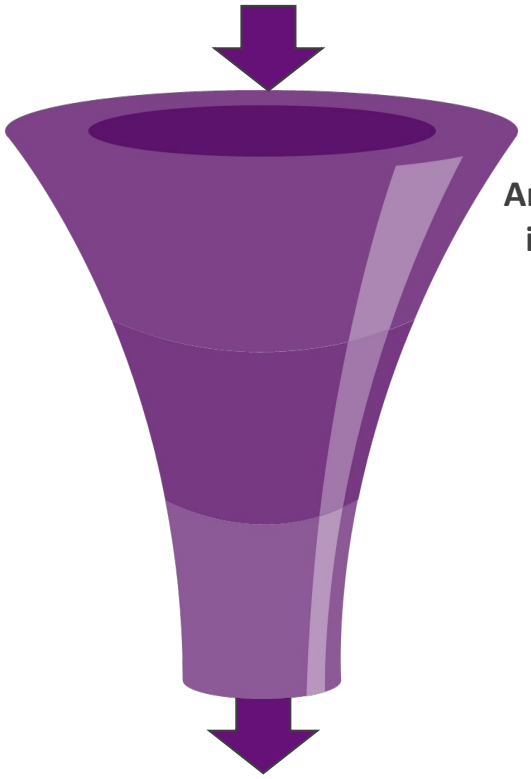
- Between flares, up to 95% of patients report some level of **fear of recurrence of pericarditis episodes**"[9]
- After acute pain resolves, **residual pain** and other effects can last weeks to months[1,2]
- Testimonials reveal **devastating impact on QoL** (anxiety, loss of sleep, lifestyle change,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



1) Patient ATU Research 2019 W1; 2) Patient & Physician Emotive Journey Qual 2019 Q2; 3) Ph2 Pilot study; 4) IQVIA PharMetrics Plus Claims Analyses; 5) Putnam Patient Journey Research 2018 Q1; 6) External Publications (Cremer, P "Complicated Pericarditis", ESC Guidelines), 7) HCP ATU Research 2019 W1; 8) ER ATU Research 2019 W1; 9) LeWinter (2020 ISPOR Abstract)

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

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



Annual pericarditis incidence ~117K

1st recurrence ~26K

Repeat Recurrences

- **~7K new patients with repeat recurrences annually**
- **~14K total patients with repeat recurrences annually at any point**

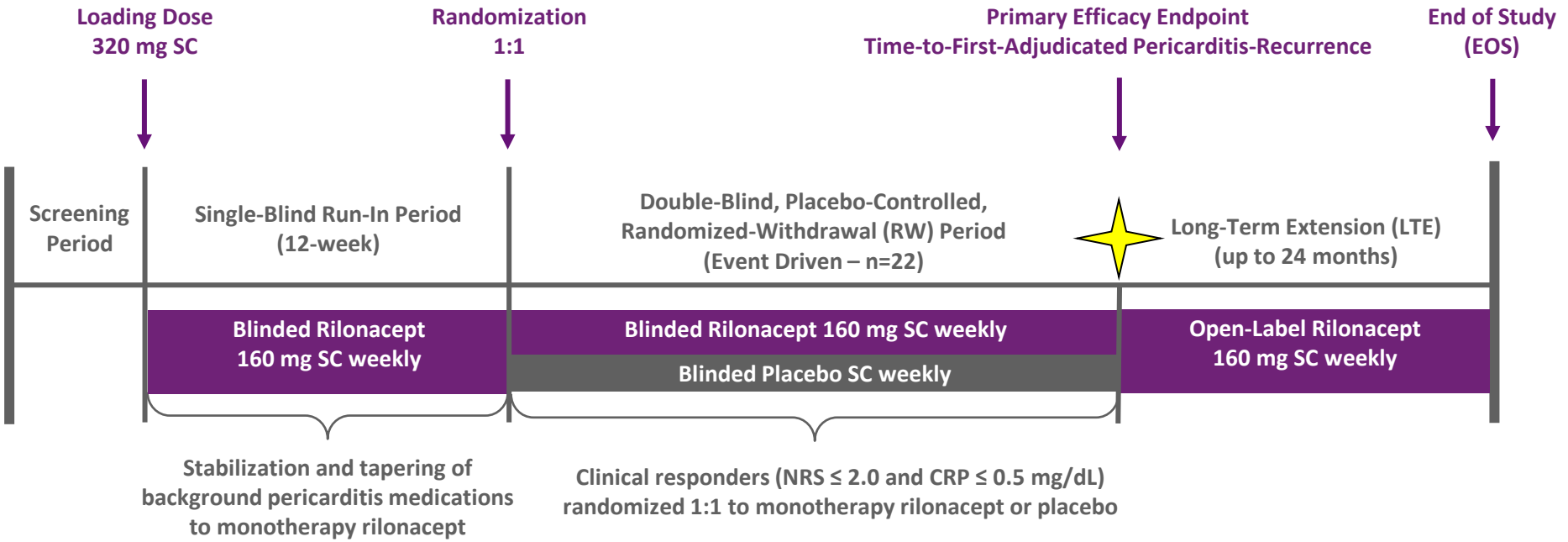
Year	-4	-3	-2	-1	0
Incident case of acute pericarditis (1st episode)[1]	117K	117K	117K	117K	117K
Incidence of initial RP patients (1st recurrence)[2]	26K	26K	26K	26K	26K
Ongoing recurrent from year-1[3]					7K
Ongoing recurrent from year-2[3]				7K	3.5K
Ongoing recurrent from year-3[3]			7K	3.5K	1.8K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

Design of Pivotal Phase 3 Trial of Rilonacept in Recurrent Pericarditis

RHAPSODY



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

CRP = C-reactive protein; NRS = Numerical Rating Scale; NSAIDs = nonsteroidal anti-inflammatory drugs; CEC = Clinical Endpoint Committee

Klein A et al. Am Heart J. 2020 Oct;228:81-90

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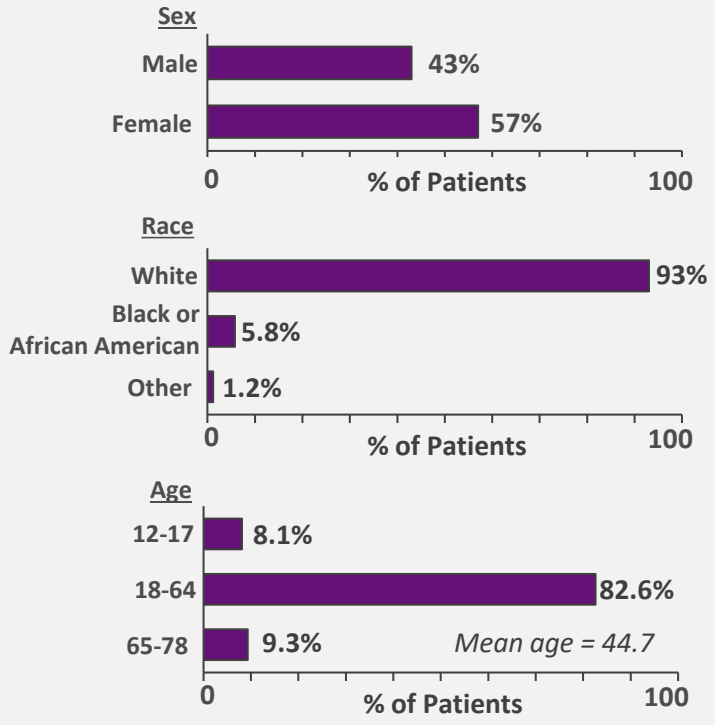
Baseline Demographics and Clinical Characteristics

Pivotal Phase 3 Rilonacept Data

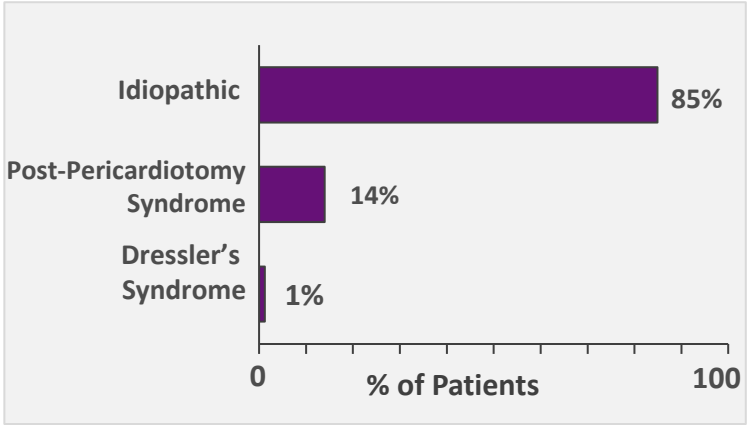
RHAPSODY

Baseline Demographics (n=86)

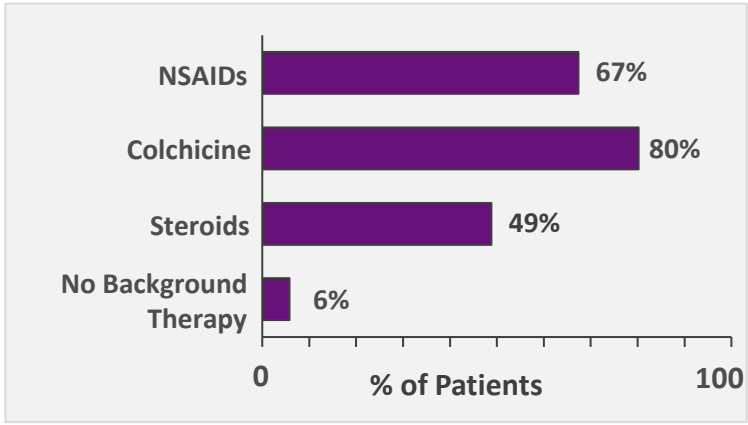


Total Number of Episodes Including Index and Qualifying Episodes	Run-in Period (n=86)
Mean	4.7

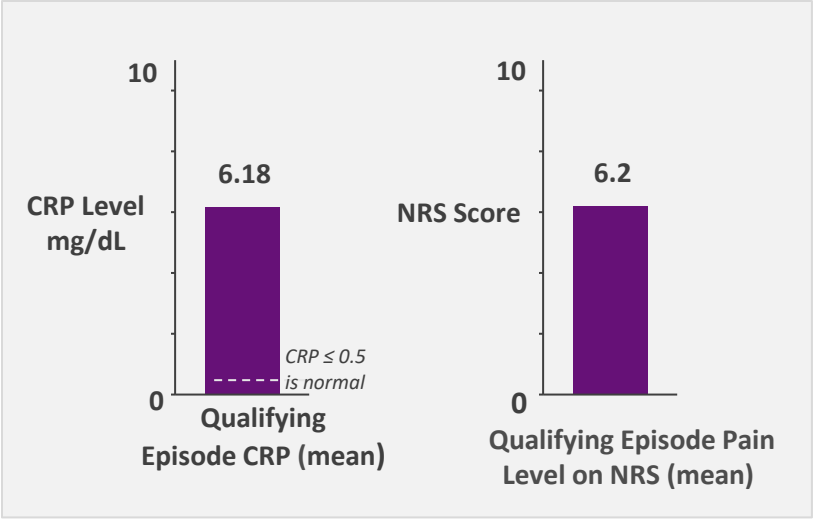
Prior Pericarditis History at Baseline (n=86)



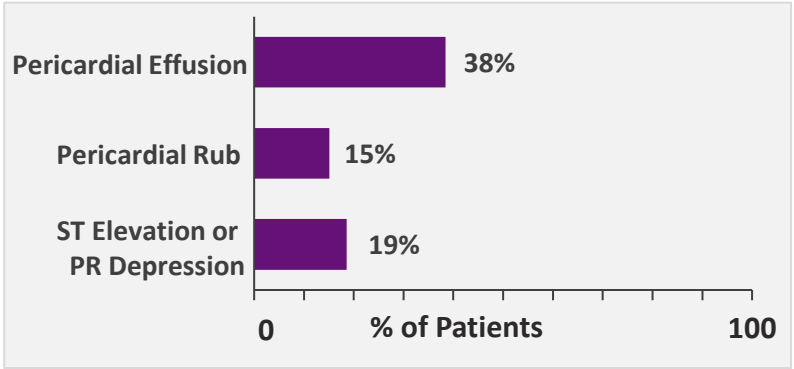
SoC Received at Qualifying Episode (n=86)



Qualifying Episode CRP & NRS (n=86)



Pericarditis Manifestations at Qualifying Episode (n=86)



CRP = C-reactive protein; NRS = Numerical Rating Scale; SoC = Standard of Care; NSAIDs = nonsteroidal anti-inflammatory drugs;

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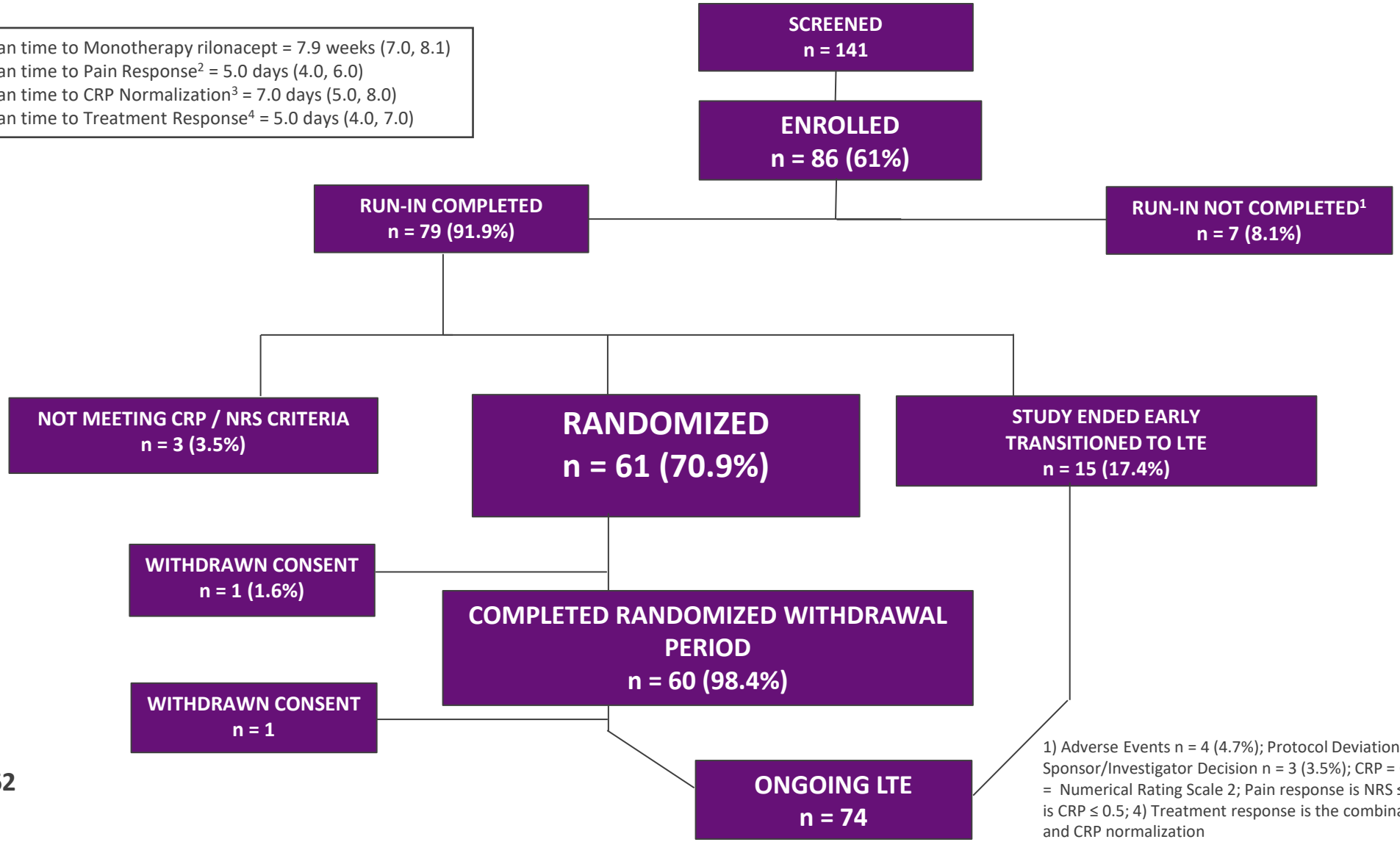
Subject Disposition

Pivotal Phase 3 Rilonacept Data

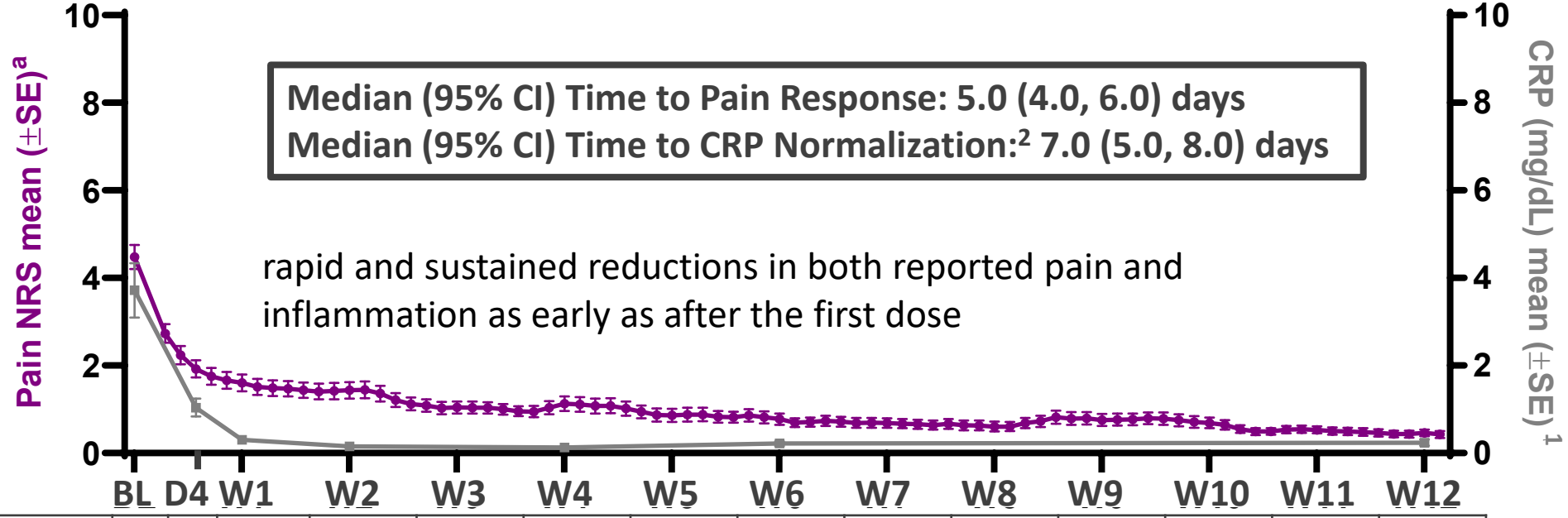
Median time to Monotherapy rilonacept = 7.9 weeks (7.0, 8.1)
Median time to Pain Response[2] = 5.0 days (4.0, 6.0)
Median time to CRP Normalization[3] = 7.0 days (5.0, 8.0)
Median time to Treatment Response[4] = 5.0 days (4.0, 7.0)



1) Adverse Events n = 4 (4.7%); Protocol Deviation /Withdrawn Consent / Sponsor/Investigator Decision n = 3 (3.5%); CRP = C-reactive protein; NRS = Numerical Rating Scale 2; Pain response is NRS ≤ 2; 3) CRP normalization is CRP ≤ 0.5; 4) Treatment response is the combination of pain response and CRP normalization

Rilonacept Initiation Resulted in [Rapid and Sustained Reductions in Reported Pain and Inflammation]

Pivotal Phase 3 Rilonacept Data



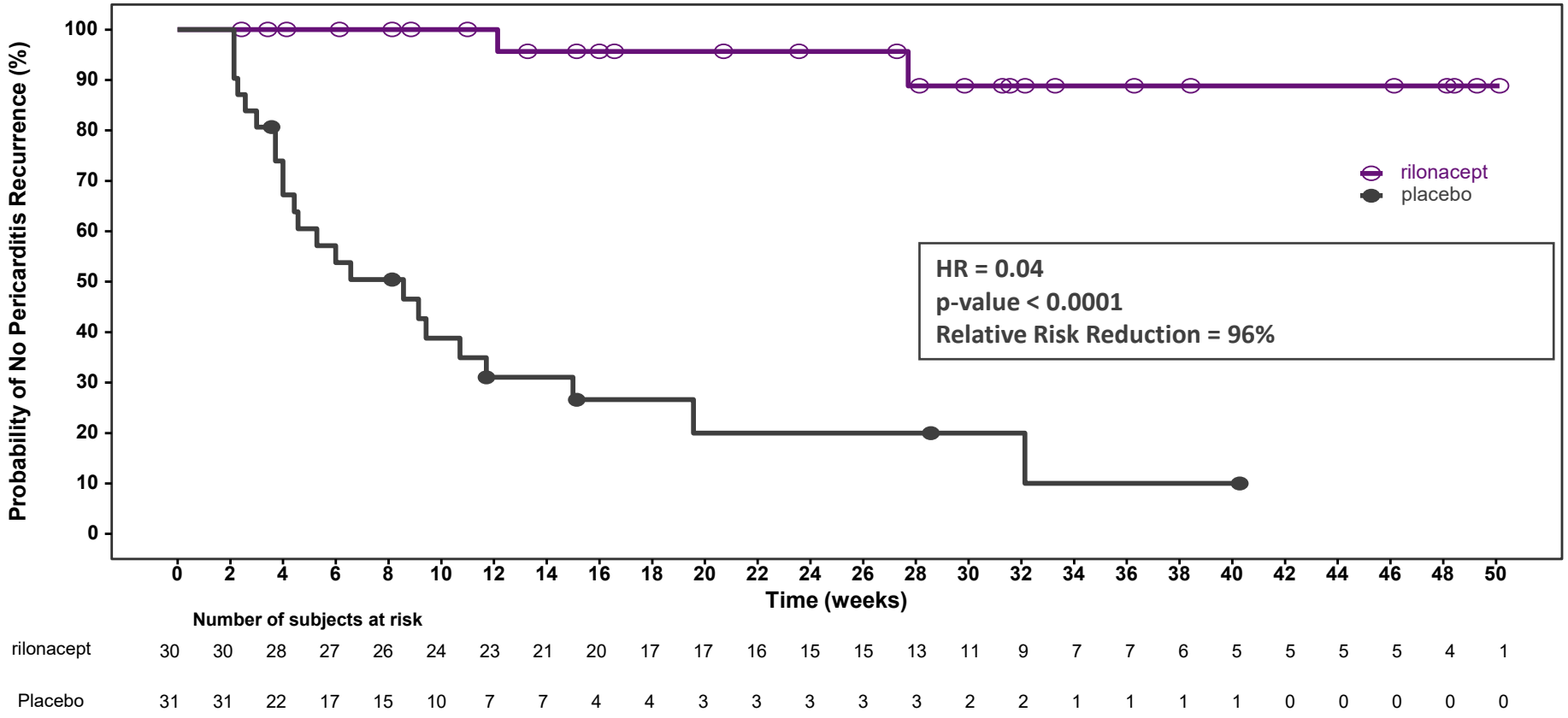
		BL	D4	W1	W2	W3	W4	W5	W6	W7	W8	W9	W10	W11	W12
CRP	# of Patients	85	79	82	81		79		82						81
	CRP Mean	3.7	1.0	0.30	0.15		0.13		0.22						0.24
Pain NRS	# of Patients	84		84	84	83	83	84	83	83	82	81	82	82	78
	Pain Mean	4.5		1.60	1.43	1.04	1.13	0.86	0.78	0.68	0.61	0.76	0.69	0.53	0.46

Pain NRS and CRP rapidly decreased after the first rilonacept dose
All patients on corticosteroids successfully tapered and transitioned to monotherapy rilonacept during the run-in

1) Mean pain NRS and CRP at BL differs from those at qualifying episode: investigator could temporarily manage pericarditis episode with SOC prior to enrollment; 2) CRP ≤0.5 mg/dL

Rilonacept Resulted in a 96% Reduction in Risk of Pericarditis Recurrence

Pivotal Phase 3 Rilonacept Data



	Number of Patients with Recurrence[1] n (%)	Number of Weeks to Recurrence[1] Median (95% CI)
Rilonacept	2 (6.7)	NE (NE, NE)
Placebo	23 (74.2)	8.6 (4.0, 11.7)

Annualized incidence of pericarditis recurrence decreased from 4.42 episodes per year prior to the study to 0.15 episodes per year while on rilonacept treatment.

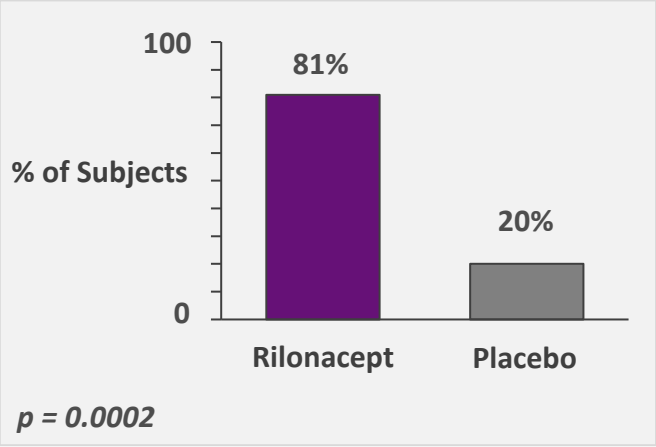
1) Mean (median, range); NE = Not Estimable; HR = hazard ratio
Klein, et. al. New England Journal of Medicine. Nov 2020

Rilonacept Resulted in 98% of Trial Days of No/Minimal Pain

Pivotal Phase 3 Rilonacept Data

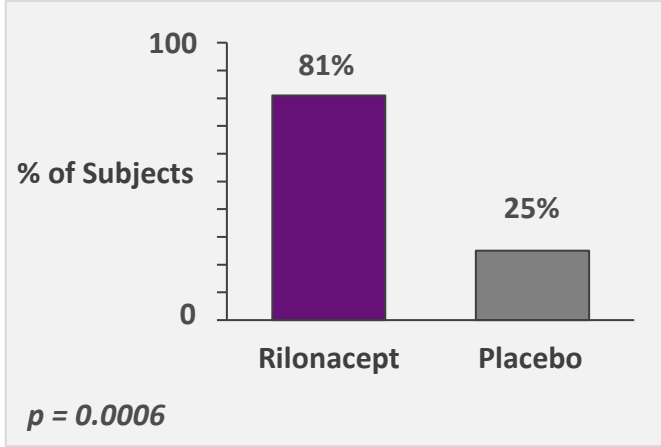
RHAPSODY

Proportion of Subjects Who Maintained Clinical Response [1]



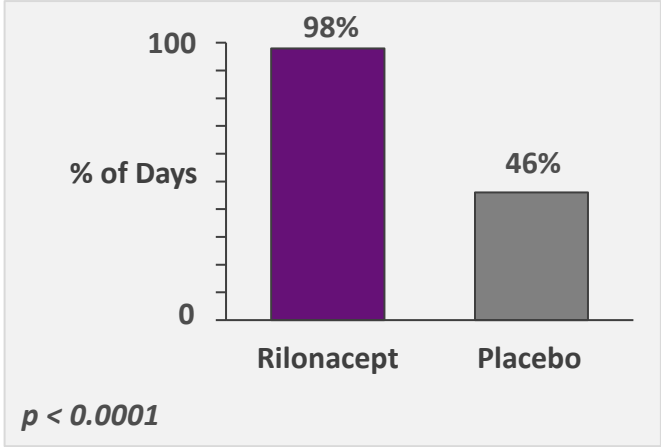
Data at Weeks 8 and 24 were consistent and statistically significant
(Week 8, p < 0.0001; Week 24, p=0.0022)

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.

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Rilonacept Was Well-Tolerated in Clinical Trials

Pivotal Phase 3 Rilonacept Data

RHAPSODY

	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
Gastrooesophageal 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

1) Subjects with multiple events are counted once in the same category; 2) A Treatment-emergent adverse events (TEAEs) are defined as AEs that start or increase in severity on or after the date of first dose and before 6 weeks after the last dose of study drug; 3) Each subject has only been represented with the maximum severity; 4) Related or possibly related or missing, as assessed by the investigator.; 5) Includes malignancy excluding basal cell carcinoma of the skin

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Summary of Adverse Events

Pivotal Phase 3 Rilonacept Data

RHAPSODY

	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
Gastrooesophageal 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

1) Subjects with multiple events are counted once in the same category; 2) A Treatment-emergent adverse events (TEAEs) are defined as AEs that start or increase in severity on or after the date of first dose and before 6 weeks after the last dose of study drug; 3) Each subject has only been represented with the maximum severity; 4) Related or possibly related or missing, as assessed by the investigator.; 5) Includes malignancy excluding basal cell carcinoma of the skin

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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)

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Summary of Adverse Events

Pivotal Phase 3 Rilonacept Data

Category [1]	Run-In Period	Randomized Withdrawal Period	
	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
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

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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 (%)
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]	Rilonacept (N=86) n (%)	Rilonacept Including Bailout Rilonacept (N=30) n (%)	Placebo Only Before Bailout Rilonacept (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

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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

1) Subjects with multiple events are counted once in the same category; 2) A Treatment-emergent adverse events (TEAEs) are defined as AEs that start or increase in severity on or after the date of first dose and before 6 weeks after the last dose of study drug; 3) Each subject has only been represented with the maximum severity; 4) Related or possibly related or missing, as assessed by the investigator.; 5) Includes malignancy excluding basal cell carcinoma of the skin

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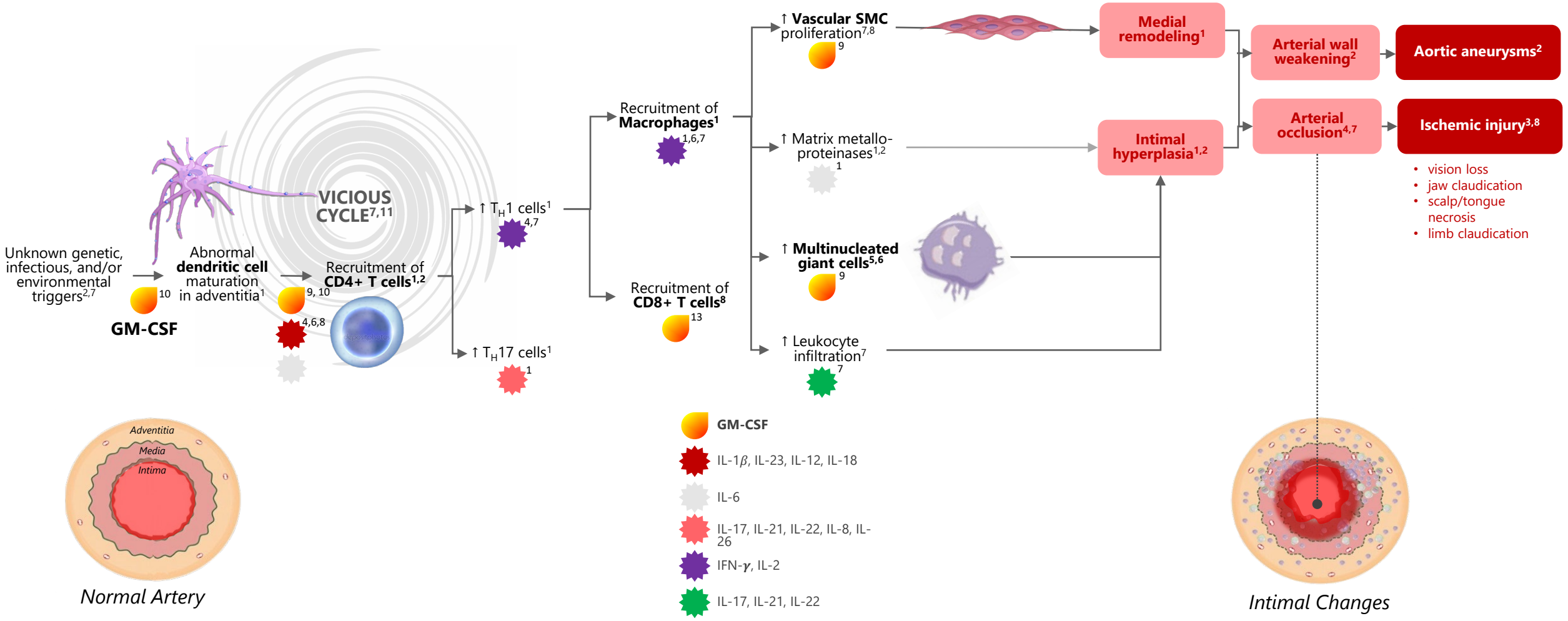
Every Second Counts!™

Appendix – Mavrilimumab

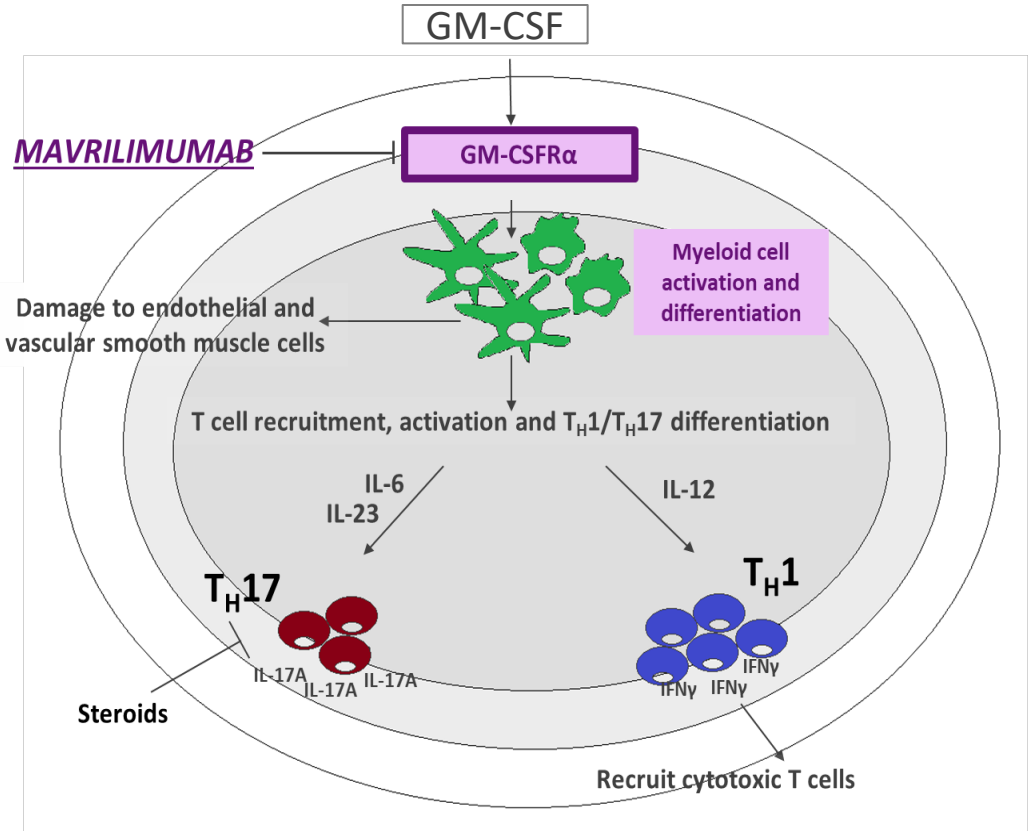
Central Role of GM-CSF in Pathophysiology of Giant Cell Arteritis



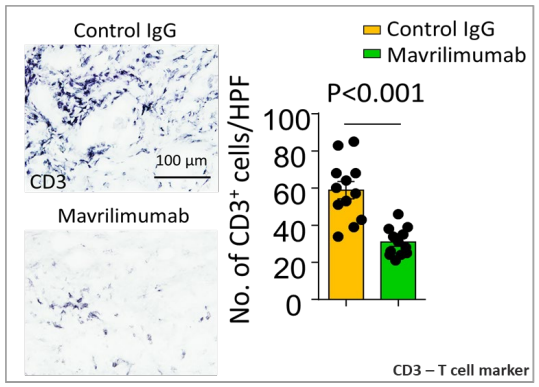
1. Al-Mousawi AZ, et al. Ophthalmol Ther 2019;8:177-193. 2. Boura P, et al. Updates in the Diagnosis and Treatment of Vasculitis. Chapter 4 2013; http://dx.doi.org/10.5772/55222. 3. Cho HJ, et al. Disease-a-Month 2017;63:88-91. 4. Ly KH, et al. Autoimm Review 2010;9:635-645. 5. Lazarewicz K, et al. BMJ 2019;365l1964 doi: 10.1136/bmj.l1964. 6. O'Neill L, et al. Rheumatol 2016;55:1921-1931. 7. Planas-Rigol E, et al. J Vasc 2016;1:2:DOI: 10.4172/2471-9544.100103. 8. Samson M, et al. Autoimmun Rev 2017;16:833-844. 9. Cid MC, et al. GM-CSF Pathway Signature Identified in Temporal Artery Biopsies of Patients With Giant Cell Arteritis. 2019 EULAR;12-15 June. Madrid, Spain. 10. Cid M, et al. Ann Rheumatol 2019; DOI: 10.1136/annrheumdis-2019-eular.2694. 11. Pupim L, et al. Rheumatology 2019;58:https://doi.org/10.1093/rheumatology/kez063.060. 12. Herndler-Brandstetter D, et al. Cell Research 2014;24:1379-1380. 13. Becher B, et al. Immunity 2016;45:963-973.

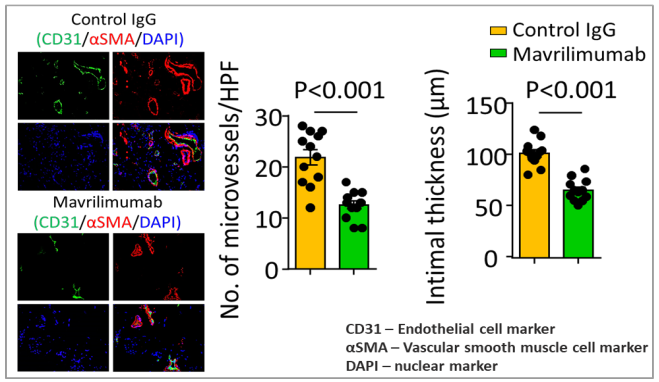
Preclinical Data Support the Mechanistic Rationale of Targeting GM-CSF in GCA

GM-CSF and its receptor, GM-CSFRα, shown to be elevated in GCA biopsies compared to control[1]

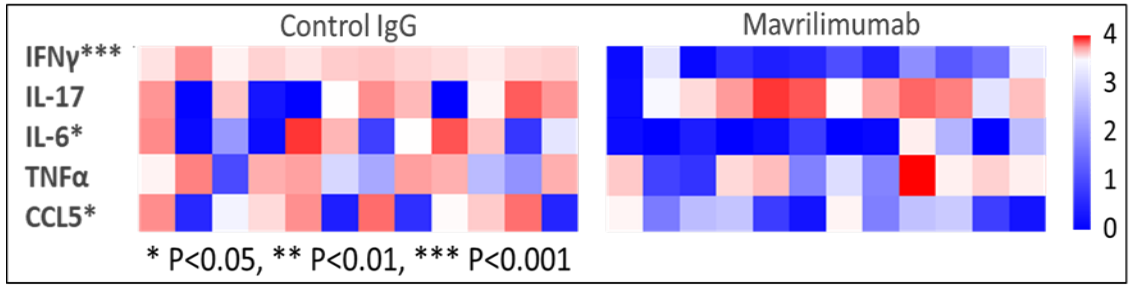


Mavrilimumab reduced arterial inflammation compared to control in an *in vivo* model of vasculitis[2]





Mavrilimumab suppressed expression of inflammatory genes in artery

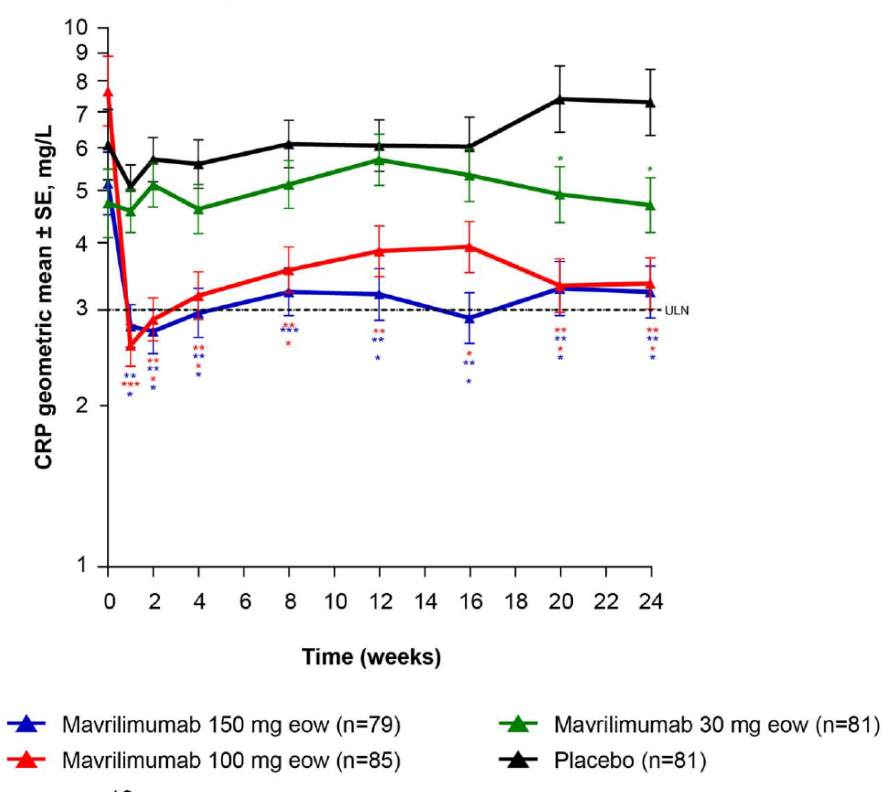


1) Poster presentation at European Congress of Rheumatology 2019 (EULAR): *GM-CSF Pathway Signature Identified in Temporal Artery Biopsies of Patients With Giant Cell Arteritis* Maria C. Cid, Rohan Gandhi, Marc Corbera-Bellalta, Nekane Terrades-Garcia, Sujatha Muralidharan, John F. Paolini; 2) Presentation at 2019 American College of Rheumatology (ACR): *GM-CSF is a Pro-Inflammatory Cytokine in Experimental Vasculitis of Medium and Large Arteries* Ryu Watanabe, Hui Zhang, Toshihisa Maeda, Mitsuhiro Akiyama, Rohan Gandhi, John F. Paolini, Gerald J. Berry, Cornelia M. Weyand

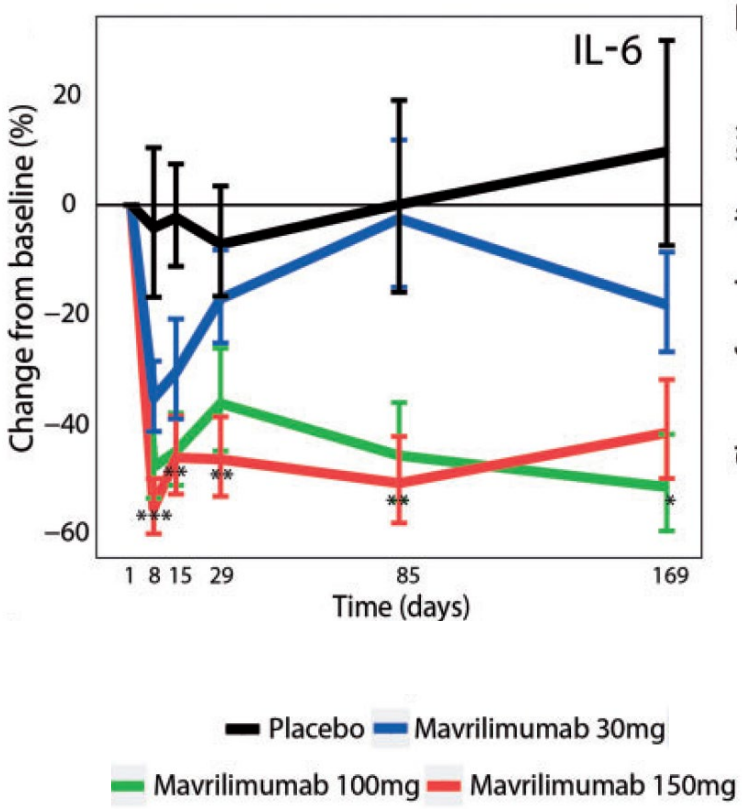
In Phase 2b Rheumatoid Arthritis Study Mavrilimumab Reduced CRP and IL-6, Key Markers of Disease Activity for Giant Cell Arteritis

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

C-reactive Protein (CRP)[1]



Interleukin-6 (IL-6)[2]



1) Burmester GR, McInnes IB, Kremer, J et al. Ann Rheum Dis 2017; 76, 1020-1030; 2) Xiang Guo et al. Rheumatology, 2017

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

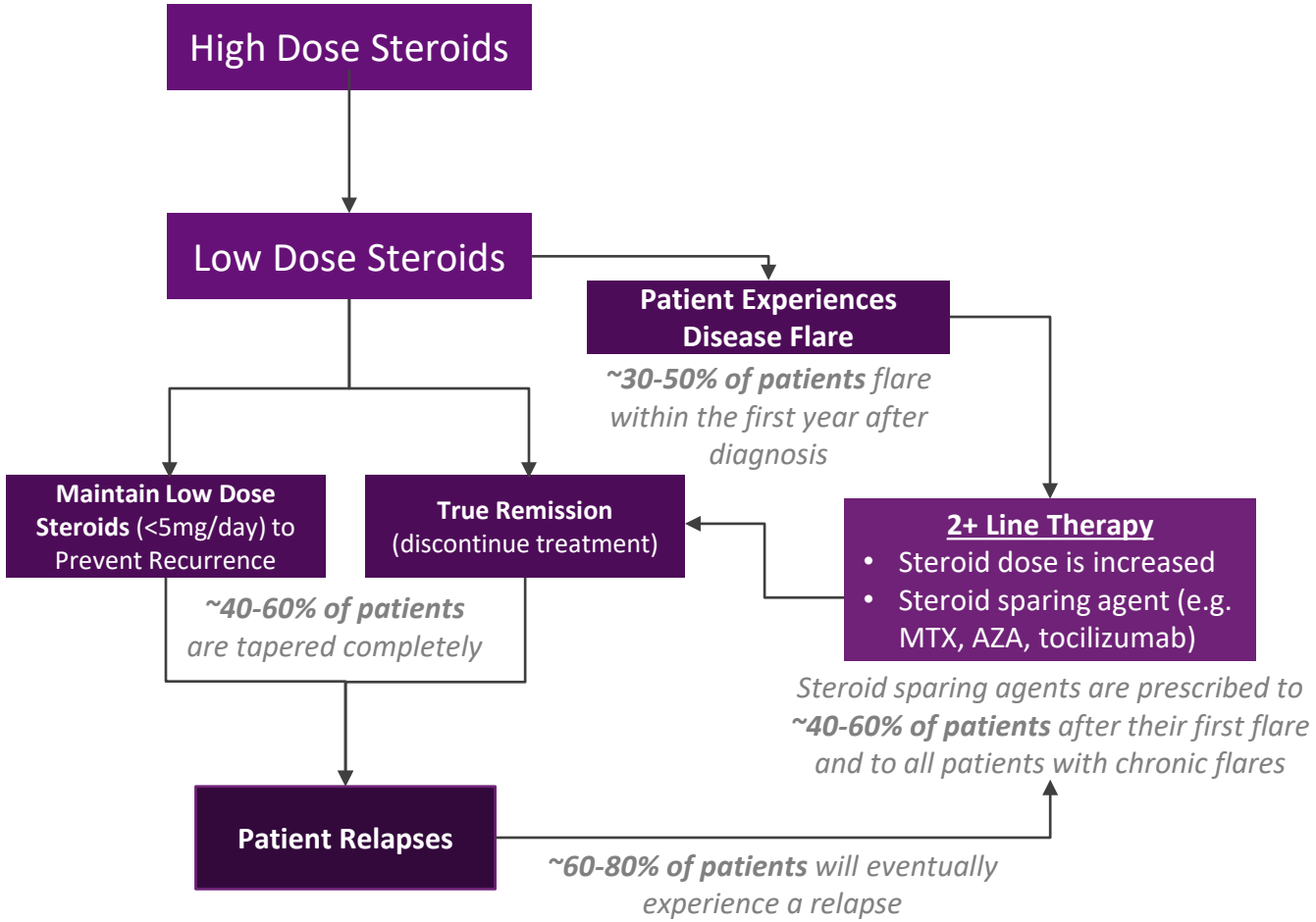
"There is an urgency of treatment with these patients, compared to other conditions it's serious."
– Rheumatologist

"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

Sources: Medcape; Trinity Partners primary market research

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

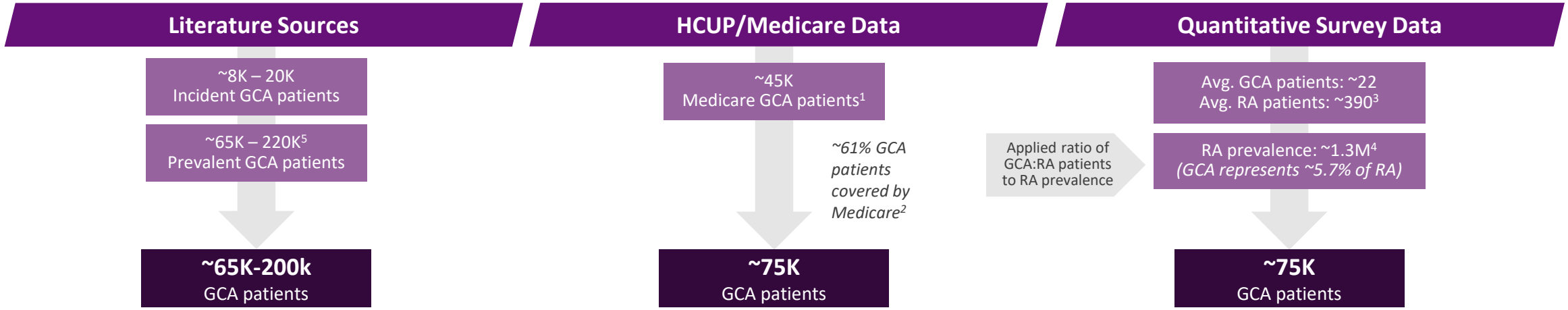


Treatment Approach:

- 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

Source: Trinity Partners Primary Market Research (n=10 Rheumatologists)

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



Key Considerations to Market Sizing Approach

Wide Range

High geographic variation

GCA prevalence estimates vary across geographies with Northern European populations showing the highest rates and Asian populations the lowest

Weighted by US demographics

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)

Under-Representation

Represents Actively Managed Patients

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

Under-Representation

Represents patients actively seen by a Rheum

Rheumatologists reported the number of GCA patients they manage. Patients who are not actively managed would likely be excluded from these estimates

Sources: 1.) Medicare analysis conducted 1/2018 2.) Trinity Partner's Quantitative Primary Market Research (n=74) 3.) Trinity Partner's Quantitative Primary Market Research (n=196) (includes data from screener portion of survey) 4.)Prevalence of rheumatoid arthritis in the United States adult population in healthcare claims databases, 2004-2014, Hunter et al. 2017, 5.) Crowson et. al, 2017

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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

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)
- While the study was not powered for disease cohorts, there was a consistent trend of efficacy across the new onset and relapsing/refractory cohorts
- **New Onset Cohort**
  - There was a 71% lower risk of flare in mavrilimumab recipients compared to placebo recipients (Hazard Ratio = 0.29, p=0.0873)
  - The sustained remission rate at Week 26 was 28.9 percentage points higher in mavrilimumab recipients (91.3%) compared to placebo recipients (62.3%) (p=0.0727)
- **Relapsing/Refractory Cohort**
  - There was a 57% lower risk of flare in mavrilimumab recipients compared to placebo recipients (Hazard Ratio = 0.43, p=0.1231)
  - The sustained remission rate at Week 26 was 30.6 percentage points higher in mavrilimumab recipients (72.2%) compared to placebo recipients (41.7%) (p=0.0668)
- 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 is ongoing, and additional analyses of this Phase 2 trial are planned. Next steps for the development program in GCA will be further informed by anticipated discussions with the U.S. Food and Drug Administration (FDA)

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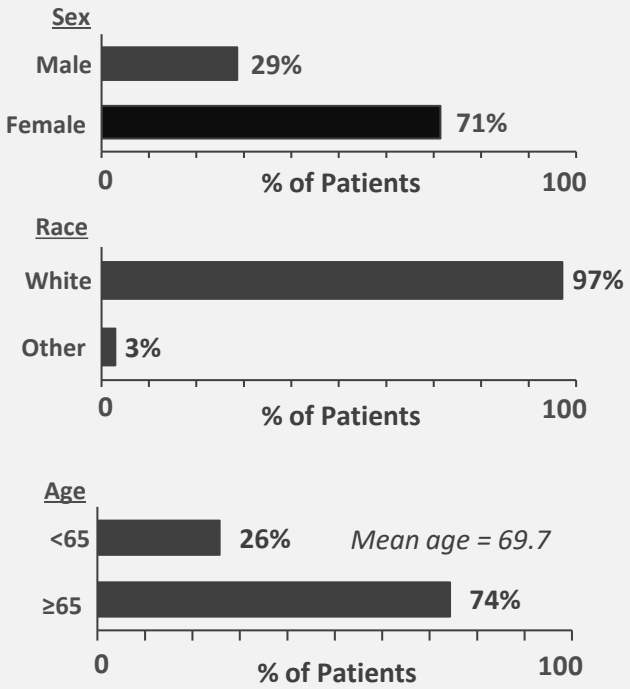
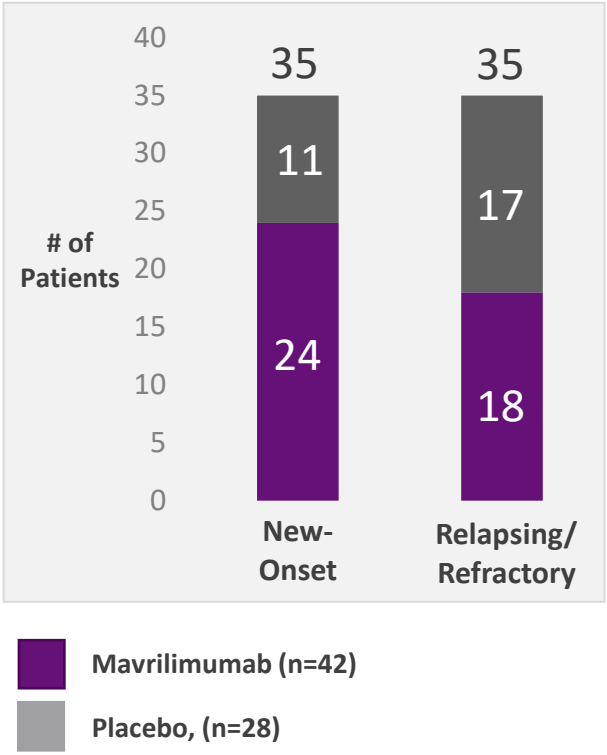
Baseline Demographics and Clinical Characteristics

Mavrilimumab Phase 2 Giant Cell Arteritis Data

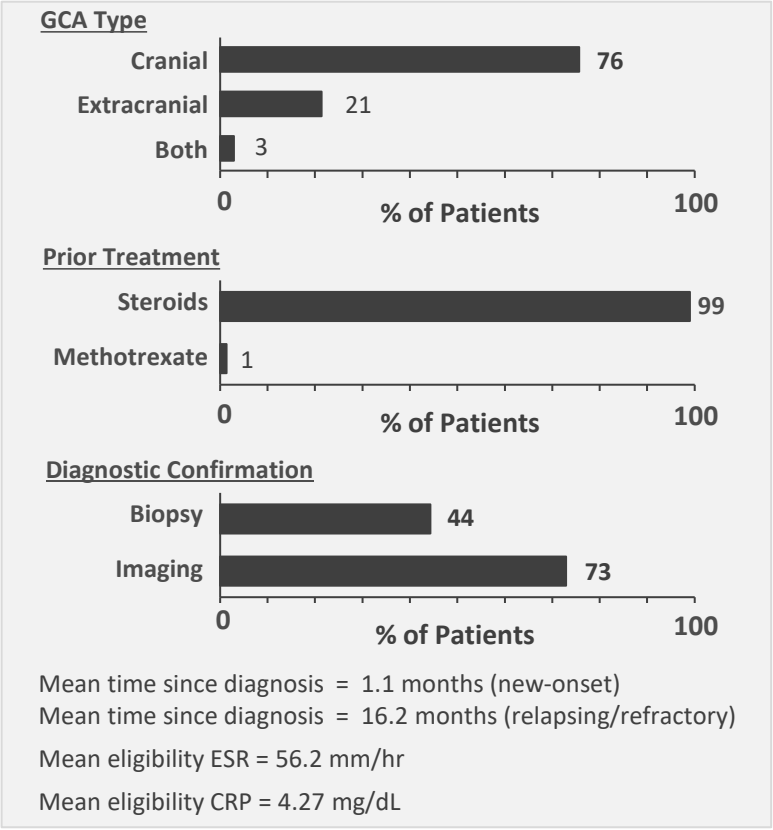
Baseline Demographics (n=70)



Randomization Strata



Baseline Disease Characteristics (n=70)



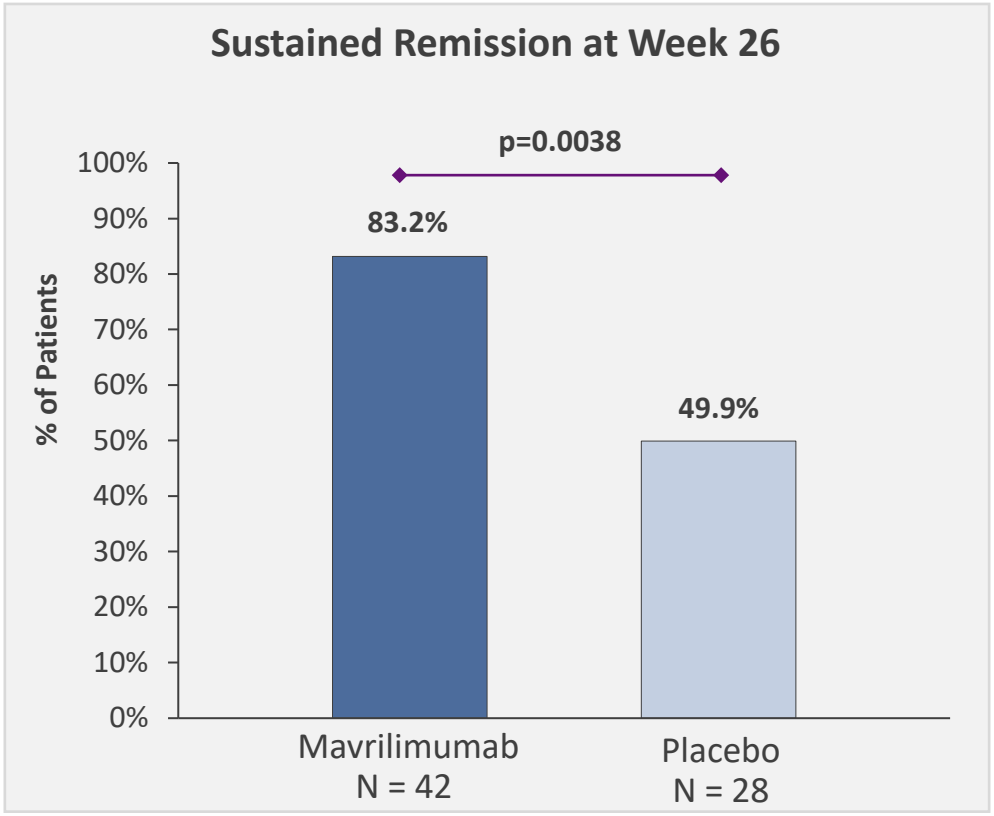
Mean time since diagnosis = 1.1 months (new-onset)
Mean time since diagnosis = 16.2 months (relapsing/refractory)

Mean eligibility ESR = 56.2 mm/hr

Mean eligibility CRP = 4.27 mg/dL

Secondary Efficacy Endpoint: Sustained Remission at Week 26

Mavrilimumab Phase 2 Giant Cell Arteritis Data



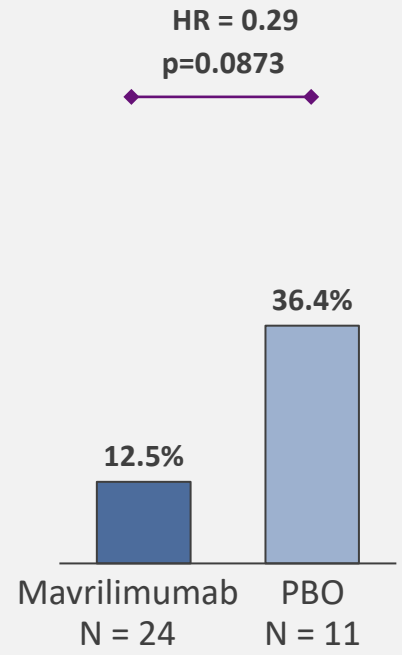
The sustained remission rate at Week 26 was 33.3 percentage points higher in mavrilimumab recipients (83.2%) compared to placebo recipients (49.9%) (p=0.0038).

Consistent Trend of Efficacy Across the New Onset and Relapsing/Refractory Cohorts

Mavrilimumab Phase 2 Giant Cell Arteritis Data

New-Onset GCA

Patients With Flare by Week 26



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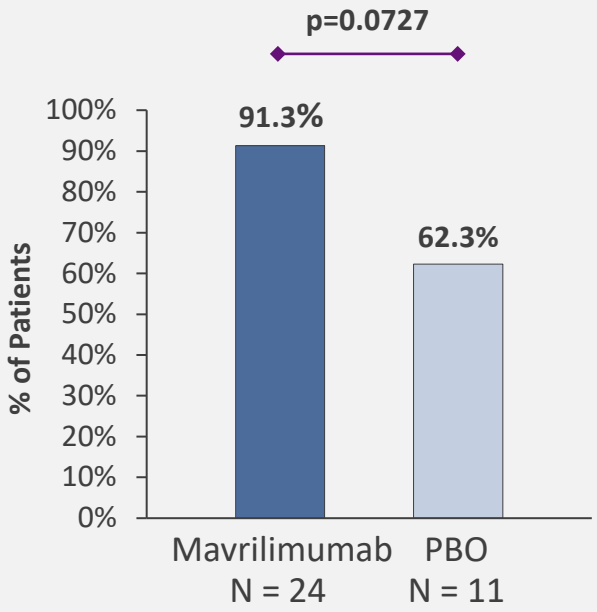
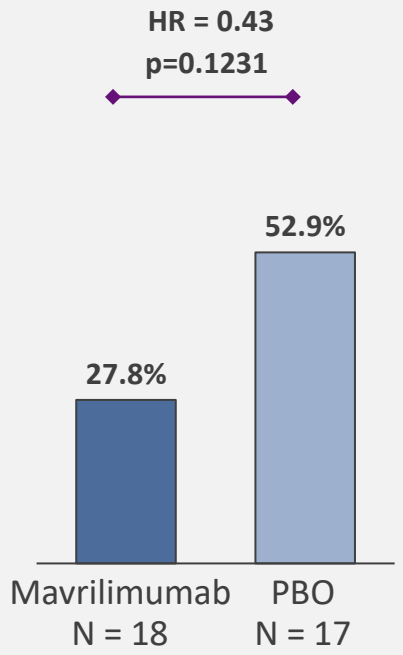
Sustained Remission at Week 26



The sustained remission rate at Week 26 was 28.9 percentage points higher in mavrilimumab recipients (91.3%) compared to placebo recipients (62.3%) (p=0.0727).

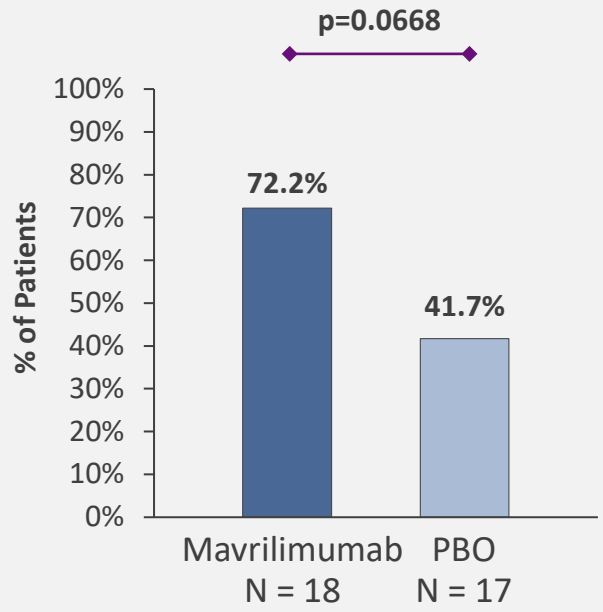
Relapsing/Refractory GCA

Patients With Flare by Week 26



There was a 57% lower risk of flare in mavrilimumab recipients compared to placebo recipients (Hazard Ratio = 0.43, p=0.1231).

Sustained Remission at Week 26



The sustained remission rate at Week 26 was 30.6 percentage points higher in mavrilimumab recipients (72.2%) compared to placebo recipients (41.7%) (p=0.0668).

*Nominal p values

Time to Flare and Sustained Remission at Week 26

Mavrilimumab Phase 2 Giant Cell Arteritis Data

Time to Flare by Week 26 and Sustained Remission at Week 26 - Total mITT Population	Mavrilimumab 150 mg (N=42)	Placebo (N=28)
Number of Subjects with Flare, n (%)	8 (19.0)	13 (46.4)
Primary Efficacy Endpoint: Time to Flare (weeks) by Week 26 [1]		
Median, 95% CI	NE (NE, NE)	25.1 (16.0, NE)
Hazard Ratio (Mavrilimumab vs Placebo), 95% CI [2]	0.38 (0.15, 0.92)	
P-value [3]	0.0263	
Secondary Efficacy Endpoint: Sustained Remission at Week 26 (%), 95% CI [4]	83.2 (67.9, 91.6)	49.9 (29.6, 67.3)
Difference in Proportions (95% CI) [5]	33.3 (10.7, 55.8)	
P-value [5]	0.0038	

Time to Flare by Week 26 and Sustained Remission at Week 26 by Randomization Strata	New-onset		Relapsing/Refractory	
	Mavrilimumab 150 mg (N=24)	Placebo (N=11)	Mavrilimumab 150 mg (N=18)	Placebo (N=17)
Number of Subjects with Flare, n (%)	3 (12.5)	4 (36.4)	5 (27.8)	9 (52.9)
Primary Endpoint: Time to Flare (weeks) by Week 26 [1]				
Median, 95% CI	NE (NE, NE)	NE (11.7, NE)	NE (16.4, NE)	22.6 (16.0, NE)
Hazard Ratio (Mavrilimumab vs Placebo), 95% CI [6]	0.29 (0.06, 1.31)		0.43 (0.14, 1.30)	
P-value [7] [8]	0.0873		0.1231	
Secondary Endpoint: Sustained Remission at Week 26 (%) , 95% CI [4]	91.3 (69.3, 97.7)	62.3 (27.7, 84.0)	72.2 (45.6, 87.4)	41.7 (17.4, 64.5)
Difference in Proportions (95% CI) [5]	28.9 (-2.7, 60.5)		30.6 (-2.1, 63.2)	
P-value [5][8]	0.0727		0.0668	

NE = Not estimable.

[1] Kaplan-Meier method used to estimate the survival functions for each treatment arm.

[2] Calculated based on a Cox proportional-hazards model with treatment as covariate and stratified by randomization strata.

[3] Comparison of KPL-301 and placebo with respect to time to flare calculated by using a log-rank test and stratified by randomization strata.

[4] Kaplan-Meier Survival Estimates with standard error and 95% CI for each arm.

[5] Two-sided p-value and 95% CI for the difference in sustained remission between two arms using normal approximation. Placebo arm is the reference.

[6] Calculated based on a Cox proportional-hazards model with treatment as covariate.

[7] Comparison of KPL-301 and placebo with respect to time to flare calculated by using a log-rank test.

[8] Subgroup analyses were not powered for significance; nominal p values reported.

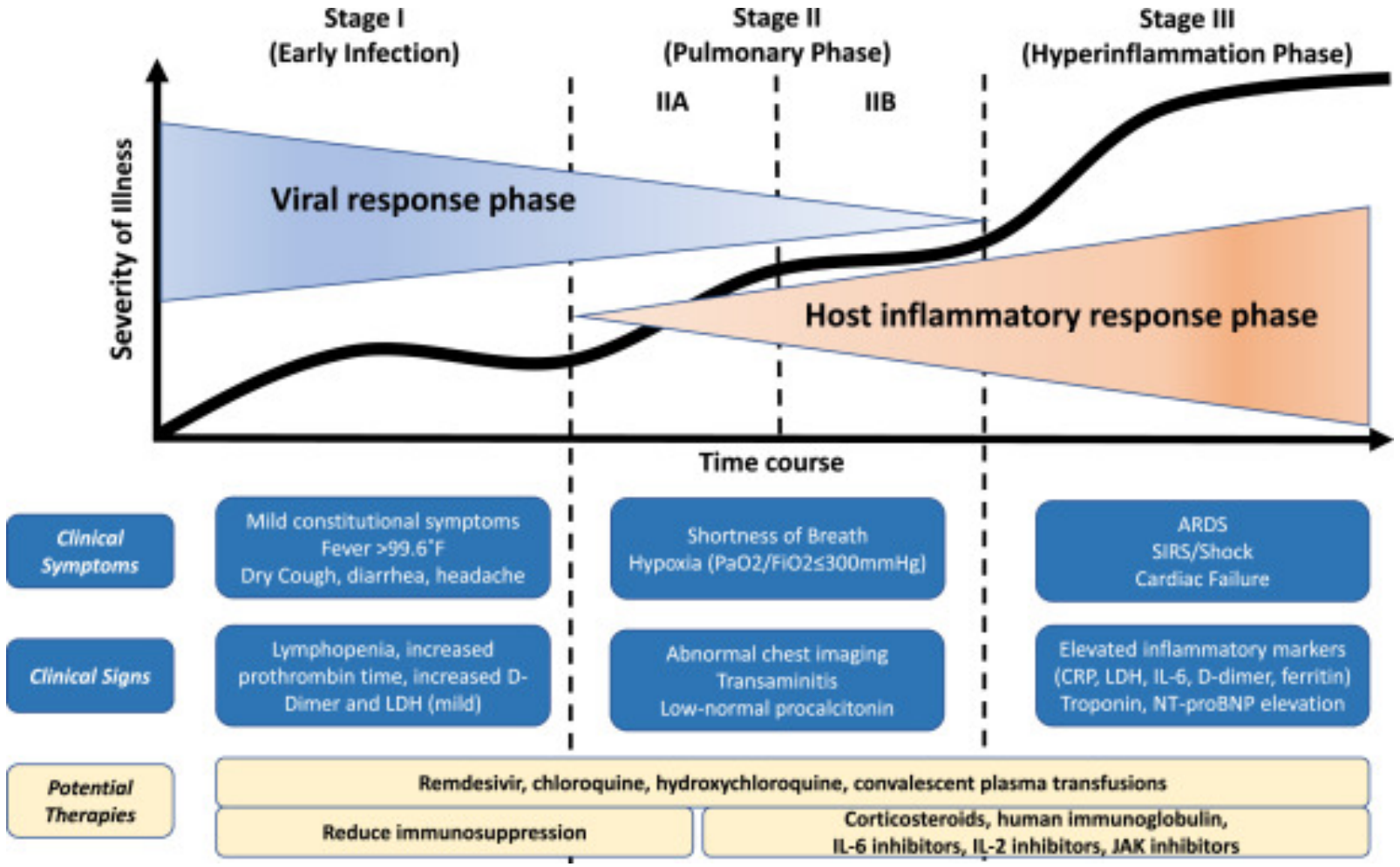
Summary of Adverse Events

Mavrilimumab Phase 2 Giant Cell Arteritis Data

	Mavrilimumab 150mg (N=42) n (%)	Placebo (N=28) n (%)
Treatment Emergent Adverse Events	33 (78.6)	25 (89.3)
By Maximum Severity [1]		
Mild	18 (42.9)	13 (46.4)
Moderate	14 (33.3)	11 (39.3)
Severe	1 (2.4)	1 (3.6)
Related to Mavrilimumab or Placebo [2]	10 (23.8)	7 (25.0)
Related to Prednisone [2]	11 (26.2)	11 (39.3)
Serious Treatment Emergent Adverse Events	2 (4.8)	3 (10.7)
Related to Mavrilimumab or Placebo [2]	0	0
Related to Prednisone [2]	0	0
Non-serious Treatment Emergent Adverse Events	33 (78.6)	25 (89.3)
Treatment Emergent Adverse Events Resulting in Death	0	0
Treatment Emergent Adverse Events Leading to Dose Interruption	1 (2.4)	2 (7.1)
Treatment Emergent Adverse Events Leading to Withdrawal of Treatment	1 (2.4)	1 (3.6)
Treatment Emergent Adverse Events of Special Interest	0	1 (3.6)

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

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

ARDS = Acute respiratory distress syndrome; CRP = C-reactive protein; IL = Interleukin; JAK = Janus Kinase; LDH=Lactate DeHydrogenase; SIRS = Systemic inflammatory response syndrome

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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.

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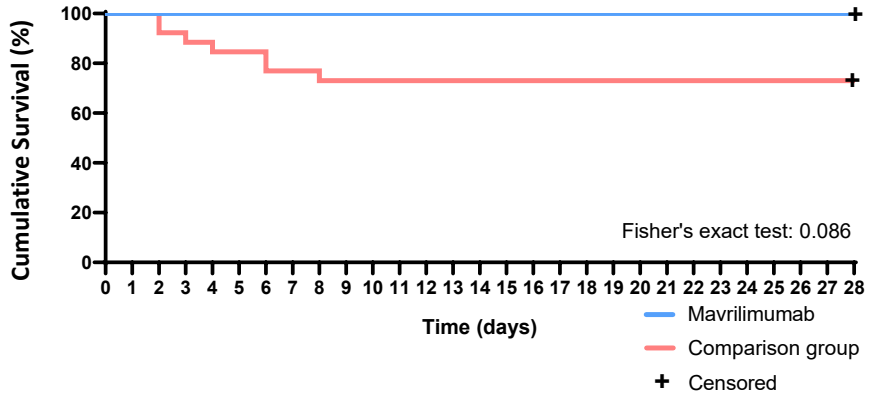
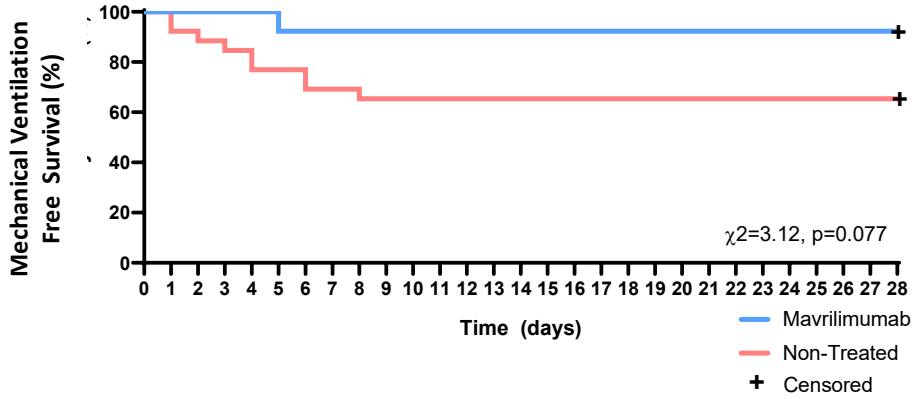
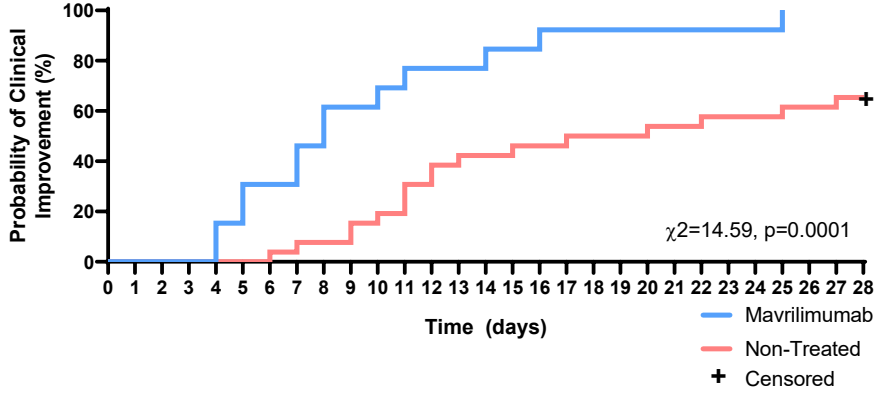
Mavrilimumab Treatment Protocol in Patients with COVID-19 Pneumonia & Hyperinflammation Showed Improved Clinical Outcomes Compared to Matched Contemporaneous Controls[1]



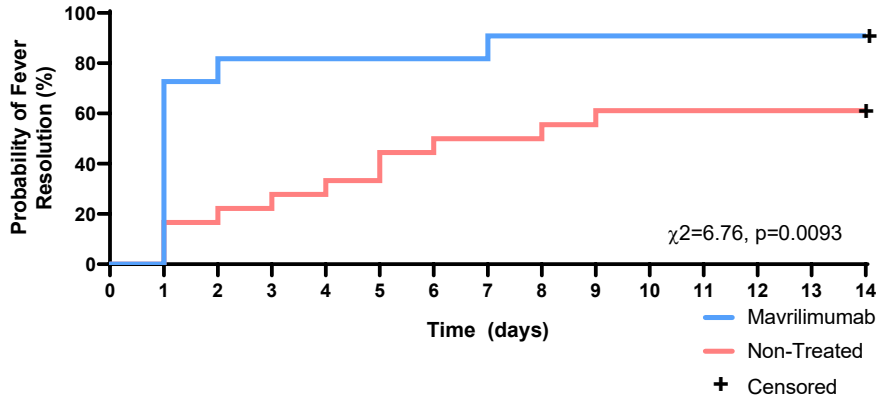
Death occurred in 0% (n=0/13) of mavrilimumab-treated patients by Day 28, compared to 27% (n=7/26) of control-group patients (p=0.086)



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)

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; 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.

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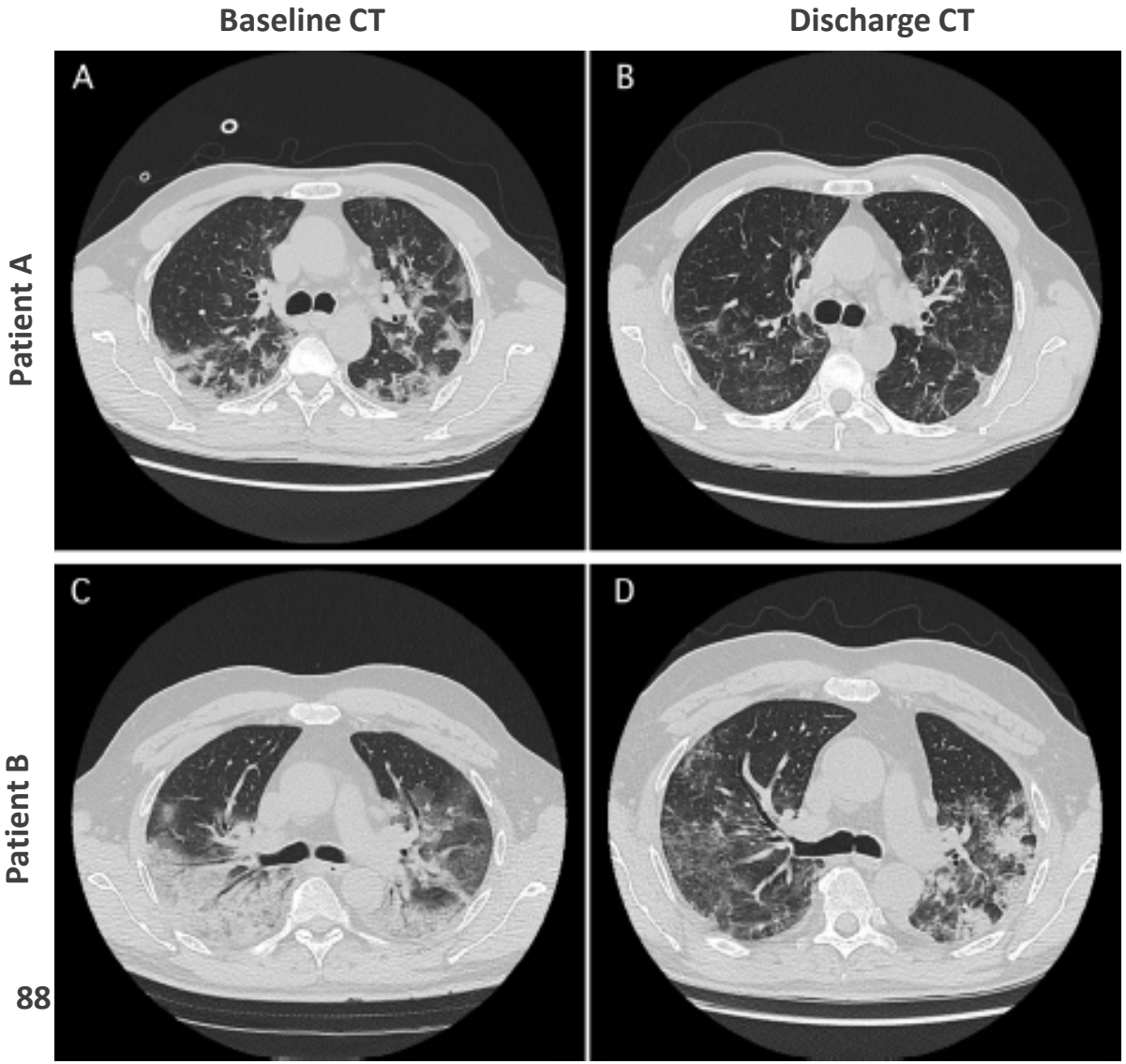
Representative mavrilimumab-treated patients showed significant improvement in lung opacification on computerized tomography (CT) scans, consistent with the overall improvement in their clinical status



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).

De Luca et al. Lancet Rheum 2020. In press.

Data from U.S. Investigator-Initiated Study of Mavrilimumab in Severe COVID-19 Pneumonia and Hyperinflammation

The investigator-initiated study was a randomized, double-blind, placebo-controlled study across a consortium of U.S. academic sites designed to evaluate the efficacy and safety of mavrilimumab versus placebo on top of standard of care therapy in patients with severe COVID-19 pneumonia and hyperinflammation.

- Enrolled 40 patients with severe COVID-19 pneumonia (all patients presented with pneumonia and hypoxia: all patients required supplemental oxygen, 50% of patients required non-invasive ventilation, none required mechanical ventilation at baseline; median PaO2/FiO2 ratio 137) and hyperinflammation (median C-reactive protein 13.1 mg/dL).
- Concomitant medications at baseline included corticosteroids (65% of patients) and remdesivir (75% of patients). Patients were randomized 1:1 to a single intravenous (IV) infusion of mavrilimumab 6mg/kg (n=21) or placebo (n=19) and were followed for at least 60 days.

Data showed an early signal of efficacy, with trends toward clinical improvement as well as lower mortality and shorter duration of mechanical ventilation in patients treated with mavrilimumab on top of corticosteroids, including dexamethasone, and/or remdesivir.

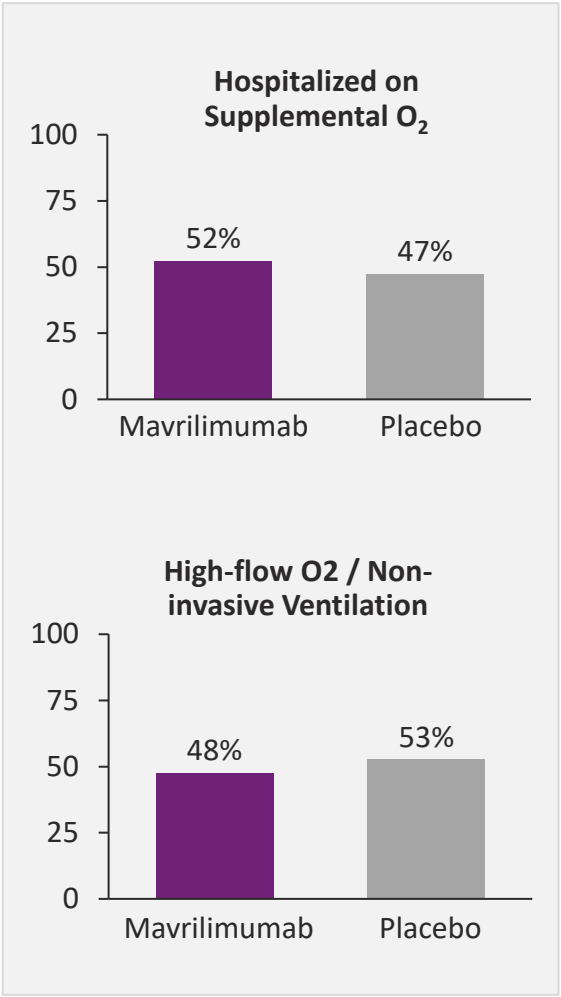
Clinical Outcomes:

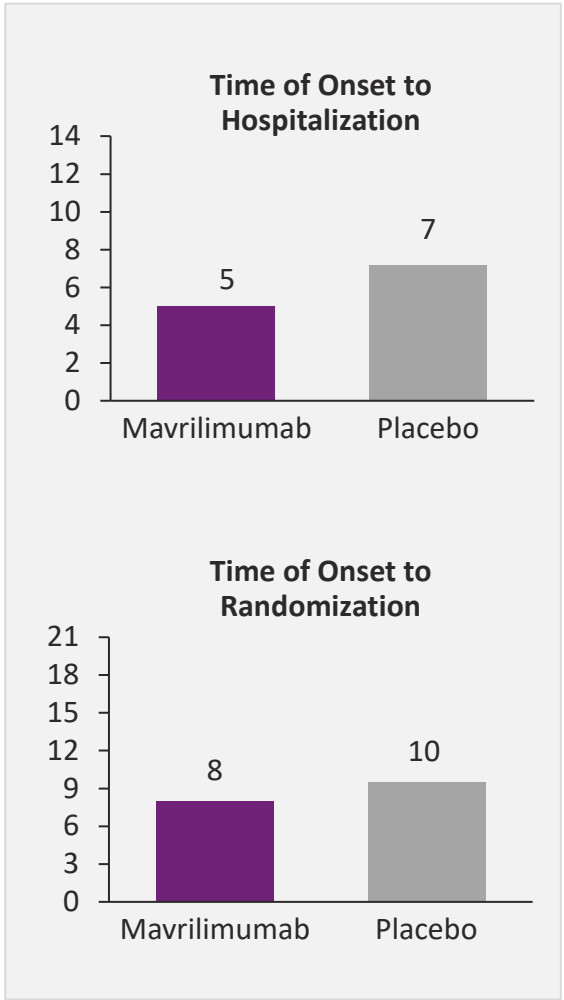
- There was a 20.5% relative increase in the primary efficacy endpoint, the proportion of patients alive and off supplemental oxygen at Day 14 (mavrilimumab: 57.1% [n=21]; placebo: 47.4% [n=19]; nominal p=0.536).
- There was a 20.7% relative increase in the secondary efficacy endpoint, the proportion of patients alive and without respiratory failure[1] at Day 28 (mavrilimumab: 95.2%; placebo: 78.9%; nominal p=0.172).
- There was 1 death (4.8%) in the mavrilimumab arm by Day 28, compared to 3 deaths (15.8%) in the placebo arm (nominal p=0.222). By Day 60 there was 1 death (4.8%) in the mavrilimumab arm, compared to 4 deaths (21.1%) in the placebo arm (nominal p=0.108).
- While the percentage of patients who progressed to mechanical ventilation was similar between treatment arms (mavrilimumab: 23.8% [n=5]; placebo: 21.1% [n=4]), the median (interquartile) duration of mechanical ventilation was shorter in the mavrilimumab arm (12 [9.0, 18.0] days) compared to the placebo arm (17 [11.0, 24.5] days). Additionally, 4 of the 5 patients who progressed to mechanical ventilation in the mavrilimumab arm had recovered by Day 28, whereas all patients in the placebo arm who progressed to mechanical ventilation had died by Day 28.
- There was no difference in serious adverse events between the mavrilimumab arm and the placebo arm.

[1] Need for mechanical ventilation, Non-Invasive Ventilation, Hi Flow Oxygen

Baseline Demographics and Baseline Characteristics

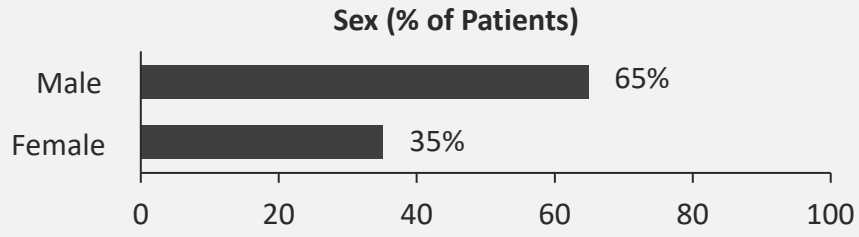
U.S. investigator-initiated study in patients with severe COVID-19 pneumonia and hyperinflammation

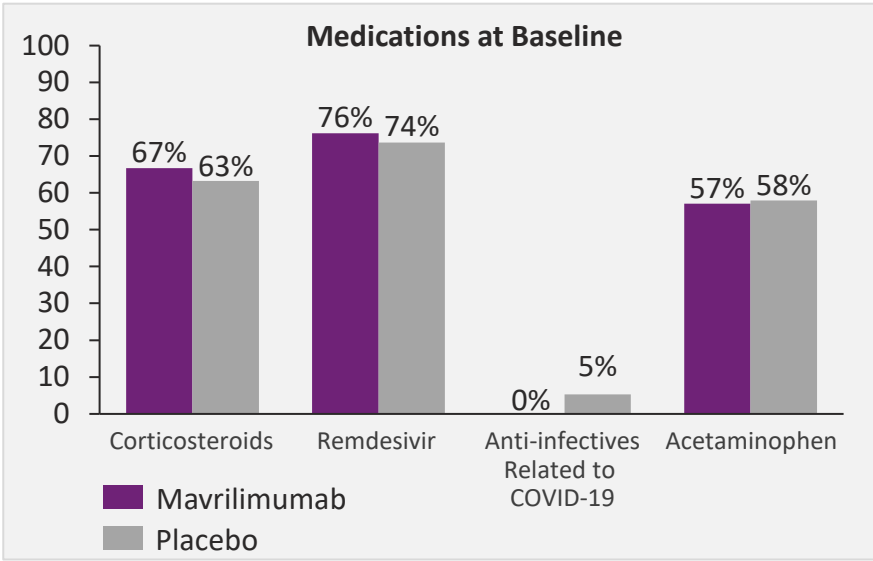




Mean Age (years): 56.1

Age Range (years): 22.6 - 82.9

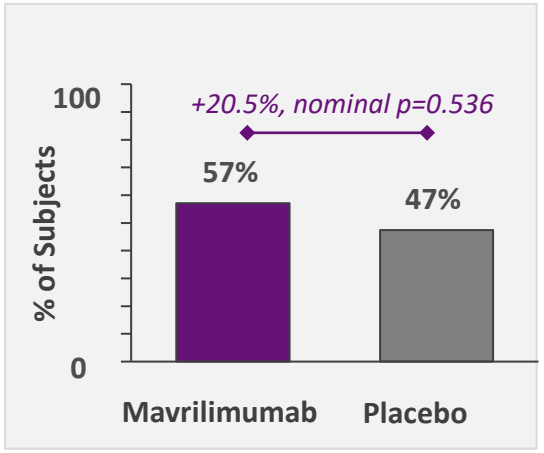




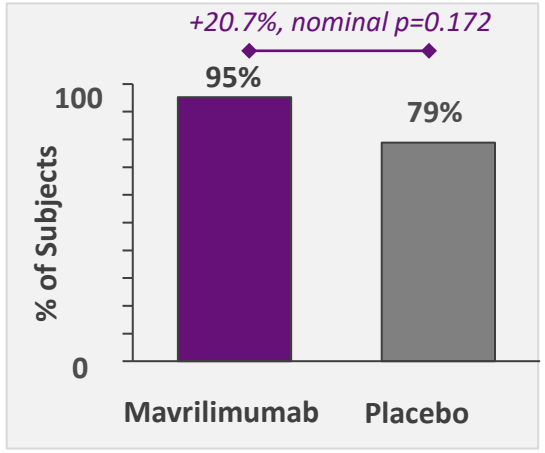
Encouraging Trends toward Reduced Mortality and Duration of Mechanical Ventilation

U.S. investigator-initiated study in patients with severe COVID-19 pneumonia and hyperinflammation

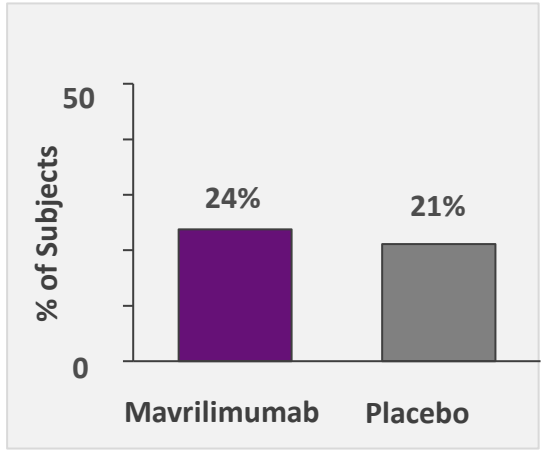
Primary Endpoint: Proportion of Patients Alive and off Supplemental Oxygen at Day 14



Secondary Endpoint: Proportion of Patients Alive and Without Respiratory Failure at Day 28

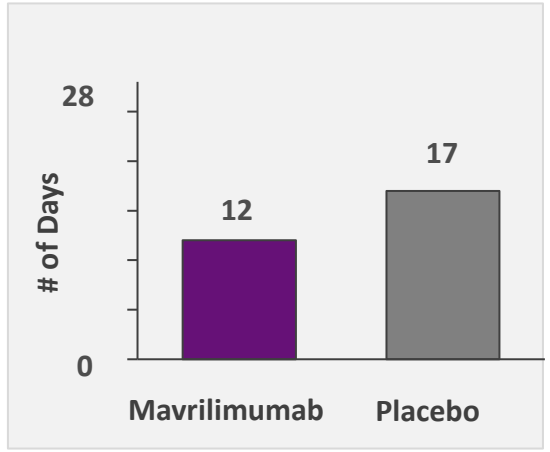


Percentage of Patients who Progressed to Mechanical Ventilation



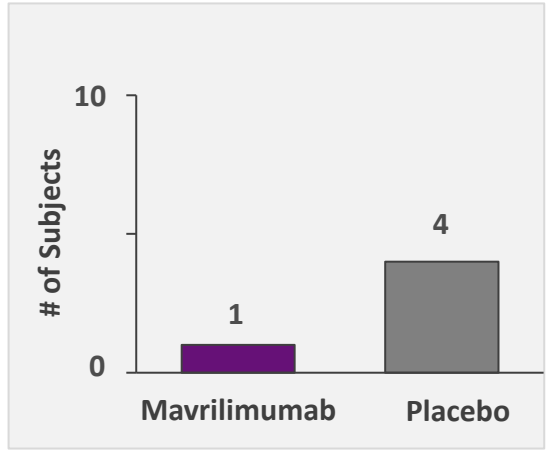
The percentage of patients who progressed to mechanical ventilation was similar between treatment arms (mavrilimumab: 23.8% [n=5]; placebo: 21.1% [n=4]).

Duration of Mechanical Ventilation



The median (interquartile) duration of mechanical ventilation was shorter in the mavrilimumab arm (12 [9.0, 18.0] days) compared to the placebo arm (17 [11.0, 24.5] days). 4 of the 5 patients who progressed to mechanical ventilation in the mavrilimumab arm had recovered by Day 28, whereas all patients in the placebo arm who progressed to mechanical ventilation had died by Day 28.

Death by Day 60



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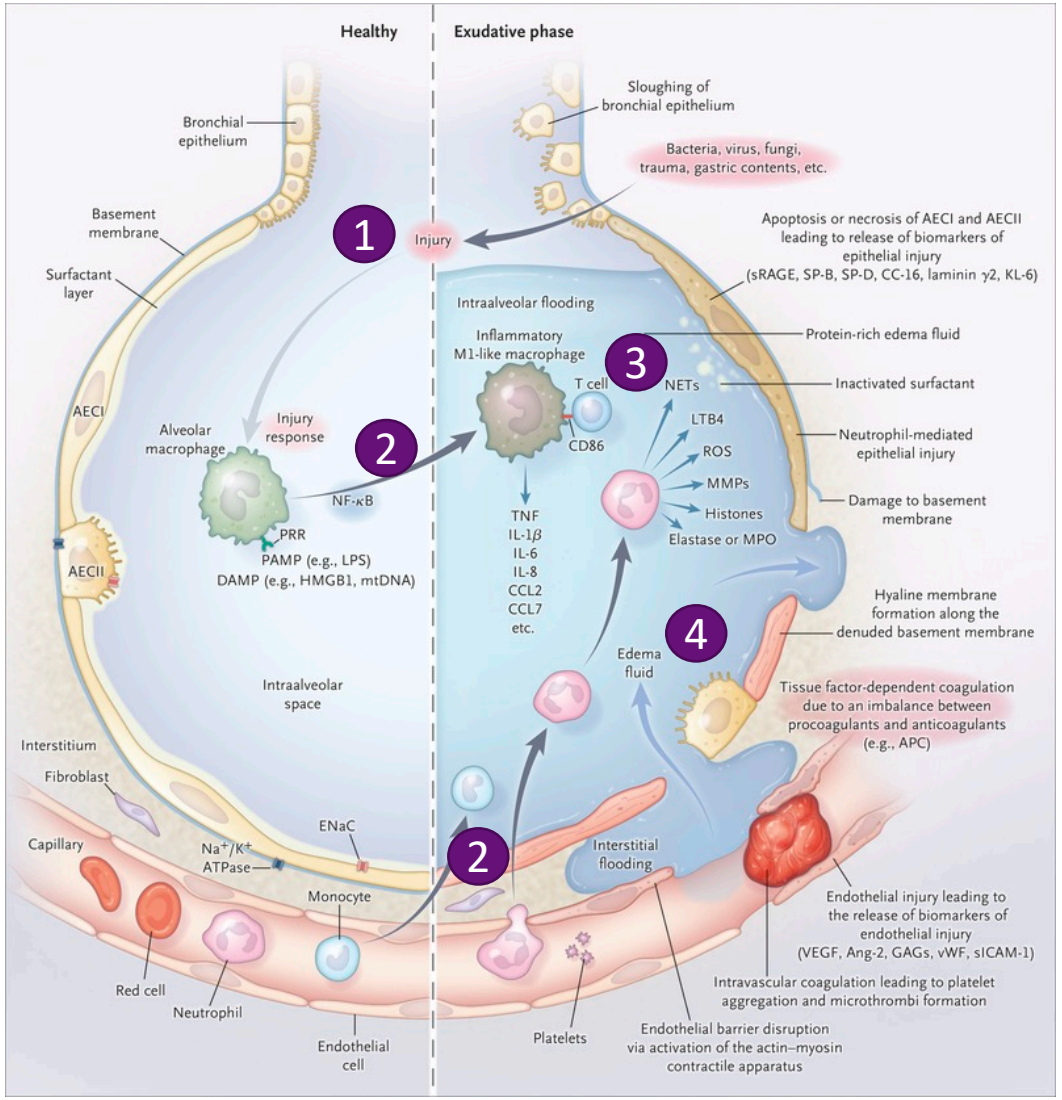
Cytokine Cascade Amplification System in the Pathophysiology of ARDS

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

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.

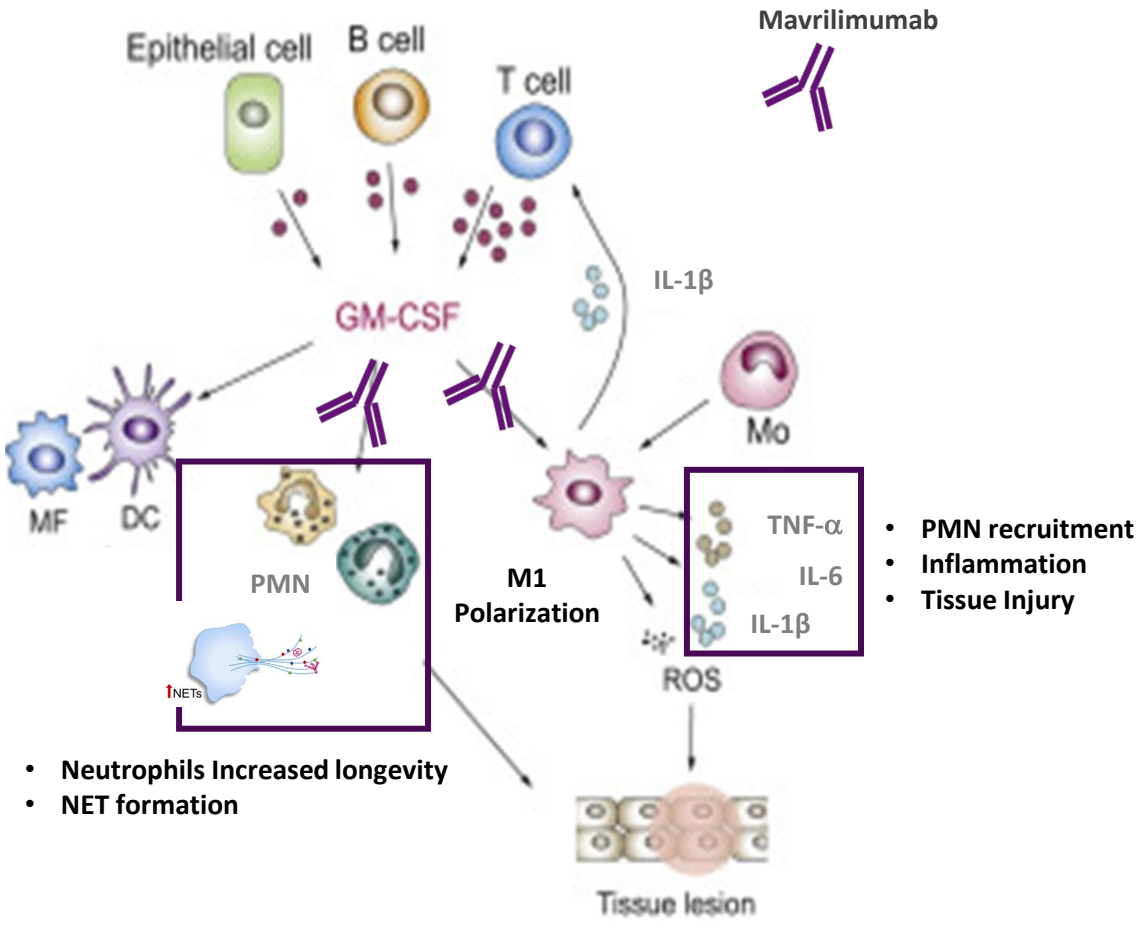
4
- Extensive damage to lung epithelia and endothelia results in an impaired alveolar-capillary barrier.
- Disruption of this barrier allows protein-rich fluid to enter the alveoli causing fluid accumulation in alveolar spaces (pulmonary edema) interfering with gas exchange

ARDS = Acute Respiratory Distress Syndrome

The New England Journal of Medicine. 2017

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

[1]Wu 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

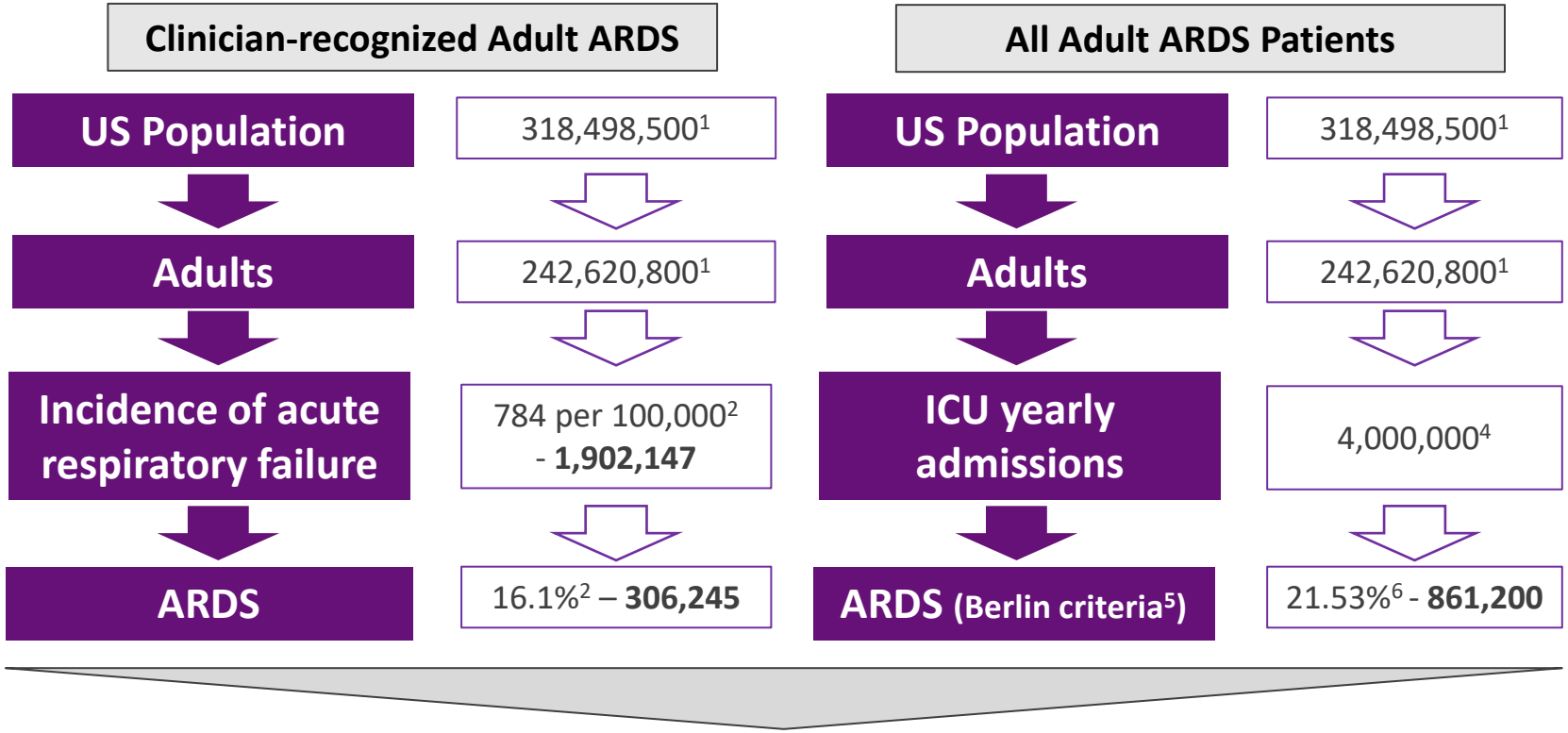
[15] Jones J Infect Dis (2006), [16] Wright Rheumatology (2014), [17] Afford JBC (1992), [18] Biffl JLB (1995), [19] Oh J Exp Med (2011), [20] Yan Sci Rep (2016).

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).

ARDS = Acute Respiratory Distress Syndrome
Becher B. et al., Immunity 45, (2016)

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 ventilation[7]
- 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 20112;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

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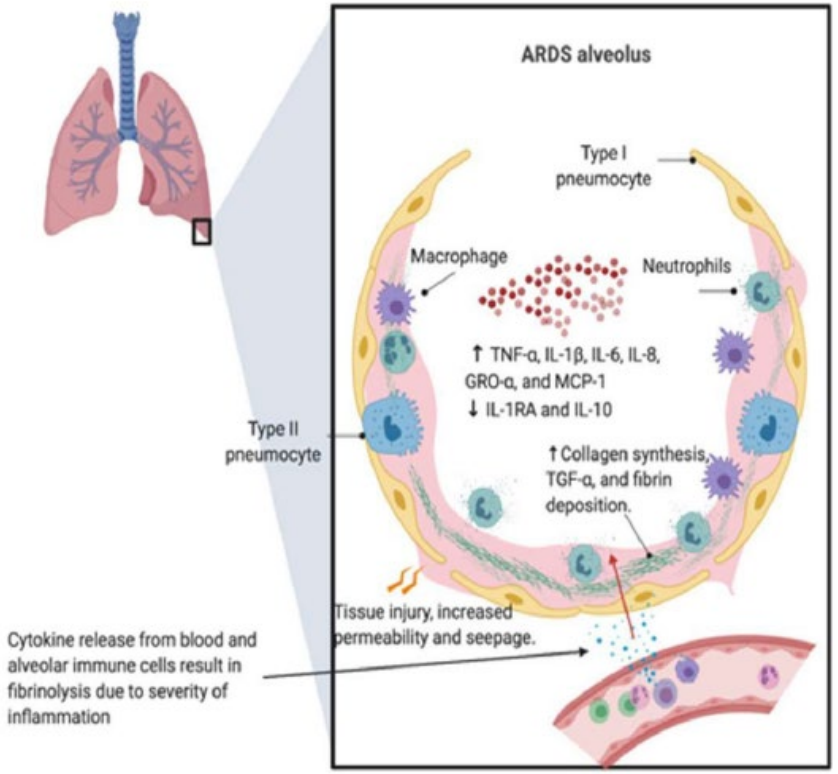
Viral Infections Causing ARDS (i.e., influenza, H1N1, RSV, COVID-19, etc.) Have an *Inflammatory* Pathophysiology, Primarily Precipitated by Cytokine Storm

- 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

1) Kalil A.C and Thomas P.G. Critical Care (2019) 23:258
2) Guo XZ, Thomas PG,. Semin Immunopathol. 2017 July ; 39(5): 541–550. doi:10.1007/s00281-017-0636-y.
3) Zhang, et al. Clinical Immunology 214 (2020) 108393

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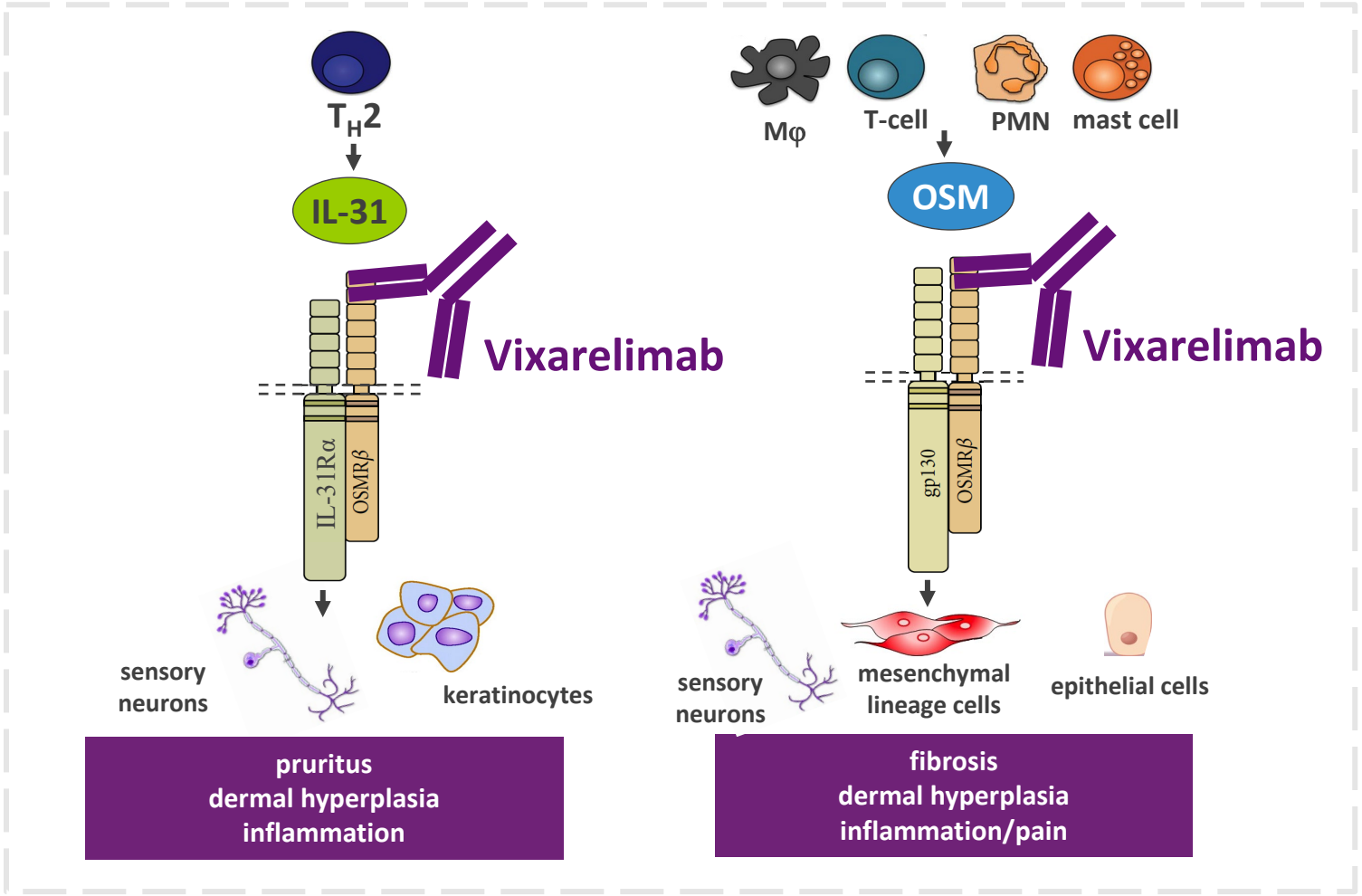
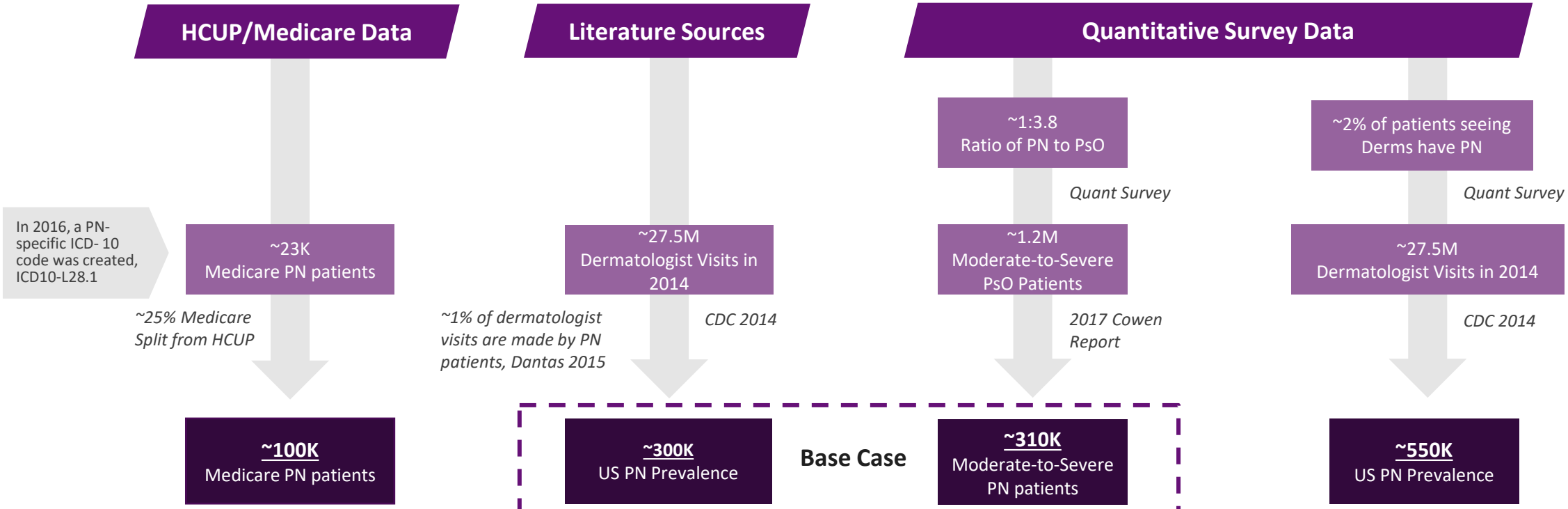
Every Second Counts!™

Appendix – Vixarelimab (KPL-716)

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

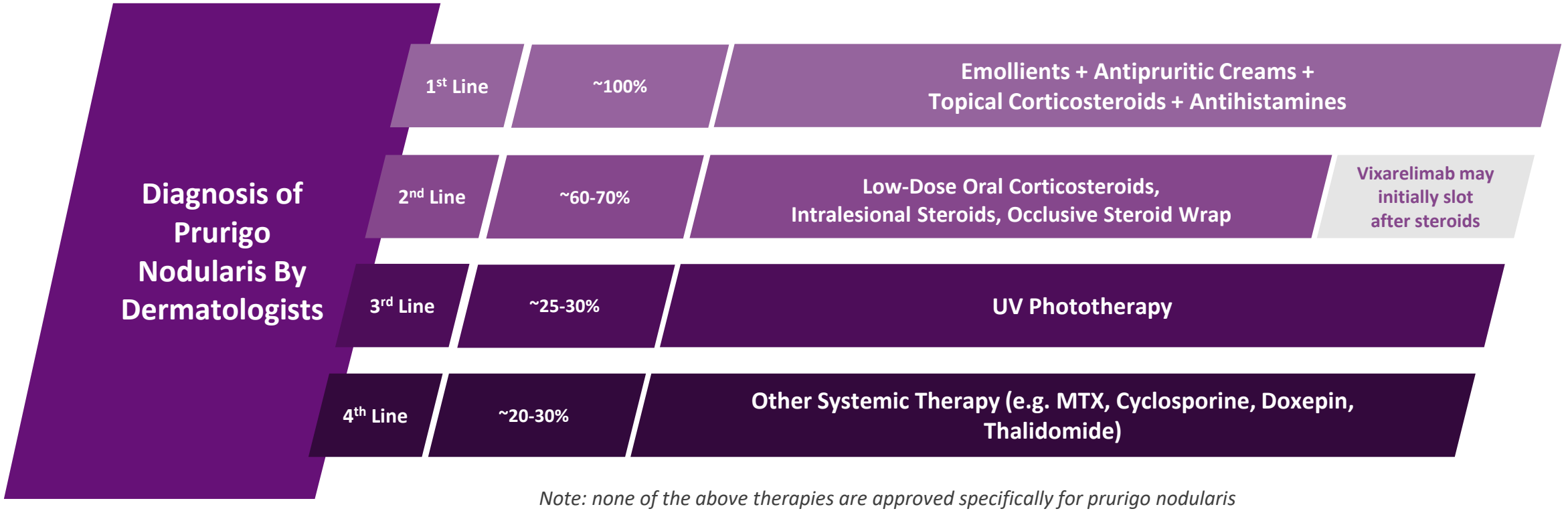


Prurigo Nodularis U.S. Prevalence Estimated to be ~300K Patients



Sources: CDC 2014: National Ambulatory Medical Care Survey: 2014 State and National Summary Tables <https://www.cdc.gov/nchs/data/ahcd/namcs_summary/2014_namcs_web_tables.pdf>; Cowen and Company, Therapeutic Categories Outlook: Comprehensive Study September 2017; Primary Market Research; 3. Dantas, 2015, "Prevalence of dermatoses in dermatologic evaluation requests from patients admitted to a tertiary hospital for 10 years"

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



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

Sources: 1. Medscape, 2. Trinity Qualitative Research

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)

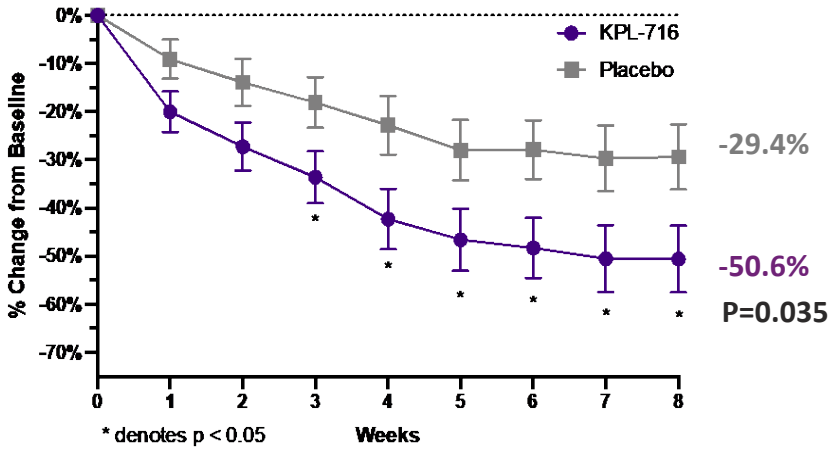
Topline Observations:

- 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

WI-NRS = Worst-Itch Numeric Rating Scale
PN-IGA = prurigo nodularis-investigator's global assessment

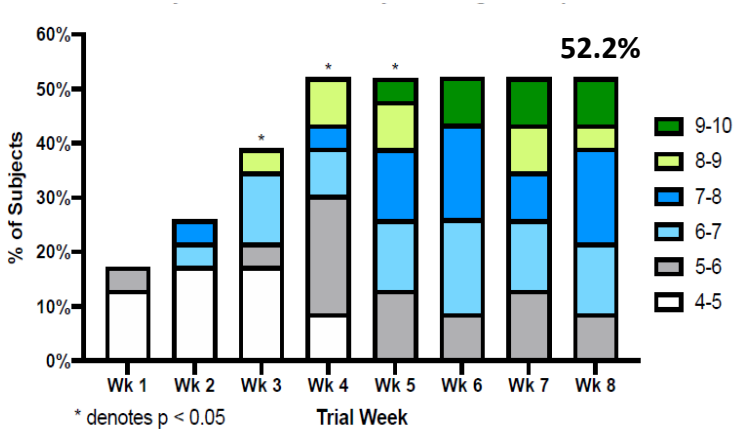
Vixarelimab Phase 2a Data in Prurigo Nodularis

LS-Mean % Change in Weekly Average WI-NRS



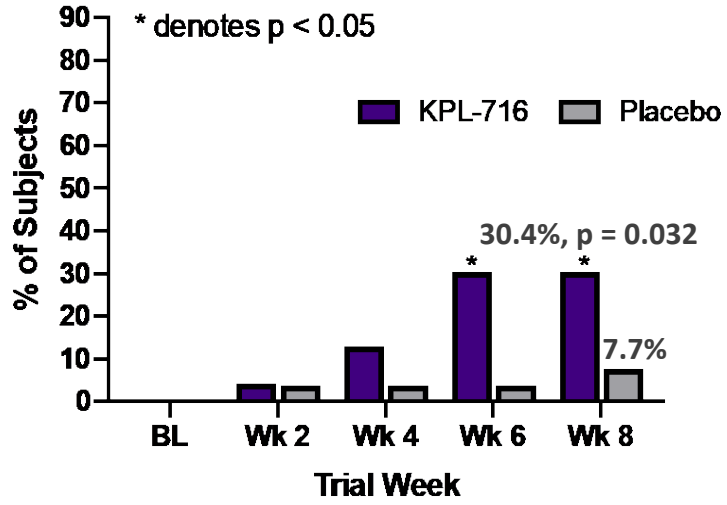
Statistically Significant Primary Efficacy Endpoint of Reduction in Weekly-Average WI-NRS at Week 8

% 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



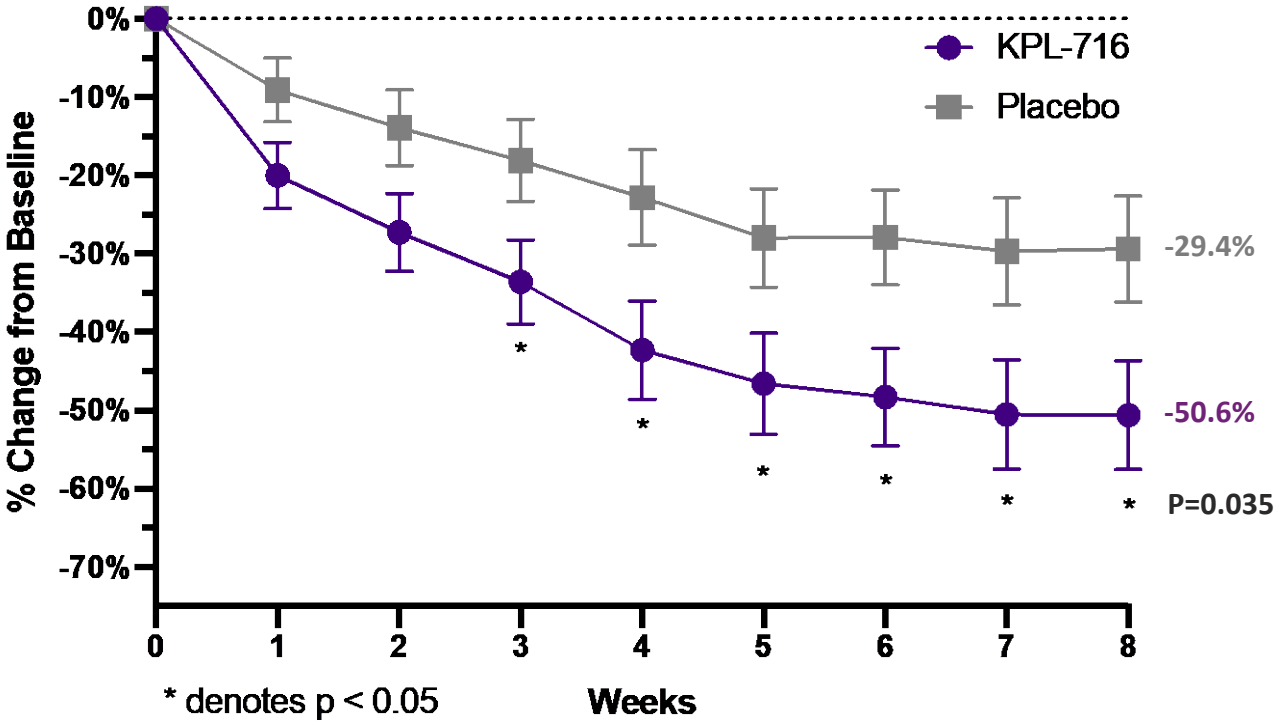
Significantly More Vixarelimab Recipients Attained A Clear/Almost Clear Lesion Score by Week 8

Vixarelimab = KPL-716
WI-NRS = Worst-Itch Numeric Rating Scale
LS = least squares

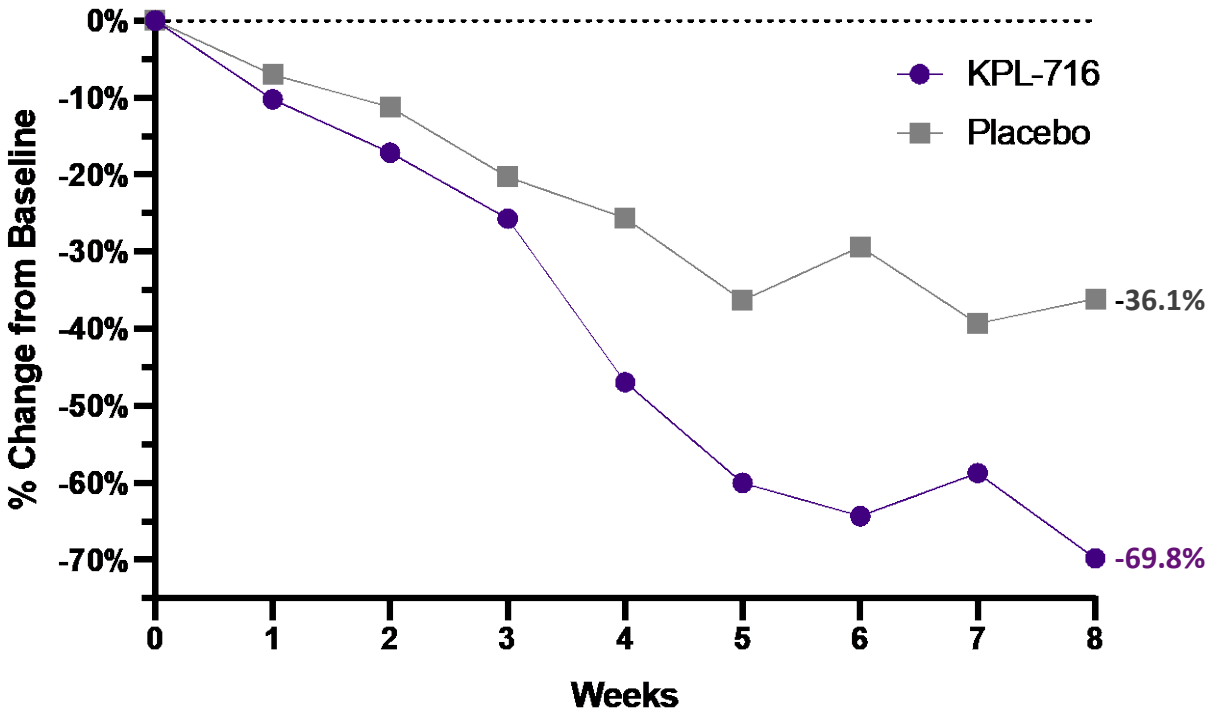
Vixarelimab Phase 2a Study in Prurigo Nodularis: Statistically Significant Primary Efficacy Endpoint of Reduction in Weekly-Average WI-NRS at Week 8

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

LS-Mean % Change in Weekly Average WI-NRS

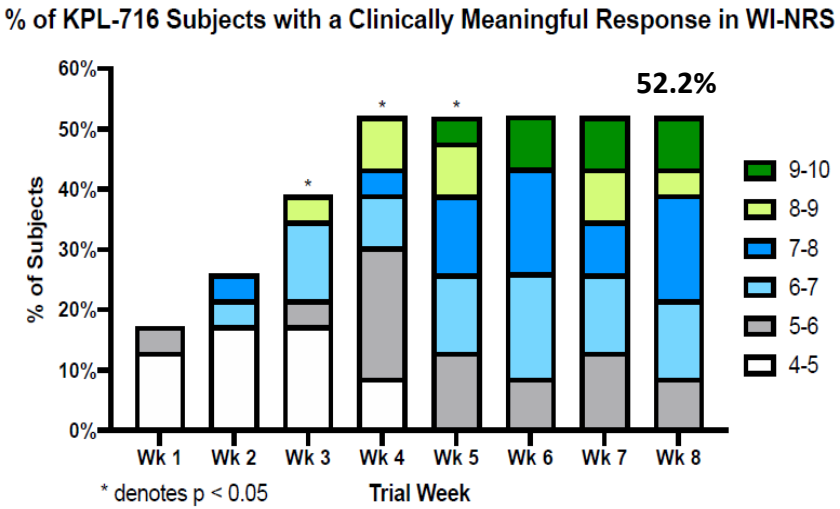


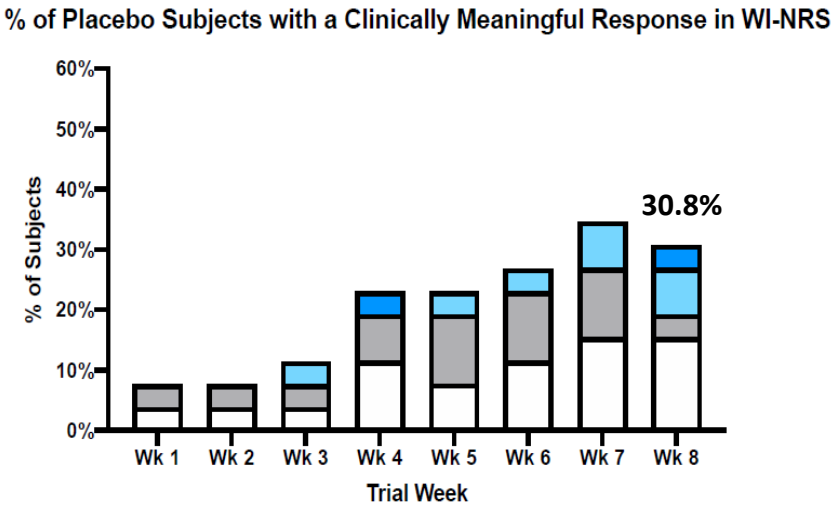
Median % Change in Weekly Average WI-NRS

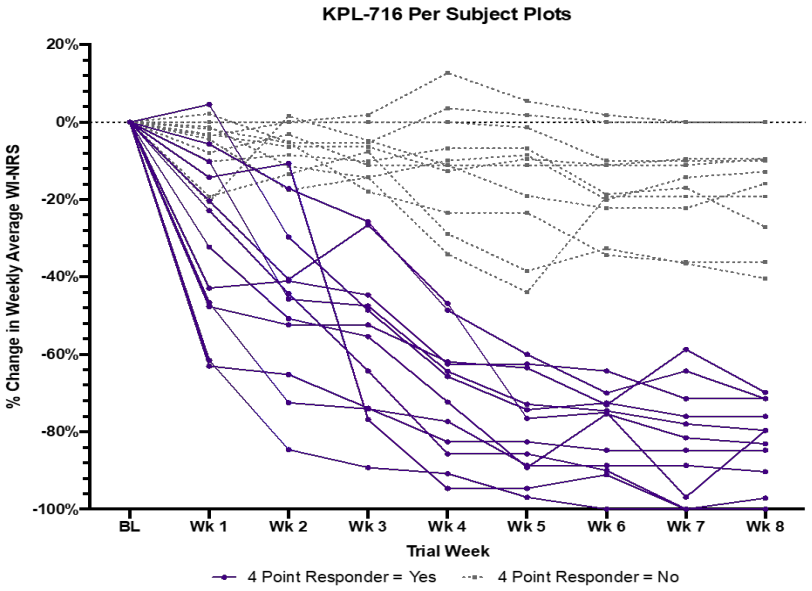


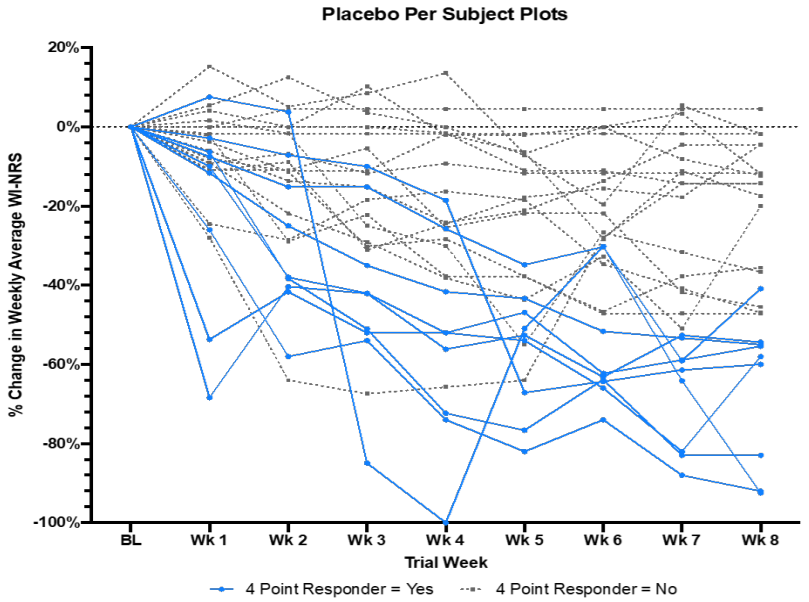
Vixarelimab = KPL-716
WI-NRS = Worst-Itch Numeric Rating Scale
LS = least squares

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





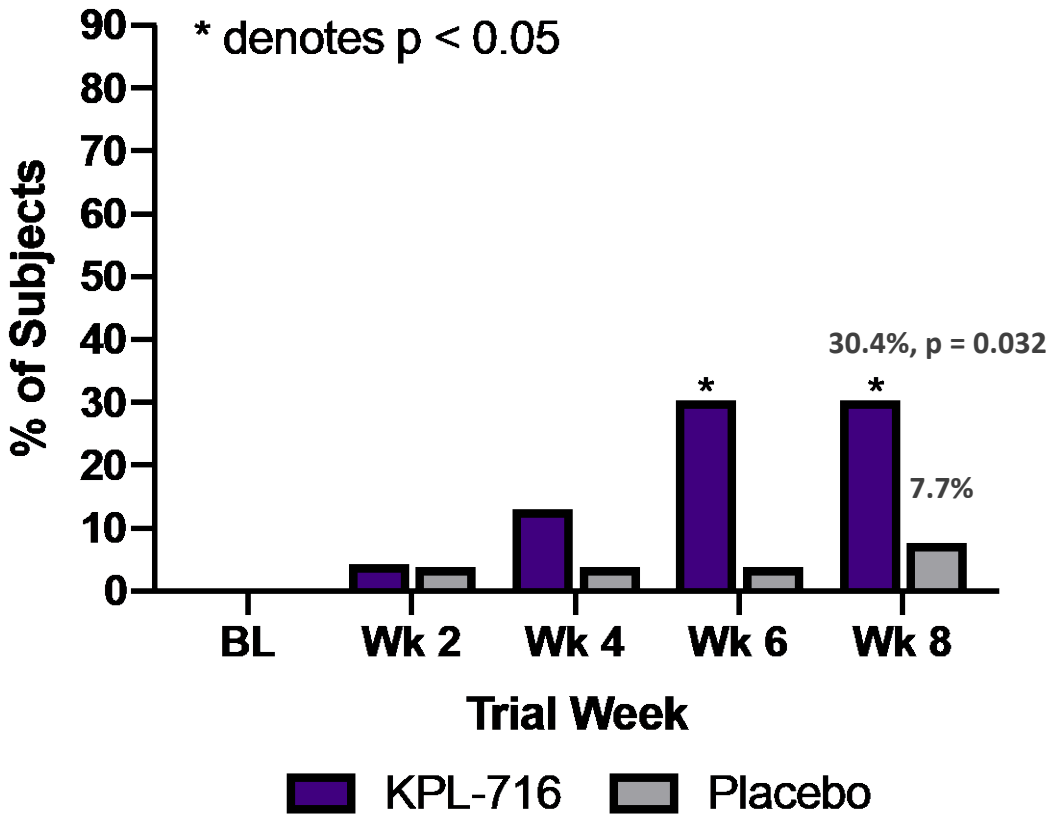




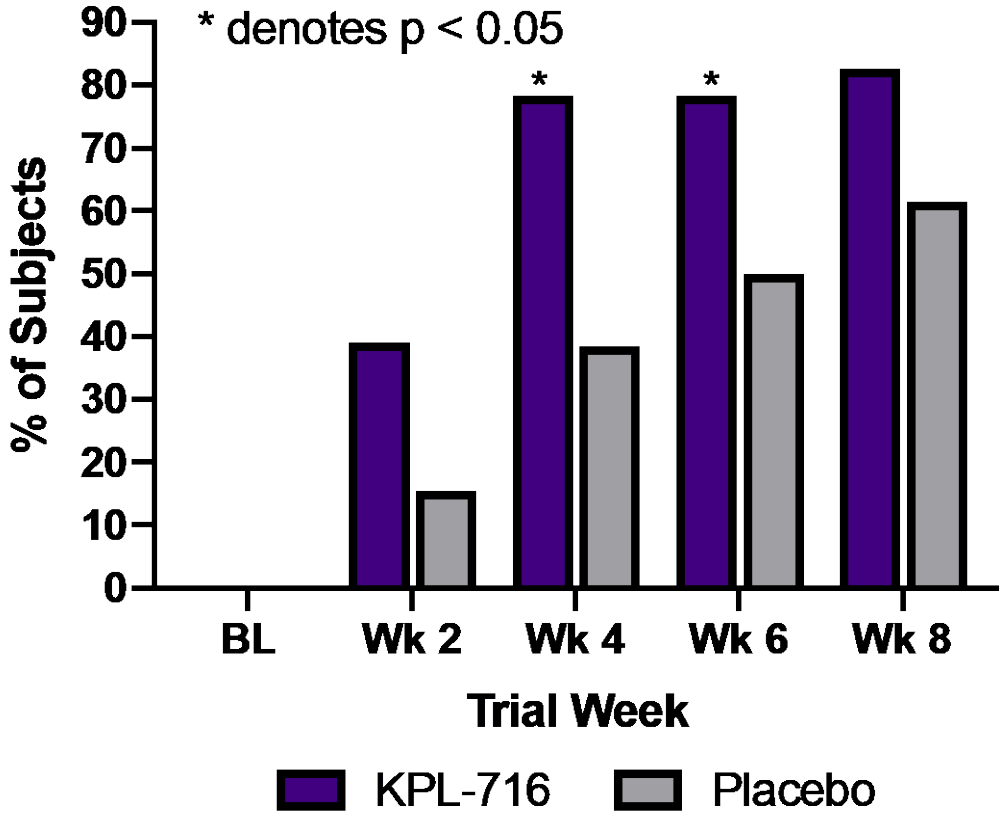
Vixarelimab = KPL-716
WI-NRS = Worst-Itch Numeric Rating Scale

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



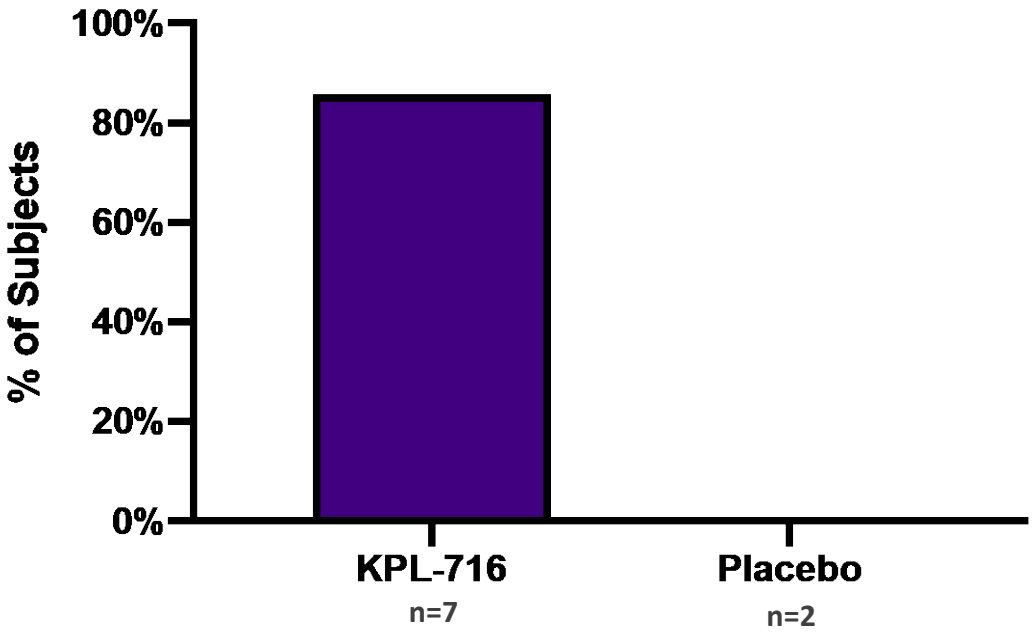
≥1 Point Change in PN-IGA



Vixarelimab = KPL-716; PN-IGA = prurigo nodularis-investigator's global assessment

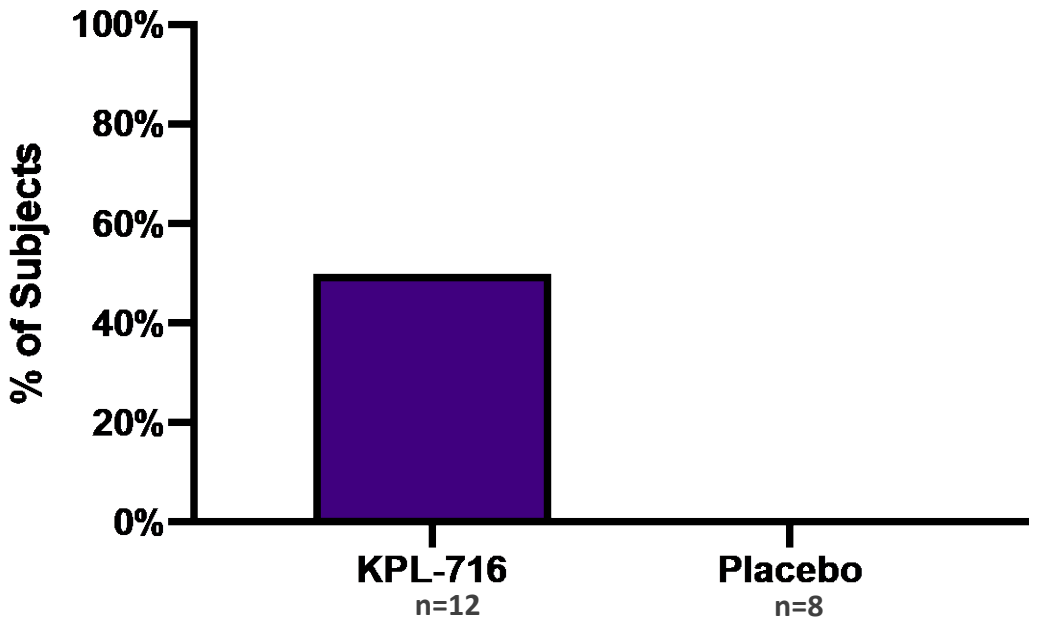
Vixarelimab Phase 2a Study in Prurigo Nodularis: Concordant Activity of Vixarelimab on PN-IGA and Pruritus

% 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

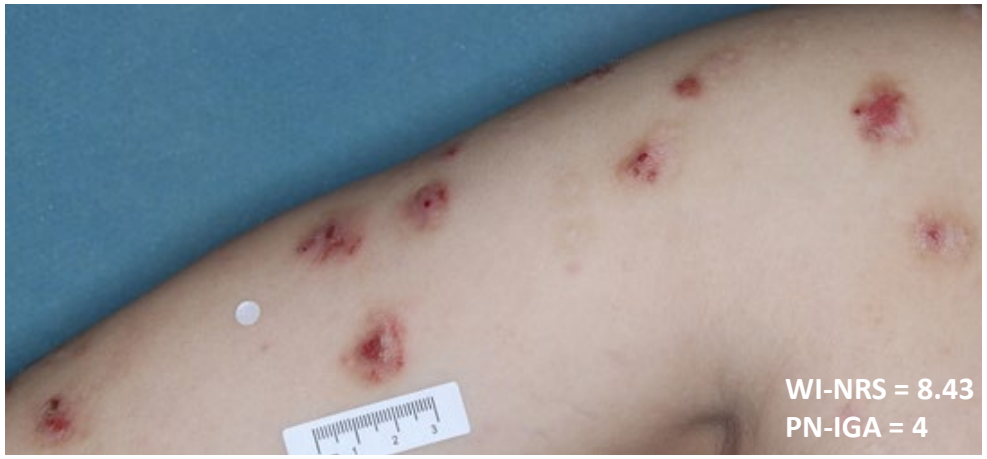
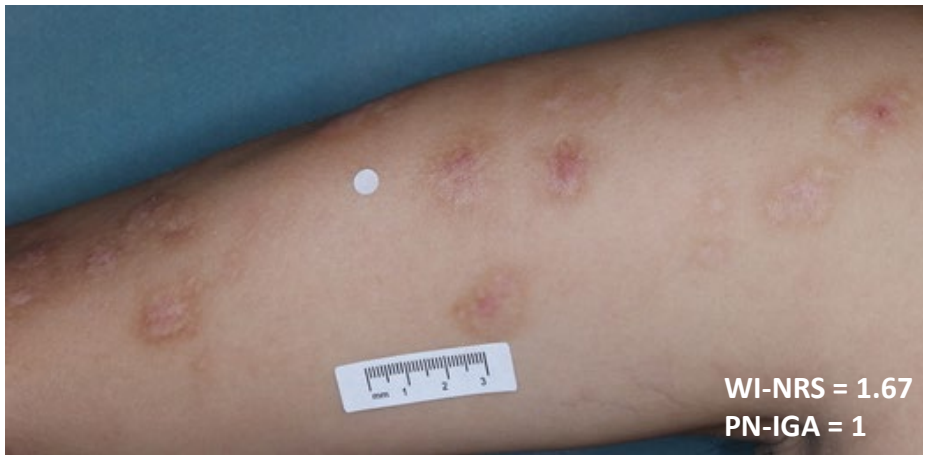
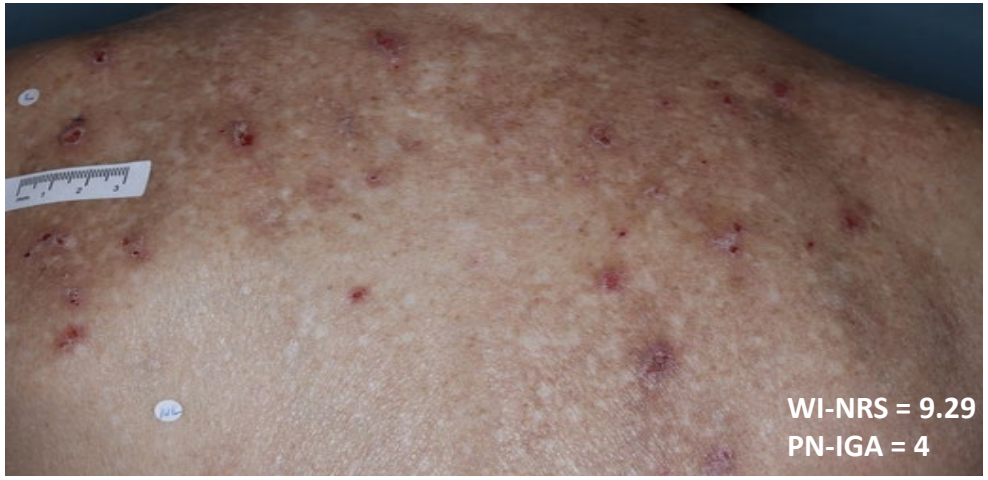
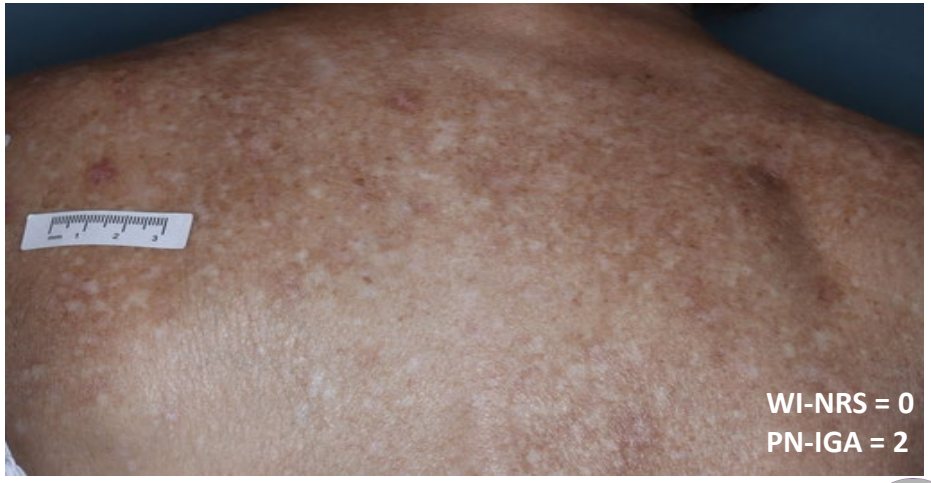
% of Subjects with ≥4 Point Change in WI-NRS and an IGA of 0-1



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 = KPL-716
WI-NRS = Worst-Itch Numeric Rating Scale
PN-IGA = prurigo nodularis-investigator's global assessment

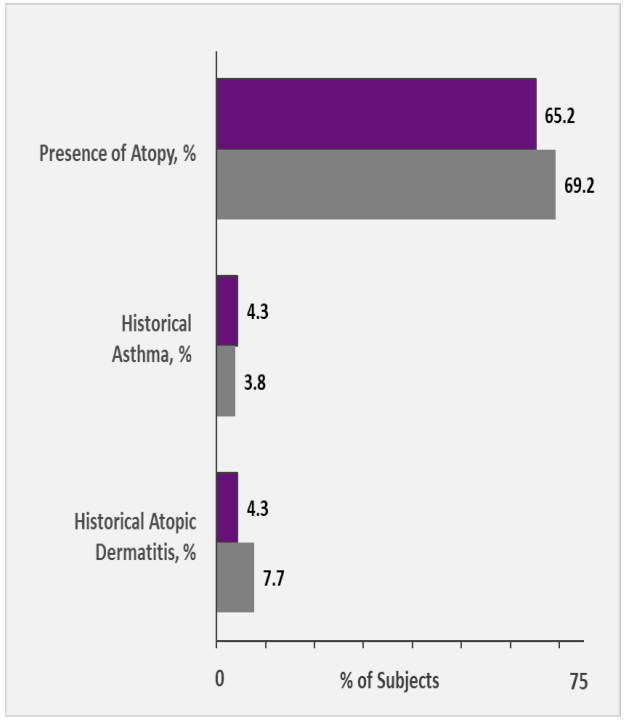
Vixarelimab Phase 2a Study in Prurigo Nodularis: Representative Images of Nodule Resolution at Week 8 in Vixarelimab-Treated Subjects

	Day 1	Week 8
Subject 1	 WI-NRS = 8.43 PN-IGA = 4	 WI-NRS = 1.67 PN-IGA = 1
Subject 2	 WI-NRS = 9.29 PN-IGA = 4	 WI-NRS = 0 PN-IGA = 2

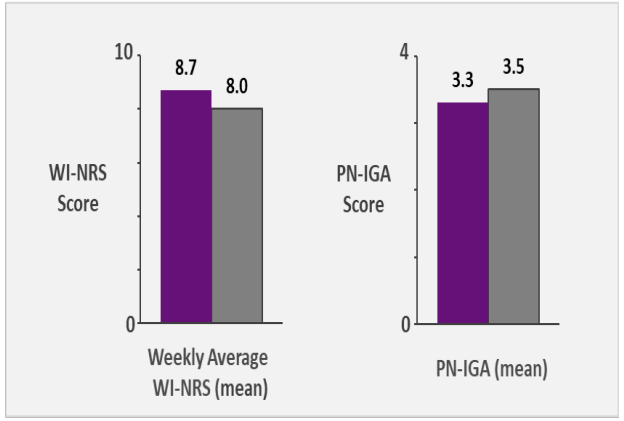
Vixarelimab Phase 2a Study in Prurigo Nodularis: Baseline Characteristics

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



*mITT Analysis Set

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

AE = adverse event
TEAE = treatment emergent adverse event

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)
Otis Media (n)	0	3.8% (1)
Skin Infection (n)	0	3.8% (1)
Tooth Abscess (n)	0	3.8% (1)

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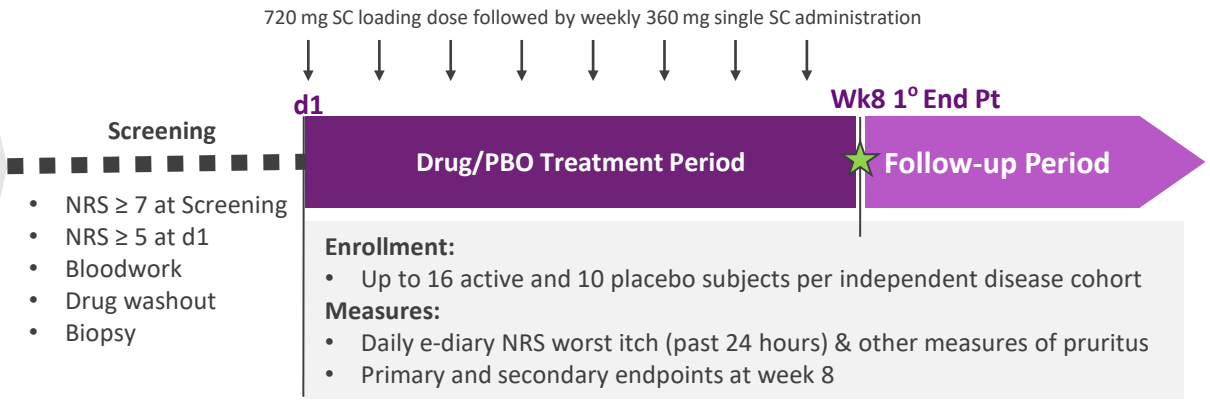
Vixarelimab Exploratory Phase 2 Study in Diseases Characterized by Chronic Pruritus

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



- NRS ≥ 7 at Screening
- NRS ≥ 5 at d1
- Bloodwork
- Drug washout
- Biopsy

Enrollment:
- Up to 16 active and 10 placebo subjects per independent disease cohort

Measures:
- Daily e-diary NRS worst itch (past 24 hours) & other measures of pruritus
- Primary and secondary endpoints at week 8

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.

WI-NRS = Worst-Itch Numeric Rating Scale

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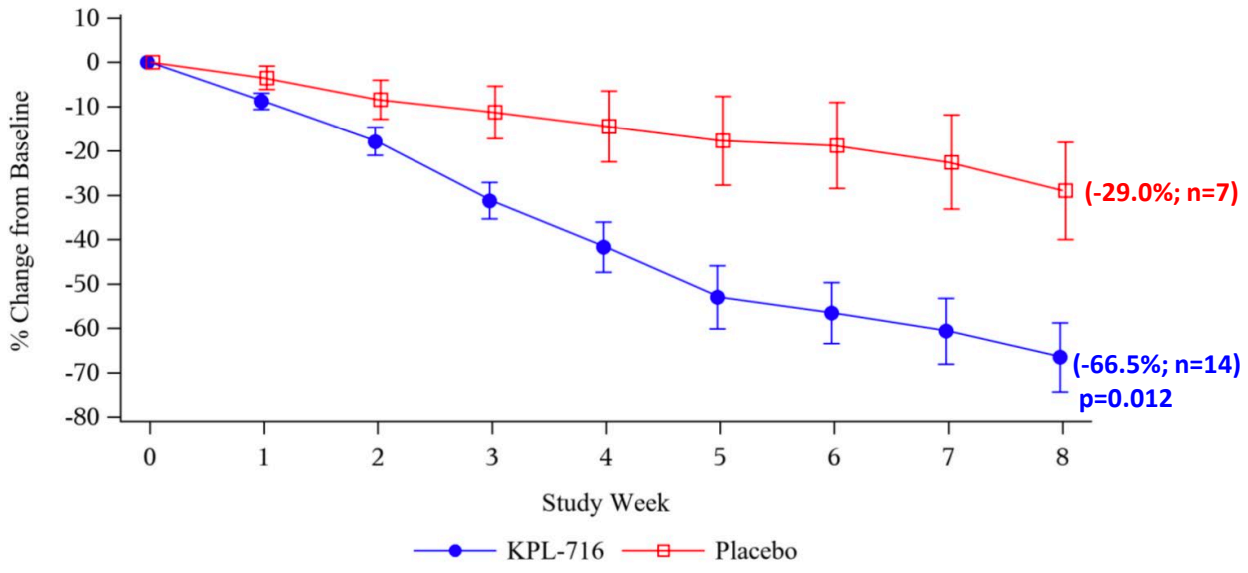
Vixarelimab Exploratory Phase 2 Study in Diseases Characterized by Chronic Pruritus: Reduction in Weekly-Average WI-NRS at Week 8

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

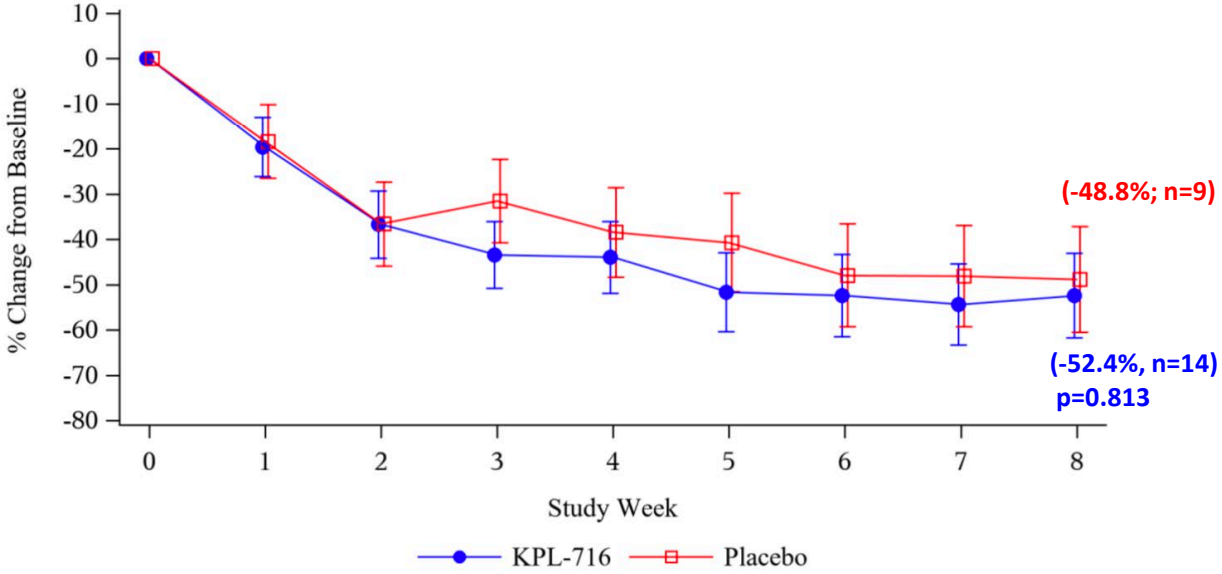
Plaque Psoriasis

LS-Mean % Change in Weekly Average WI-NRS



Chronic Idiopathic Pruritus

LS-Mean % Change in Weekly Average WI-NRS

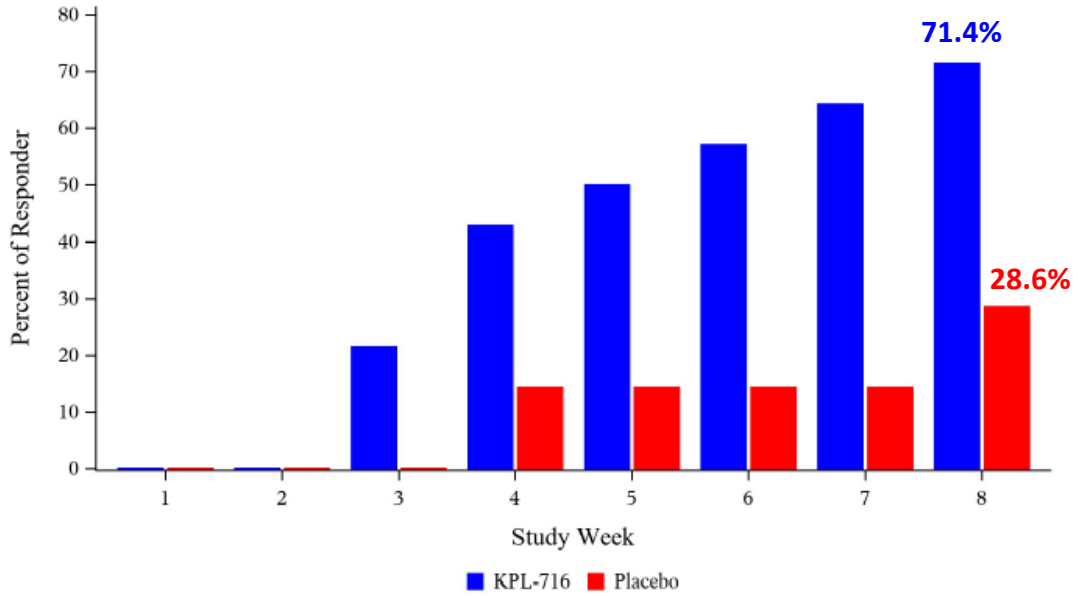


Vixarelimab = KPL-716
WI-NRS = Worst-Itch Numeric Rating Scale
Data as of May 2020

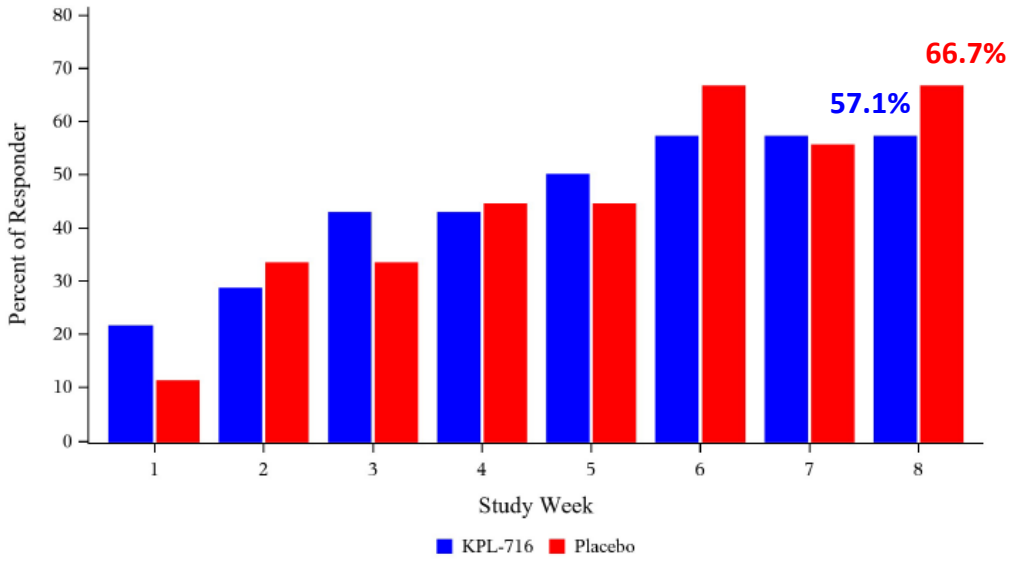
Vixarelimab Exploratory Phase 2 Study in Diseases Characterized by Chronic Pruritus: ≥ 4-Point Weekly-Average WI-NRS Reduction at Week 8

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

Plaque Psoriasis



Chronic Idiopathic Pruritus



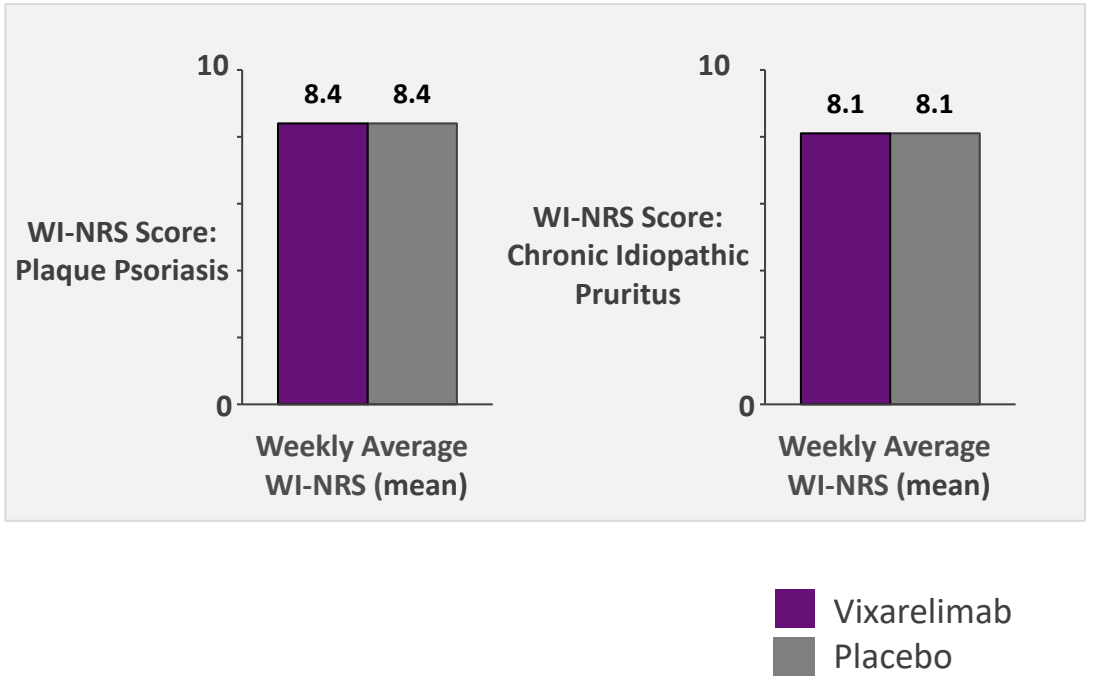
Vixarelimab = KPL-716
WI-NRS = Worst-Itch Numeric Rating Scale
Data as of May 2020

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



*mITT Analysis Set

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Appendix – KPL-404

Preliminary Data from KPL-404 Single-Ascending-Dose Phase 1 Study

The randomized, double-blind, placebo-controlled first-in-human (FIH) study is designed to investigate the safety, tolerability, PK and PD properties of single-ascending intravenous (IV) and subcutaneous (SC) doses of KPL-404 in healthy subjects.

- 2 single-ascending-dose arms (SAD):
  - Single-dose KPL-404 0.03 mg/kg, 0.3 mg/kg, 1 mg/kg, 3 mg/kg or 10 mg/kg IV and
  - Single-dose KPL-404 1 mg/kg or 5 mg/kg SC

Primary Endpoint: Safety and tolerability of single ascending intravenous (IV) and subcutaneous (SC) doses of KPL-404 in healthy subjects.

- KLH challenge in 1 mg/kg, 3 mg/kg, and 10 mg/kg IV and 1 mg/kg and 5 mg/kg SC cohorts

Secondary Endpoints: Pharmacokinetics and anti-drug antibody response following single IV and SC doses of KPL-404 in healthy subjects, receptor occupancy of KPL-404 on CD40 in healthy subjects, serum anti- keyhole limpet hemocyanin (KLH) IgG levels.

- KLH re-challenge only in 1 mg/kg, 3 mg/kg, and 10 mg/kg IV

Topline Observations:

- All dose escalations occurred as per protocol with no dose limiting safety findings. All 6 subjects dosed with KPL-404 3 mg/kg IV showed full receptor occupancy through Day 29, which corresponded with complete suppression of the T-cell Dependent Antibody Response (TDAR) to KLH through Day 29. Consistent dose relatedness was shown in the lower dose level cohorts, including 0.03 mg/kg, 0.3 mg/kg, 1 mg/kg IV and 1 mg/kg SC. Data collection for the higher dose level cohorts, 10 mg/kg IV and 5 mg/kg SC, is ongoing.
- The data to-date support subsequent study in patients, including potential IV or SC monthly administration. Kiniksa expects final data and safety follow-up from all cohorts in the first half of 2021.

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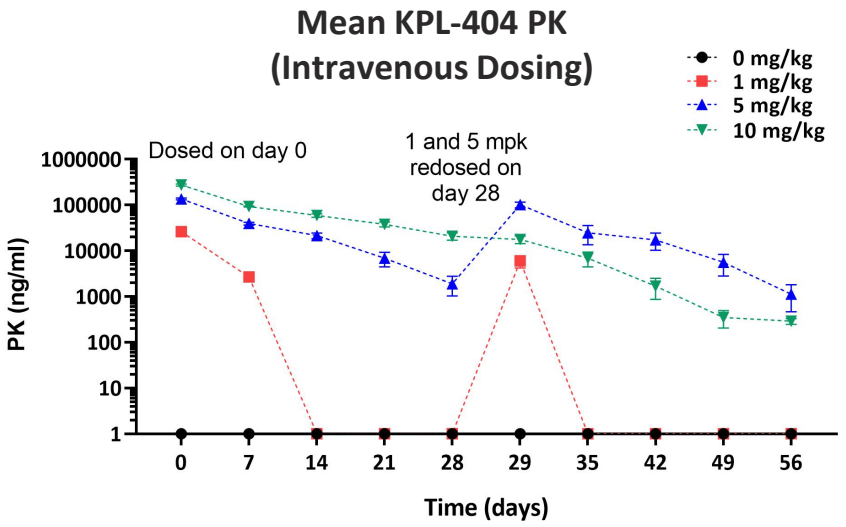
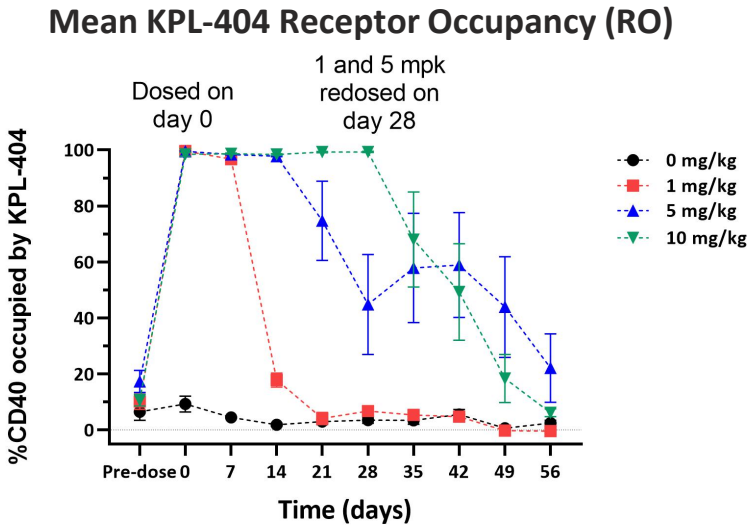
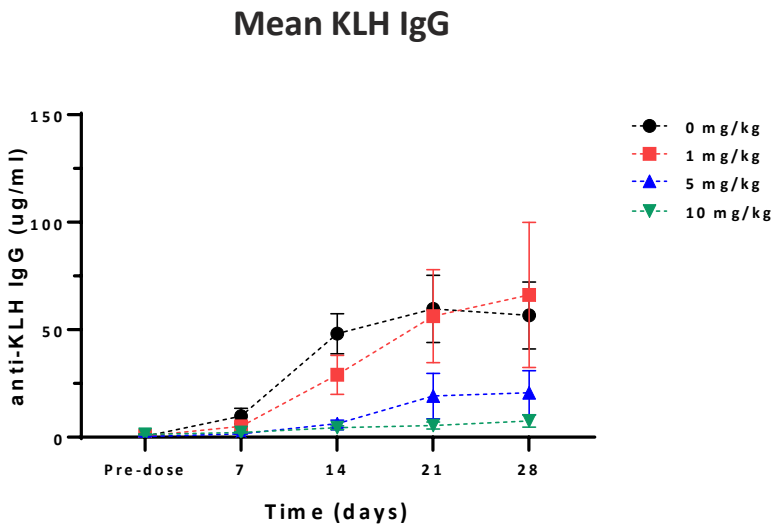
KPL-404 Showed Encouraging Results in a Non-Human Primate Model of TDAR







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

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

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

Source = 1) Poster presentation at the Keystone Symposia: Antibodies as Drugs: New Horizons in the Therapeutic Use of Engineered Antibodies: KPL-404, a CD40 antagonist, blocked antigen-specific antibody responses in an in vivo NHP model and demonstrated strong PK/PD correlation; TDAR = T-cell dependent antibody response; KLH = keyhole limpet hemocyanin

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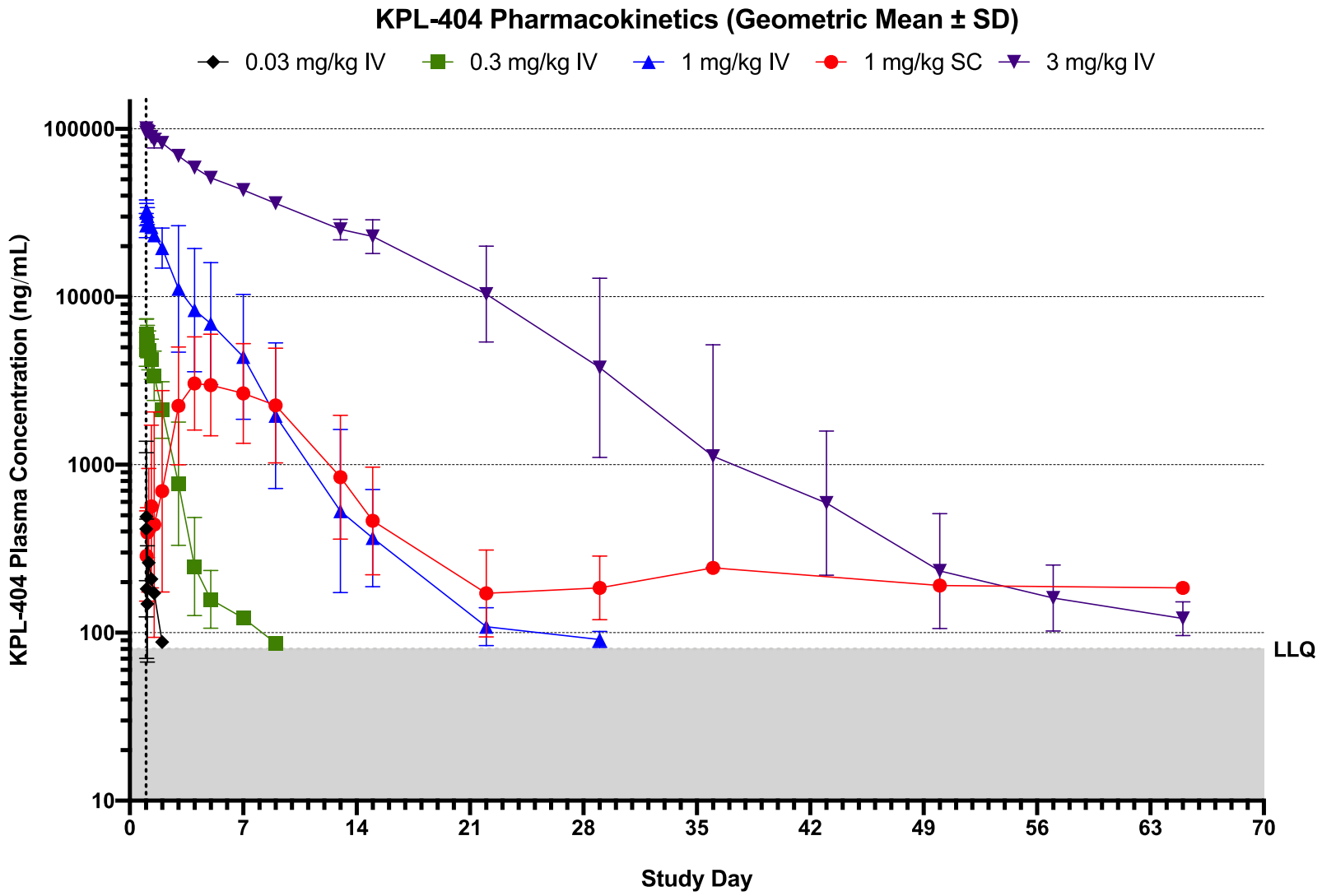
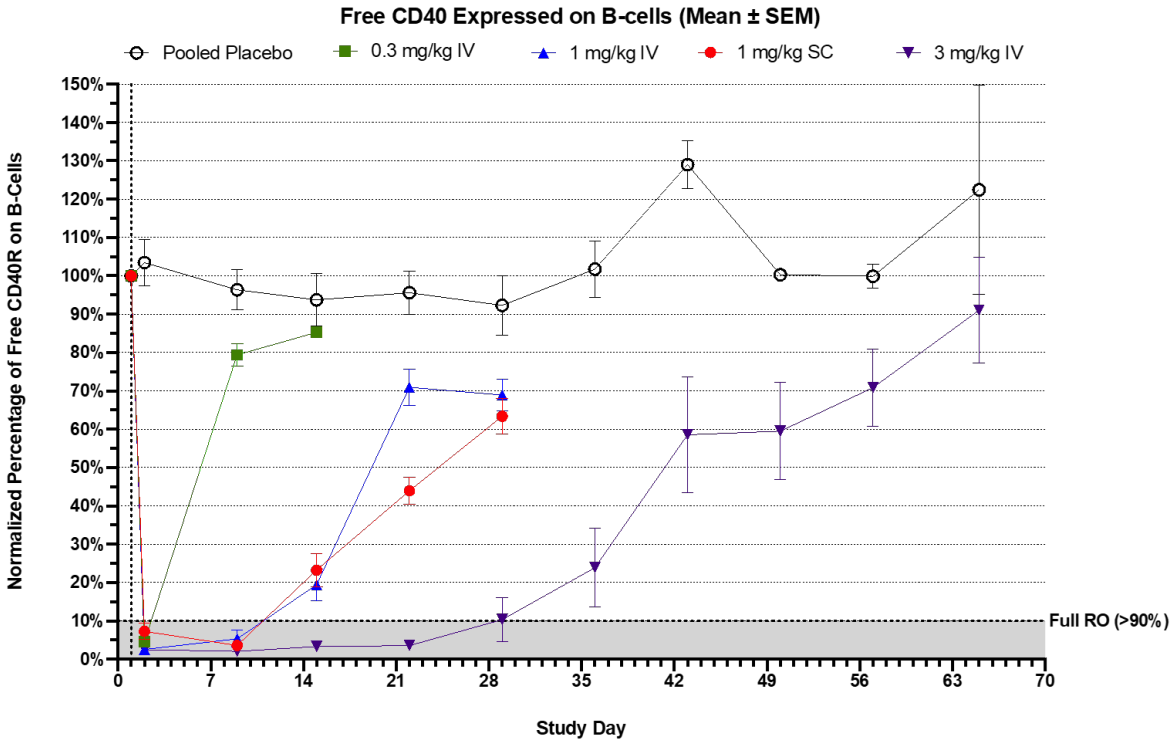
Preliminary Data from KPL-404 Single-Ascending-Dose Phase 1 Study

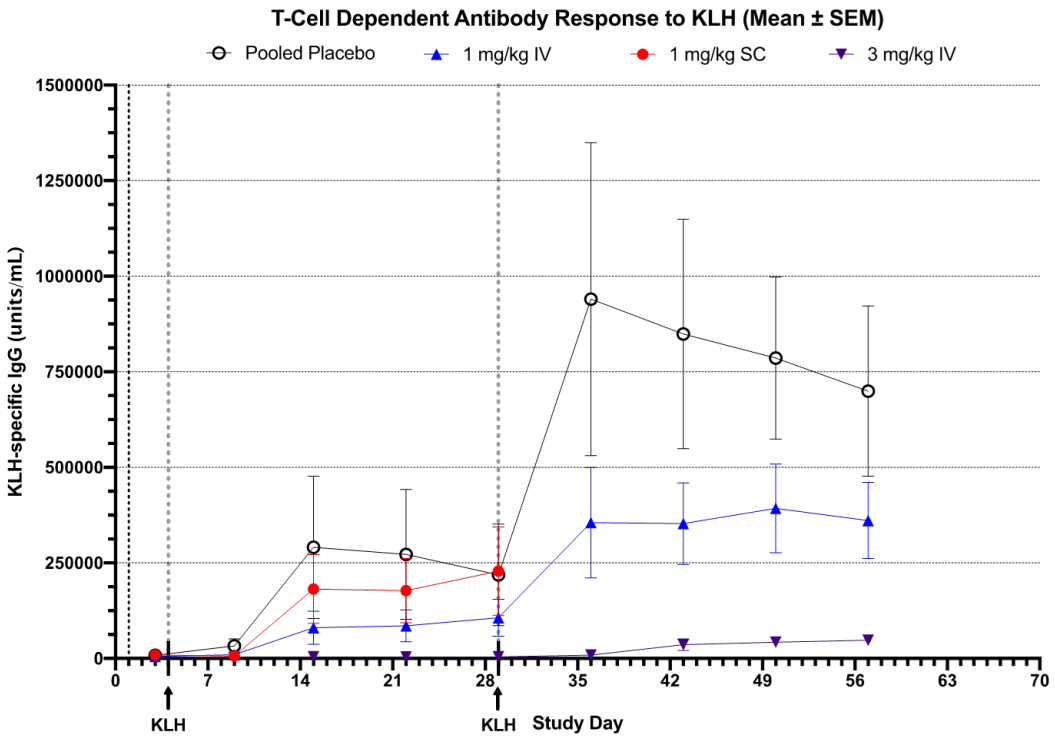
Pharmacokinetic summary



Preliminary Data from KPL-404 Single-Ascending-Dose Phase 1 Study

Receptor occupancy and KLH antigen challenge TDAR summary





1) Free CD40R = inverse of receptor occupancy; KLH = keyhole limpet hemocyanin; TDAR = T-cell dependent antibody response

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