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Every Second Counts!™

Corporate Presentation

June 2020

Forward Looking Statements

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

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

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

A Clinical-Stage Pipeline of Immune-Modulating Product Candidates

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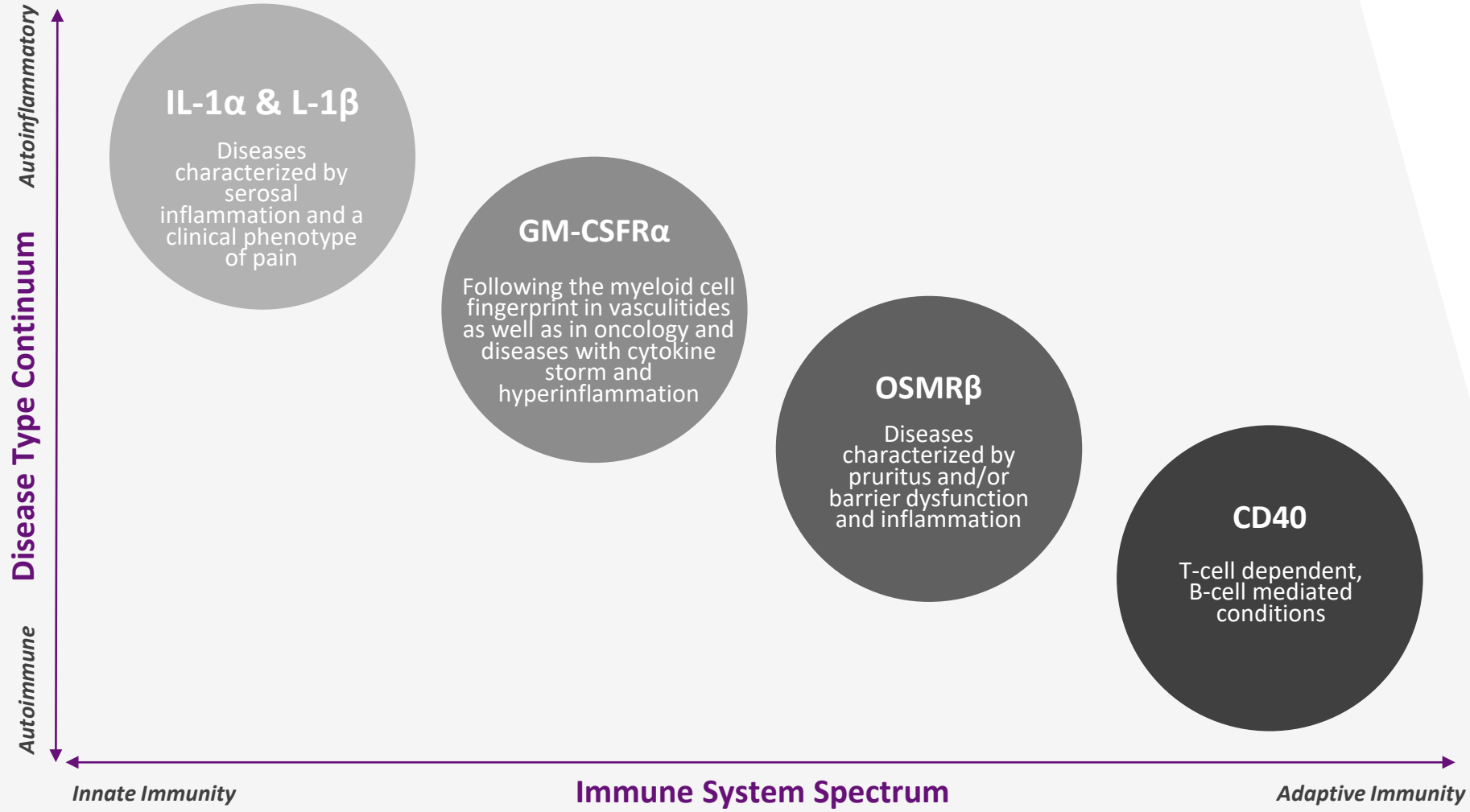
- Focused on modulating different parts of the innate and adaptive immune system
- Product candidates based on validated mechanisms and/or strong biologic rationale
- Target underserved conditions and offer potential differentiation
- Allocate capital across portfolio relative to opportunity

Development Strategy Focused on Modulating Central Nodes of the Immune System



Multiple Product Candidates and Expected Clinical Data Readouts in 2H 2020

Indication	Program & Target	Preclinical	Phase 1	Phase 2	Phase 3	Status
Recurrent Pericarditis	**Rilonacept**[1] IL-1α & IL-1β					Pivotal Phase 3 Data Expected in Q3 2020
Giant Cell Arteritis	**Mavrilimumab** GM-CSFRα					Phase 2 Data Expected in Q4 2020
CAR T Induced Cytokine Release Syndrome[2]	**Mavrilimumab** GM-CSFRα					Phase 2 Initiation Expected in 2H 2020
COVID-19 Pneumonia & Hyperinflammation	**Mavrilimumab** GM-CSFRα					Active US IND for Phase 2/3 Clinical Trial
Prurigo Nodularis	**Vixarelimab** OSMRβ					Phase 2a Data Announced in Q2 2020
Diseases Characterized by Chronic Pruritus[3]	**Vixarelimab** OSMRβ					Phase 2 Data Announced in Q2 2020
Severe Autoimmune Diseases	**KPL-404** CD40					Phase 1 Data Expected in Q4 2020

1) Rilonacept (ARCALYST®) is approved and marketed for cryopyrin-associated periodic syndrome, in the United States by Regeneron Pharmaceuticals, Inc.; 2) Clinical collaboration with Kite, a Gilead Company, in relapsed or refractory large B-cell lymphoma; 3) Chronic Idiopathic Pruritus, Chronic Idiopathic Urticaria, Plaque Psoriasis, Lichen Simplex Chronicus, Lichen Planus. IL-1α = interleukin-1α ; IL-1β = interleukin 1β; GM-CSFRα = granulocyte macrophage colony stimulating factor receptor alpha; OSMRβ = oncostatin M receptor beta

Product Candidates Based on Validated Mechanisms and/or Strong Biologic Rationale

Mechanism of Action	Rationale	Therapeutic Area
Rilonacept IL-1α and IL-1β cytokine trap	IL-1α and IL-1β cytokines shown to play key role in inflammatory diseases[1]	Phase 2 data in **recurrent pericarditis** showed resolution of pericarditis episodes, reduction in recurrences while on treatment, and tapering/discontinuation of corticosteroids[6]
Mavrilimumab monoclonal antibody inhibitor targeting GM-CSFRα	GM-CSF is a key growth factor and cytokine in autoinflammation and autoimmunity[2]	GM-CSF and GM-CSFRα have been observed to be highly expressed in biopsies of **giant cell arteritis** patients vs. normal healthy controls[7] Preclinical data suggest the potential for interruption of GM-CSF signaling to disrupt **CAR T induced cytokine release syndrome** without disrupting anti-tumor efficacy[8] 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**[9]
Vixarelimab monoclonal antibody inhibitor targeting OSMRβ	IL-31 and oncostatin M (OSM) are key cytokines implicated in chronic pruritic diseases[3,11]	Phase 2a data in **prurigo nodularis** achieved statistical significance in both reduction in weekly-average WI-NRS and attainment of PN-IGA 0/1 score at Week 8[3] Exploratory Phase 2 study in diseases characterized by chronic pruritus achieved statistically significant reduction in weekly-average WI-NRS at Week 8 in **plaque psoriasis** cohort[11]
KPL-404 monoclonal antibody inhibitor of CD40 / CD40L interaction	CD40-CD40L interaction is an attractive mechanism for targeting T-cell dependent, B-cell–mediated autoimmune diseases[4,5]	External proof-of-concept for inhibition of pathway has been established in a broad range of **autoimmune diseases**[10]

1) Dinarello CA, et al. Nat Rev Drug Discov 2012;11:633-652 and Brucato A, et al. Int Emerg Med 2018; 13:839–844; 2) Wicks, Roberts, Nature Review Immunology, 2015; Hamilton, Expert Review of Clinical Immunology, 11:4, 457-465; 3) Vixarelimab Phase 2a data in prurigo nodularis (www.investors.Kiniksa.com); 4) Elgueta, et al. Immunol Rev 2009, 229 (1), 152-172; 5) Peters, et al. Semin Immunol 2009, 21 (5) 293-300; 6) Final open-label Phase 2 data - Poster presentation at American Heart Association (AHA) Scientific Sessions 2019: Efficacy and Safety of Rilonacept in Recurrent Pericarditis: A Multicenter Phase 2 Clinical Trial; 7) Poster presentation at European Congress of Rheumatology 2019 (EULAR): *GM-CSF Pathway Signature Identified in Temporal Artery Biopsies of Patients With Giant Cell Arteritis*; 8) Sterner et al., Blood 2018; 9) Zhou et al. bioRxiv. 2020; 10) National Center for Biotechnology Information - *Targeting the CD40-CD154 Signaling Pathway for Treatment of Autoimmune Arthritis*: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6721639/; 11) Vixarelimab exploratory Phase 2 data in diseases characterized by chronic pruritus (www.investors.Kiniksa.com); WI-NRS = Worst-Itch Numeric Rating Scale; PN-IGA = prurigo nodularis-investigator's global assessment

Product Candidates Target Underserved Diseases and Offer Potential Differentiation

Recurrent Pericarditis	• No FDA-approved therapies • **Rilonacept:** IL-1α and IL-1β cytokine trap offers potential dosing, tolerability and mechanistic benefit relative to other marketed IL-1 agents[1]
Giant Cell Arteritis	• Only one FDA-approved therapy and unmet need remains • **Mavrilimumab:** GM-CSFRα inhibition may offer upstream blockade and potential to address underlying mediator of inflammation
CAR T Induced CRS	• Only one FDA-approved therapy for CAR T induced cytokine release syndrome (CRS) and unmet need remains • **Mavrilimumab:** GM-CSFRα blockade potentially prevents pathogenic cells from infiltrating into the target tissue, and suppresses multiple pro-inflammatory cytokines (e.g., IL-2Rα, IL-6, CRP)[2,3,4]
COVID-19 Pneumonia & Hyperinflammation	• Only one anti-viral therapy available under FDA emergency use authorization for COVID-19 and unmet need remains • **Mavrilimumab:** GM-CSFRα blockade potentially prevents pathogenic cells from infiltrating into the target tissue, and suppresses multiple pro-inflammatory cytokines (e.g., IL-2Rα, IL-6, CRP)[2,3,4]
Prurigo Nodularis	• No FDA-approved therapies • **Vixarelimab (KPL-716):** First-in-class mechanism designed to inhibit IL-31 and OSM, two pathways shown to be upregulated in diseased skin
Severe Autoimmune Diseases	• External proof-of-concept for inhibition of CD40-CD40L pathway established in patients with Sjogren's disease, systemic lupus, rheumatoid arthritis, liver transplant and Grave's disease[5] • **KPL-404:** Potential differentiation vs. competition

1) Dinarello CA, et al. Nat Rev Drug Discov 2012;11:633-652; 2) De Alessandris et al., J Leukoc Biol. 2019; 3) Sterner et al., Blood 2019; 4) Guo et al., Rheumatology 2017; 5) National Center for Biotechnology Information - Targeting the CD40-CD154 Signaling Pathway for Treatment of Autoimmune Arthritis: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6721639/

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Rilonacept

Indication[1]	**Recurrent Pericarditis:** Painful and debilitating autoinflammatory cardiovascular disease
Mechanism of Action[2]	IL-1α and IL-1β cytokine trap
Scientific Rationale[2]	IL-1α and IL-1β are cytokines shown to play key role in inflammatory diseases
Prevalence[3]	~40k prevalent in U.S.; addressable opportunity of ~14k in U.S.
Competition[4]	No FDA-approved therapies for recurrent pericarditis
Status	Breakthrough Therapy designation granted; data from pivotal Phase 3 clinical trial expected in Q3 2020
Economics	Regulatory milestones; 50/50 profit split upon commercialization excluding certain expenses
Rights	BLA transfers to Kiniksa after receipt of positive Phase 3 clinical data; upon approval Kiniksa has the rights to recurrent pericarditis worldwide (excluding MENA)

1) Rilonacept (ARCALYST®) is approved and marketed for cryopyrin-associated periodic syndrome (CAPS), in the United States by Regeneron Pharmaceuticals, Inc.; 2) Brucato et al. JAMA. 2016, 316 (18): 1906-1912; Arcalyst Prescribing Information; 3) 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; 4) 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;

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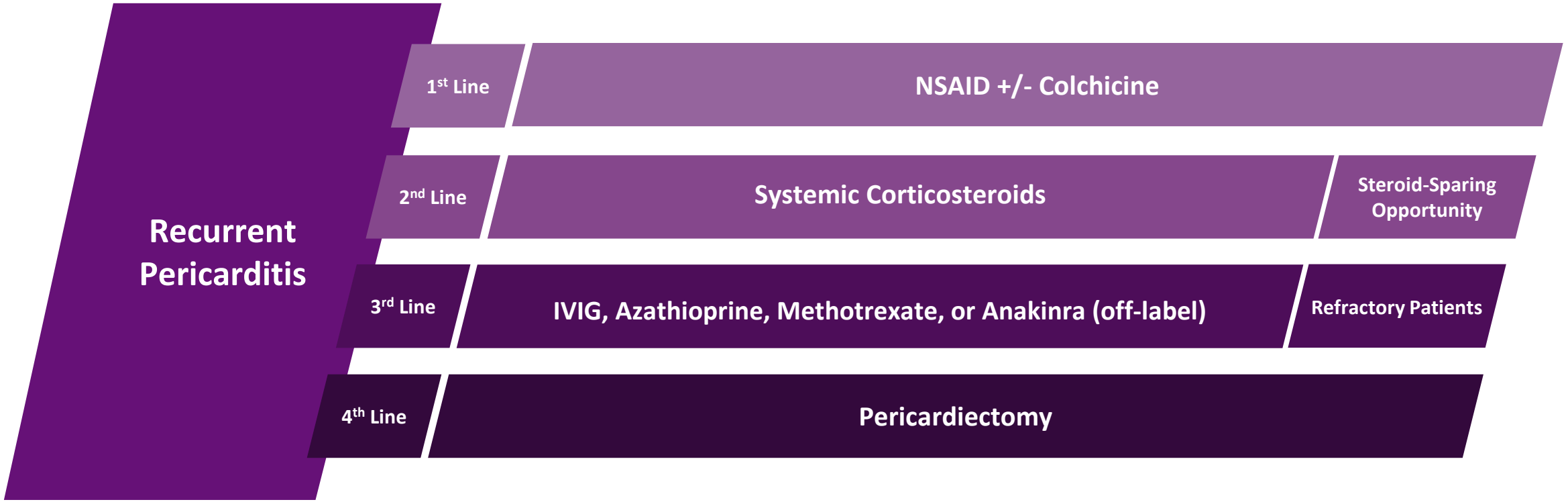
Recurrent Pericarditis Patients Currently Have Limited Treatment Options

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

Key Areas of Unmet Need in Patients with Recurrent Pericarditis

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

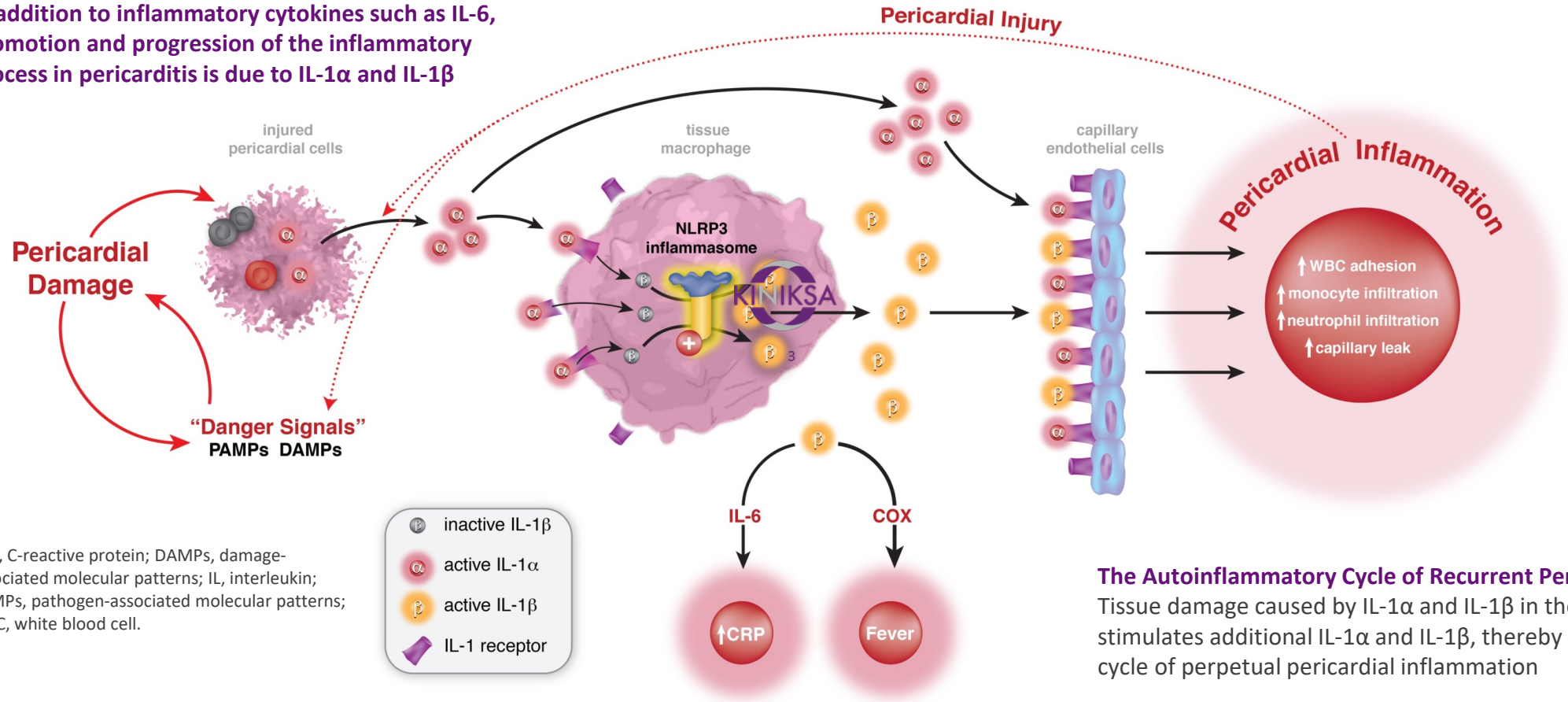
"The worst thing about pericarditis is its unpredictability and its chronicity. It's a permanent condition, so it has the potential to impact everything…work, exercise, family plans, travel."

- Patient quote, 2019

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

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

Clinical Development Plan for Rilonacept in Recurrent Pericarditis

Designed to generate data on clinically meaningful outcomes

Phase 2

- Open-label, 5-part clinical trial with rilonacept in range of recurrent pericarditis populations
- Provided first evidence that rilonacept treatment improved clinically meaningful outcomes in study[1]
- Rilonacept was well-tolerated in study, with safety results consistent with FDA-approved label for CAPS[2]

Completed

Phase 3 (RHAPSODY)

- **Enrollment completed**
- Pivotal clinical trial of rilonacept for treatment of recurrent pericarditis
- 24-week, double-blind, placebo-controlled, randomized-withdrawal (RW) study with open-label extension
- Primary efficacy endpoint is time-to-first-adjudicated pericarditis-recurrence in the RW period

Data expected Q3 2020

Rilonacept in Recurrent Pericarditis is for Investigational Use Only; Kiniksa Clinical Protocols, Phase 2: KPL-914-C001, Phase 3: KPL-914-C002; NCT03737110

1) Final open-label Phase 2 data - Poster presentation at American Heart Association (AHA) Scientific Sessions 2019: *Efficacy and Safety of Rilonacept in Recurrent Pericarditis: A Multicenter Phase 2 Clinical Trial;*

2) CAPS = Cryopyrin-Associated Periodic Syndromes

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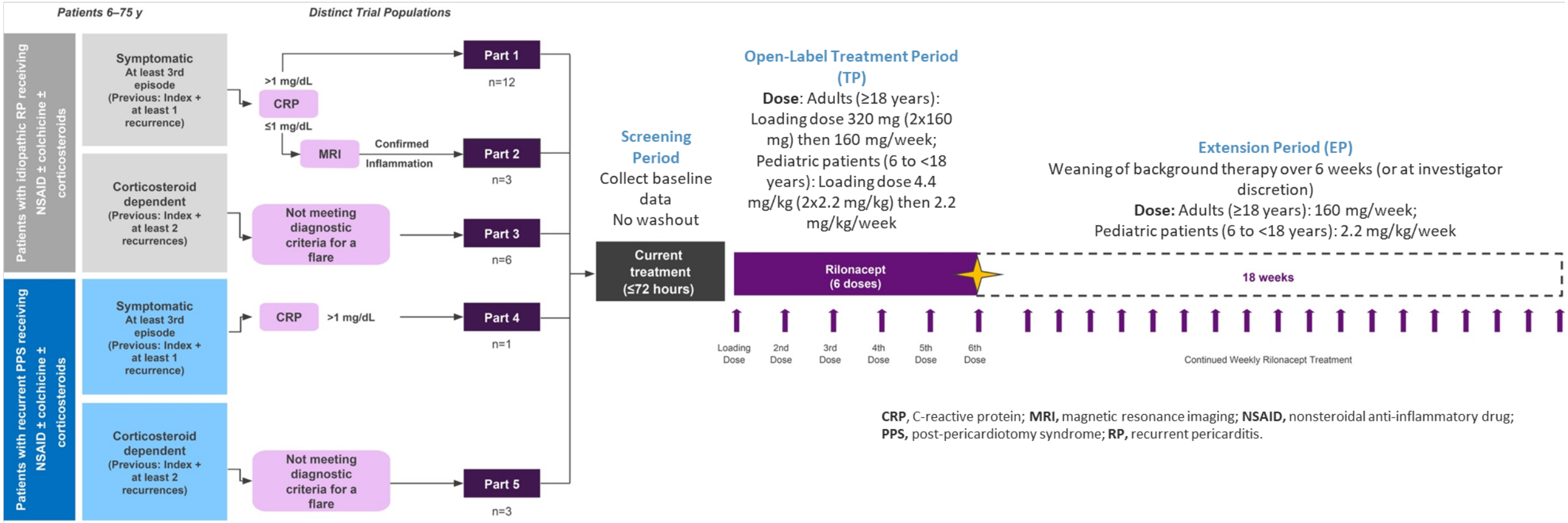
Open-Label Phase 2 Clinical Trial of Rilonacept in Pericarditis Populations



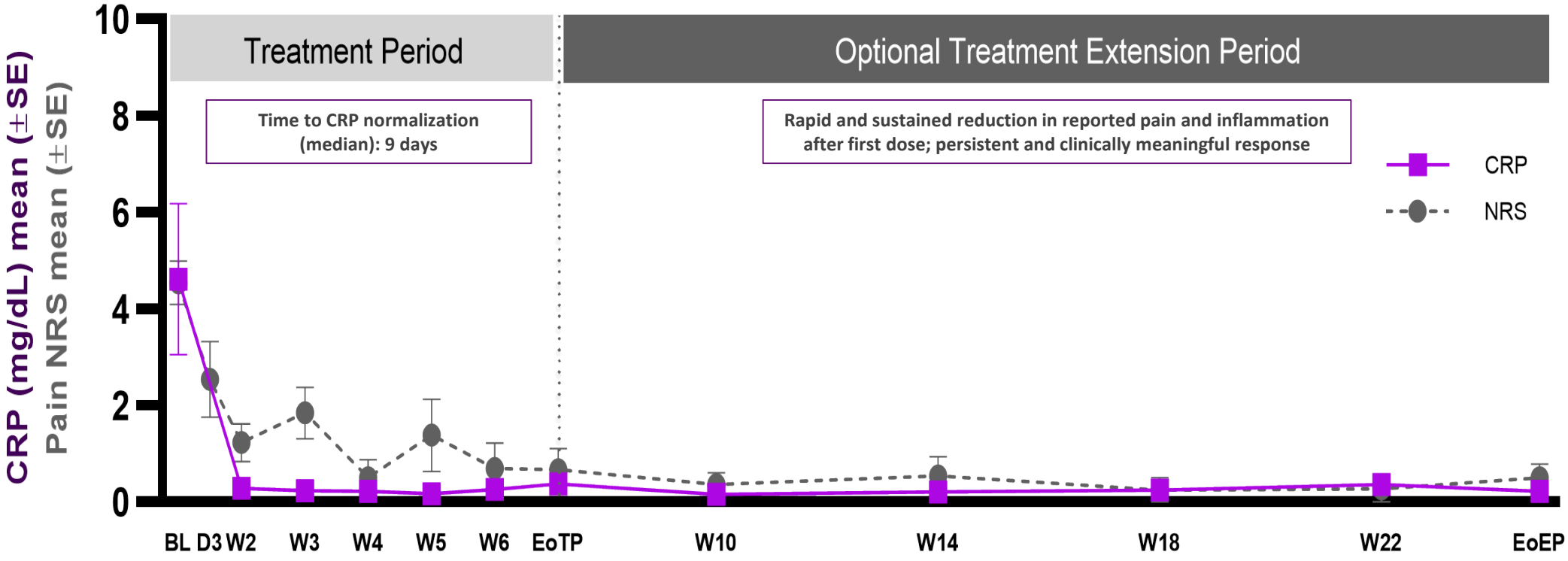
CRP, C-reactive protein; **MRI,** magnetic resonance imaging; **NSAID,** nonsteroidal anti-inflammatory drug; **PPS,** post-pericardiotomy syndrome; **RP,** recurrent pericarditis.

Rilonacept in Recurrent Pericarditis is for Investigational Use Only; Clinicaltrials.gov: NCT03980522
Klein A. Et al. Circulation. 2019;140:A12851 | AHA Scientific Sessions 2019: Poster SA1094

Phase 2 Rilonacept Data

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

Symptomatic Recurrent Pericarditis Patients with Elevated CRP[1] (n=13)



		BL	D3	W2	W3	W4	W5	W6	EoTP	W10	W14	W18	W22	EoEP
CRP	# of Patients	13		11	13	8	12	7	12	11	10	7	11	12
	CRP Mean	4.62		0.29	0.23	0.22	0.17	0.27	0.38	0.16	0.22	0.25	0.37	0.22
Pain NRS	# of Patients	13	11	13	13	8	13	10	9	11	11	8	11	12
	Pain Mean	4.5	2.5	1.2	1.8	0.5	1.4	0.7	0.7	0.4	0.5	0.3	0.3	0.5

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

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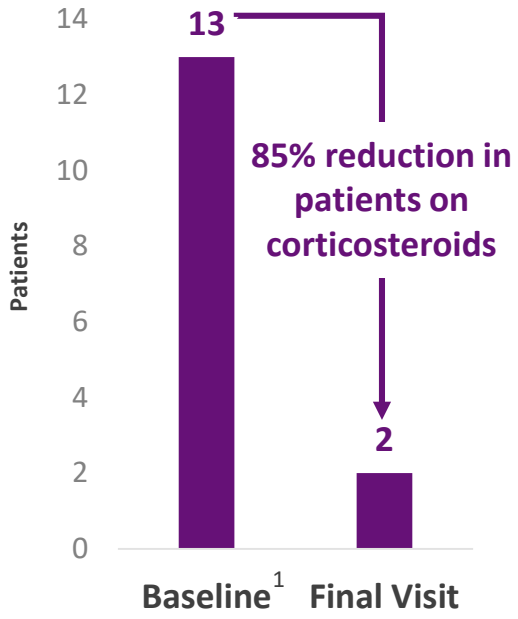
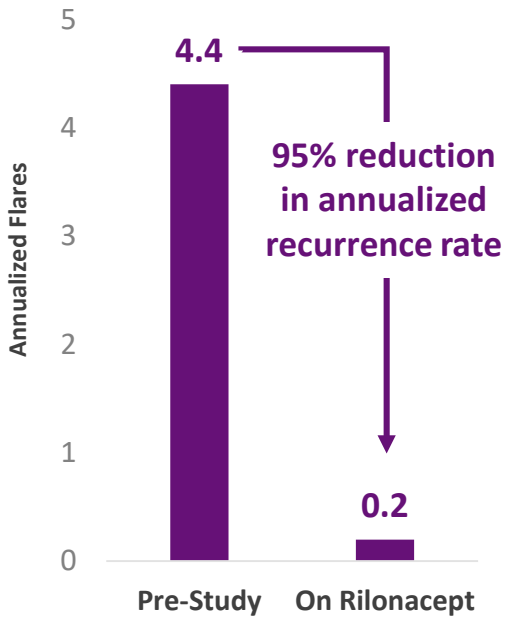
Phase 2 Rilonacept Data

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

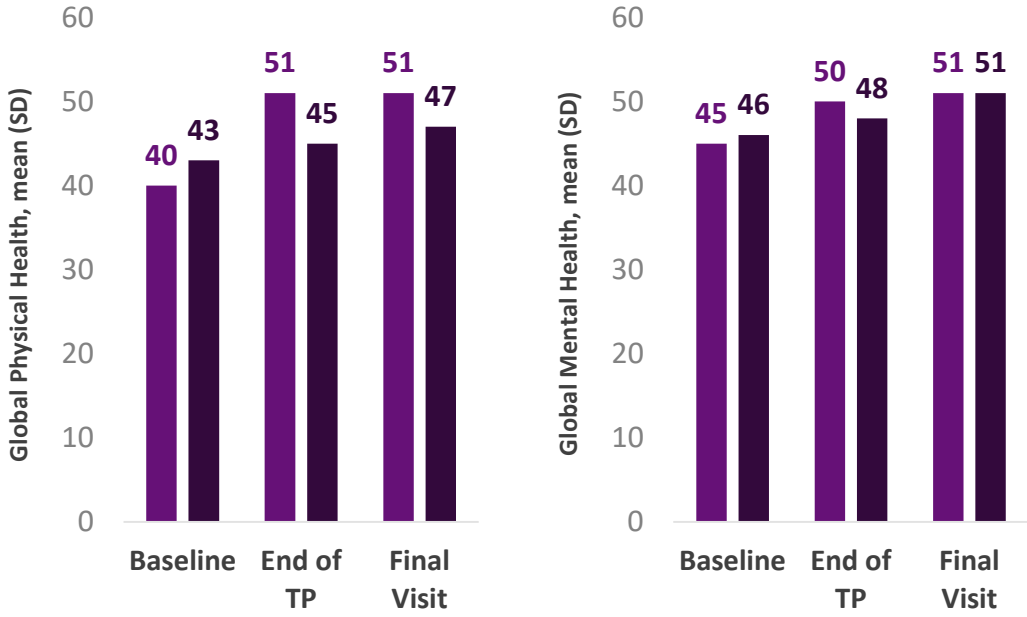
Discontinuation of Corticosteroids Without Pericarditis Recurrence



Decrease in Annualized Incidence of Pericarditis Episodes While on Treatment



Improved Quality of Life Scores[2]



Idiopathic or PPS: Active[3] (n=16) CS-dependent[4] (n=9)

1) 15 recurrent pericarditis patients on corticosteroids at baseline enrolled in the 6-week base treatment period, and 13 continued into the optional 18-week extension treatment period and completed 24 weeks of treatment; 2) PROMIS® - Patient Reported Outcomes Measurement Information System. The higher the score, the better global health is. US national average score for Global Physical and Mental Health is 50 (SD 10); 3) Parts 1, 2, and 4; 4) Parts 3 and 5

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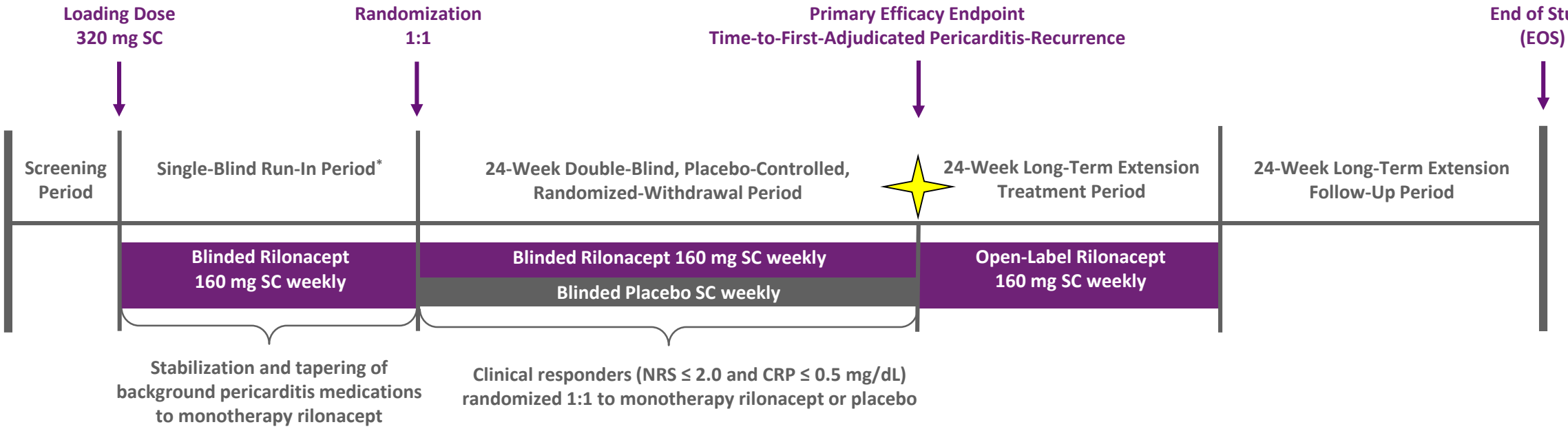
Pivotal Phase 3 Clinical Trial of Rilonacept for Recurrent Pericarditis



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 Outcome Measure (24 weeks):

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

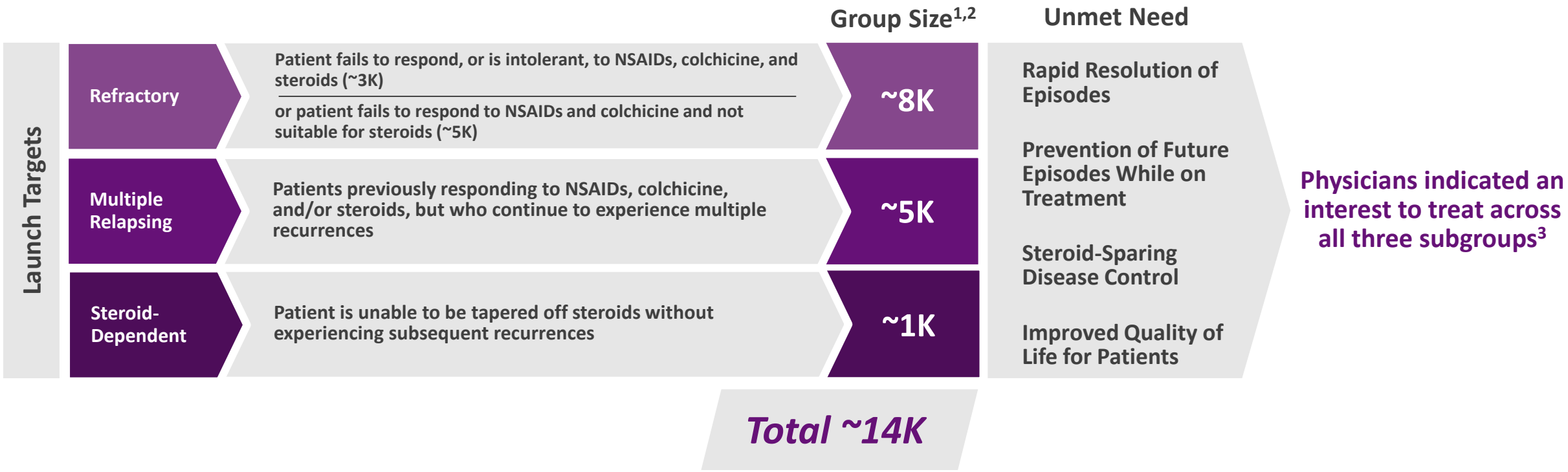
Secondary Outcome Measures (24-weeks):

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

* Duration of the run-in period undisclosed in order to maintain study subjects blinded to the start of the randomized-withdrawal period.

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

Addressable U.S. opportunity for rilonacept estimated to be ~14K patients

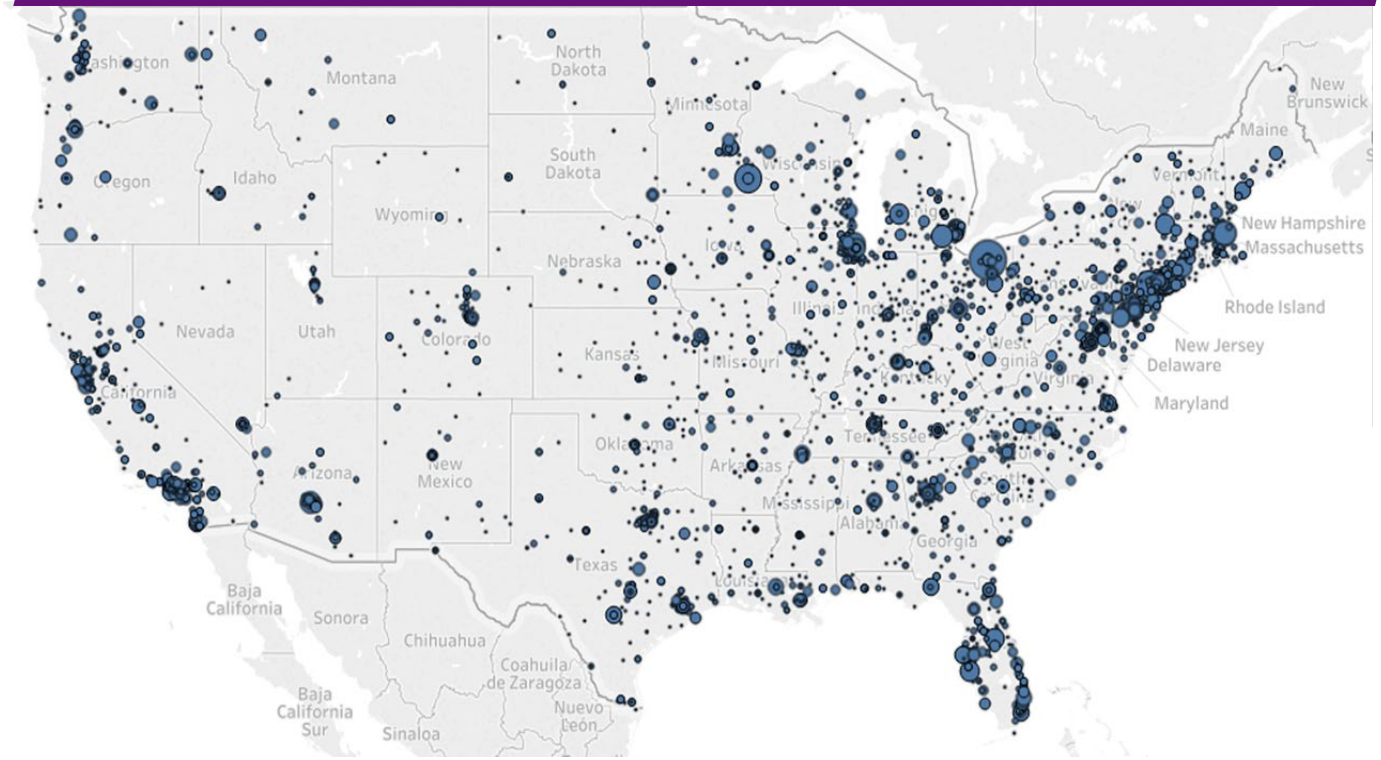


1) Klein A, Cremer P, Kontzias A, Furqan M, Tubman R, Roy M, Magestro M. Annals of Epidemiology. 2019;36:71; 2) Lin D, Majeski C, DerSarkissian M, Magestro M, Cavanaugh C, Laliberte F, Lejune D, Mahendran M, Duh M, Klein A, Cremer P, Kontzias A, Furqan M, Tubman R, Roy M, Mage. (Nov, 2019). *Real-World 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

Commercial Strategy

Potential launch would focus on high-volume specialists

Recurrent Pericarditis Patient Volume by Account



Commercialization Plan Linked to Opportunity

- Specialty cardiology sales force of ~30 reps to call on high volume specialists
- Supported by current MSL team
- Efficient digital marketing to educate lower volume specialists
- Patient services capabilities to maintain appropriate patients on therapy
- Duration of therapy expected to be at least 6-12 months
- Pricing in-line with high unmet need in rare disease

Source: IQVIA HPD Targeting Data, Komodo INTERGRITY Data, & Decision Resources Group RWD Data
Dataset generated by Kiniksa analysis

Summary of Rilonacept Profit Share Arrangement with Regeneron[1]

Rilonacept Net Sales (CAPS + Recurrent Pericarditis)[2]

Minus 100% of Cost of Goods Sold[3]

Minus 100% of Certain Maintenance Costs

Minus 100% of Field Force Costs

Minus Marketing & Certain Other Commercial Expenses (Subject to Specified Limits)

Calculated Rilonacept Operating Profit to be Shared

Minus 50% of Shared Rilonacept Operating Profit (Booked as COGS on P&L)

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 Rilonacept

- Upfront payment: $5 million
- Future regulatory milestones: $27.5 million in aggregate
- Kiniksa covers 100% of development expenses related to approval of additional indications
- In the U.S. and Japan, the initial license covers all indications other than CAPS[4], DIRA[5], oncology, and local application for eye and inner ear
- Kiniksa has rights to develop and commercialize rilonacept in our field worldwide, with the exception of MENA[6]
- After receipt of positive Phase 3 clinical data, the BLA[7] for rilonacept transfers to Kiniksa
- Upon approval for a new indication, the scope of the license expands to include CAPS and DIRA in the US and Japan, and we will assume the sales and distribution of rilonacept in these additional indications
- Profits on sales of rilonacept will be equally split after deducting certain commercialization expenses subject to specified limits

1) Subject to description contained in definitive agreement; 2) Global net sales for CAPS and recurrent pericarditis recognized as revenue on Kiniksa's income statement; 3) Including cost of product purchased from Regeneron; 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

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Mavrilimumab

Indications	**Giant Cell Arteritis (GCA):** Chronic inflammatory disease of medium-to-large arteries **CAR T Induced Cytokine Release Syndrome (CRS)[7]** **Severe COVID-19 Pneumonia and Hyperinflammation**
Mechanism of Action[1]	Monoclonal antibody inhibitor targeting GM-CSFRα
Scientific Rationale[2]	GM-CSF is a key growth factor and cytokine in autoinflammation and autoimmunity
Prevalence	GCA[3]: ~75k - 150k prevalent in U.S.; similar prevalence in other major markets CAR T Induced CRS in R/R LBCL[4]: ~7,500 in U.S. COVID-19 Pneumonia and Hyperinflammation (based on ARDS associated w/ the seasonal flu)[5]: ~150,000 in U.S.
Competition[6]	Only one FDA-approved therapy for GCA, CAR T induced CRS and COVID-19, but unmet needs remain
Status	Phase 2 data in GCA expected in Q4 2020; Phase 2 initiation in CAR T Induced CRS expected in 2H 2020; Active US IND for Phase 2/3 clinical trial in severe COVID-19 pneumonia and hyperinflammation
Economics	Clinical, regulatory and sales milestones; tiered royalty on annual net sales
Rights	Worldwide

1) Wicks, Roberts, Nature Review Immunology, 2015; Hamilton, Expert Review of Clinical Immunology, 11:4, 457-465; 2) Wicks & Roberts. Nature Reviews. Rheumatology, 2016; 12(1):37-48; 3) Chandran et al., Scand J Rheumatol, 2015; Trinity Consulting – HCUP/Medicare Data, Quantitative Survey (n=102 rheumatologists); 4) Kite, a Gilead Company, press release: http://www.businesswire.com/news/home/20171018006639/en/; 5) https://www.cdc.gov/flu/about/burden/index.html; https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3192778/ ; https://www.atsjournals.org/doi/pdf/10.1164/rccm.201401-0066LE; https://pdfs.semanticscholar.org/f3cb/d0574dc85304366dfadbd477b5eb7a271f43.pdf; https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3198489/ ; 6) Cortellis,;UpToDate; Correspondence, Trial of Tocilizumab in Giant-Cell Arteritis, NEJM, 2017; 7) Clinical collaboration with Kite, a Gilead Company, in relapsed or refractory large B-cell lymphoma (R/R LBCL)

Clinical Development Plan for Mavrilimumab

Phase 2
Giant Cell Arteritis

- **Enrollment completed**
- 26-week, double-blind, randomized, placebo-controlled clinical trial of mavrilimumab with a corticosteroid taper in subjects with new-onset or refractory GCA
- Primary efficacy endpoint involves measuring GCA flares during 26-week treatment period

Data expected 2H 2020

Phase 2
CAR T Induced Cytokine Release Syndrome

- **Clinical collaboration with Kite, a Gilead Company**
- Study of mavrilimumab with Yescarta®[1] (axicabtagene ciloleucel) in patients with relapsed or refractory large B-cell lymphoma
- Preclinical evidence suggests the potential for granulocyte macrophage colony stimulating factor (GM-CSF) to disrupt chimeric antigen receptor T (CAR T) cell mediated inflammation without disrupting anti-tumor efficacy[2]

Initiation expected 2H 2020

Phase 2/3
Severe COVID-19 Pneumonia and Hyperinflammation

- **Active investigational new drug (IND) application with the U.S. Food and Drug Administration (FDA) for a Phase 2/3 clinical trial of mavrilimumab in severe COVID-19 pneumonia and hyperinflammation.**
- **Placebo-controlled investigator-initiated study in the U.S. enrolling patients**
- Evidence of treatment response with mavrilimumab observed in an open-label treatment protocol in 13 non-mechanically ventilated patients with severe COVID-19 pneumonia and hyperinflammation in Italy[3]

Active US IND for Phase 2/3 Trial

1) Yescarta® is a registered trademark of Gilead Sciences, Inc., or its related companies; 2) Sterner, et al. Blood, 2019 Feb 14;133(7):697-709; 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

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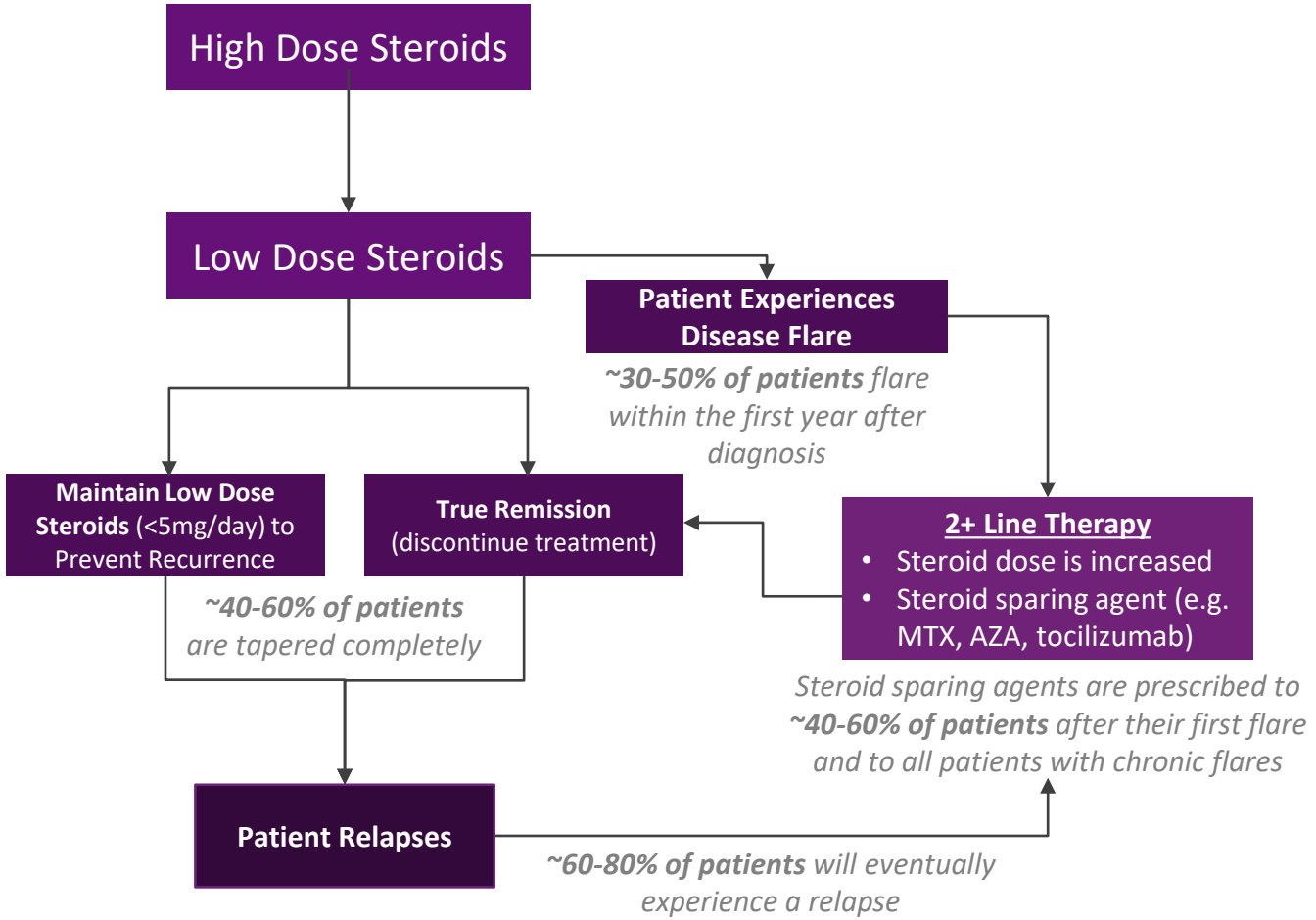
Current Treatment Paradigm for GCA Involves High-Dose Steroids Upon Clinical Suspicion

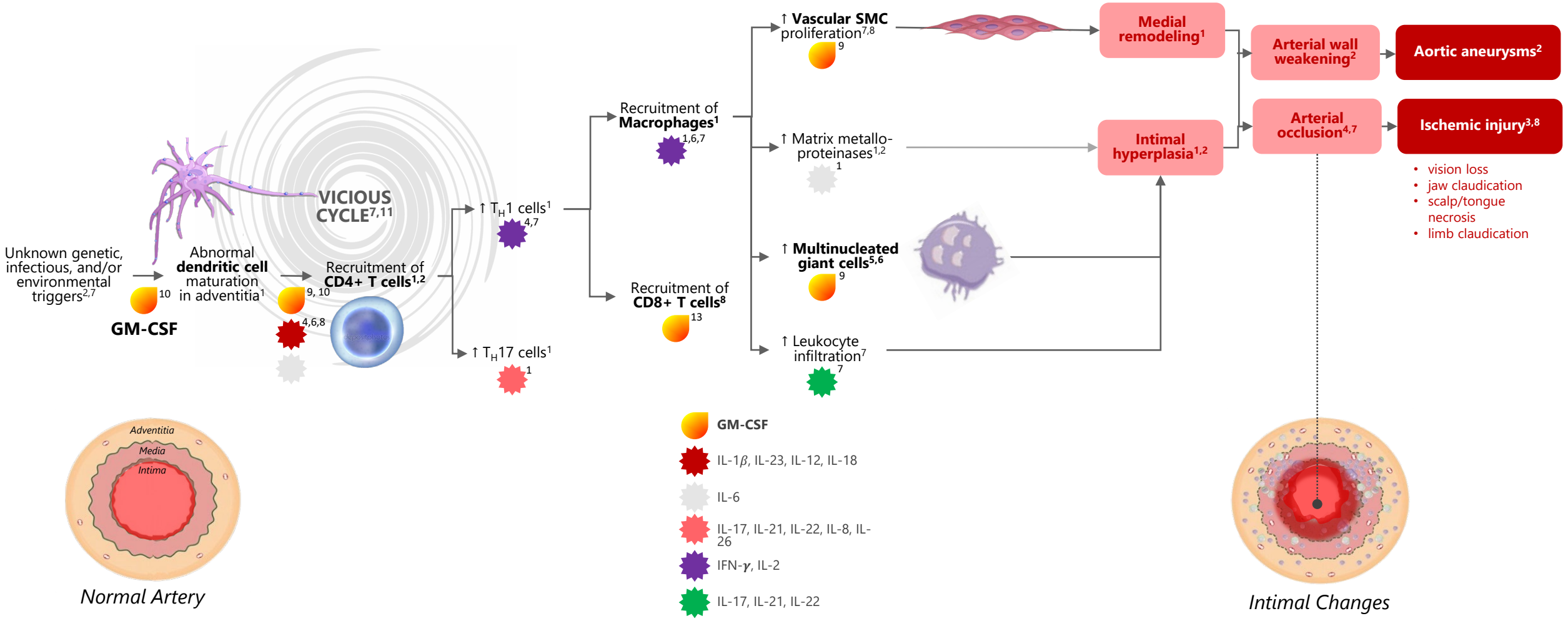


Treatment Approach:

- 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)

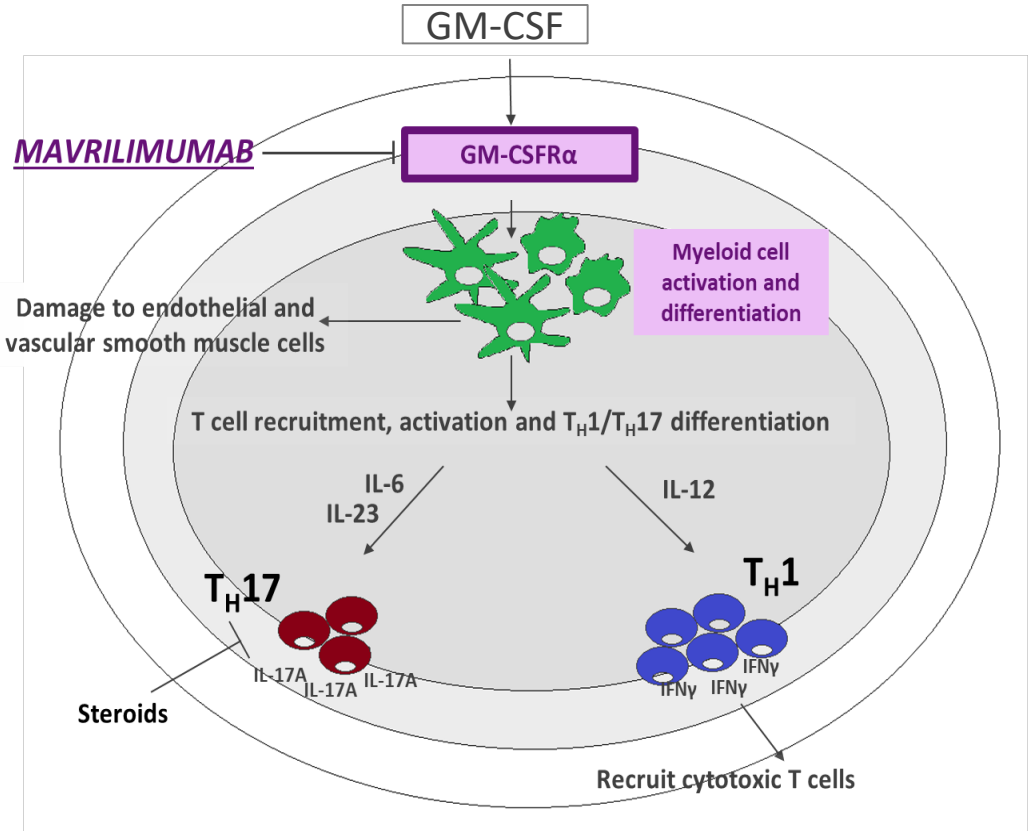
Central Role of GM-CSF in Pathophysiology of Giant Cell Arteritis



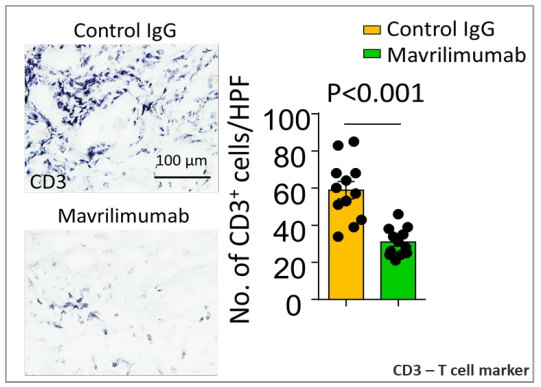
1. Al-Mousawi AZ, et al. Ophthalmol Ther 2019;8:177-193. 2. Boura P, et al. Updates in the Diagnosis and Treatment of Vasculitis. Chapter 4 2013; http://dx.doi.org/10.5772/55222. 3. Cho HJ, et al. Disease-a-Month 2017;63:88-91. 4. Ly KH, et al. Autoimm Review 2010;9:635-645. 5. Lazarewicz K, et al. BMJ 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.

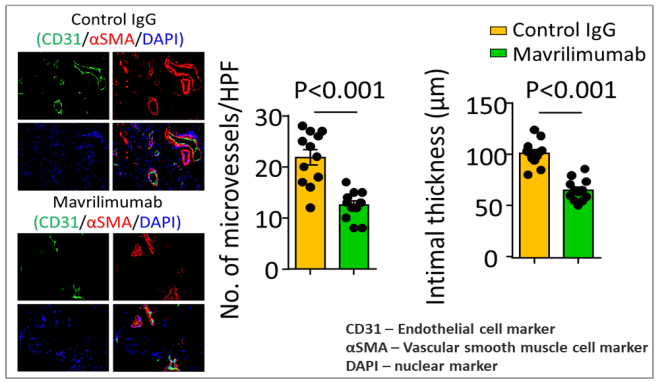
Preclinical Data Support the Mechanistic Rationale of Targeting GM-CSF in GCA

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

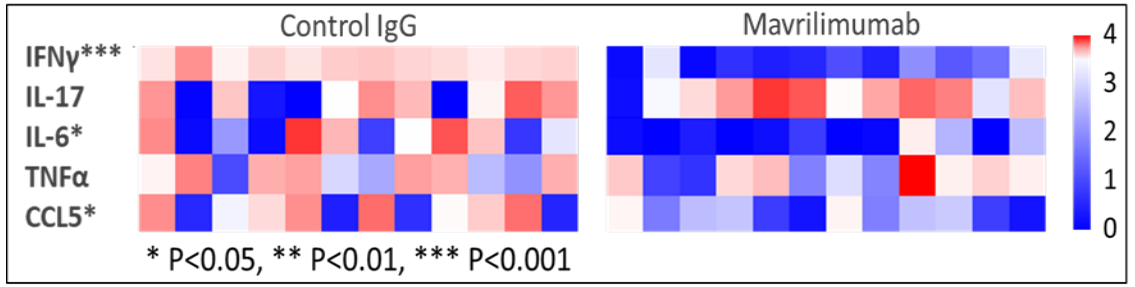


Mavrilimumab reduced arterial inflammation compared to control in an *in vivo* model of vasculitis[2]



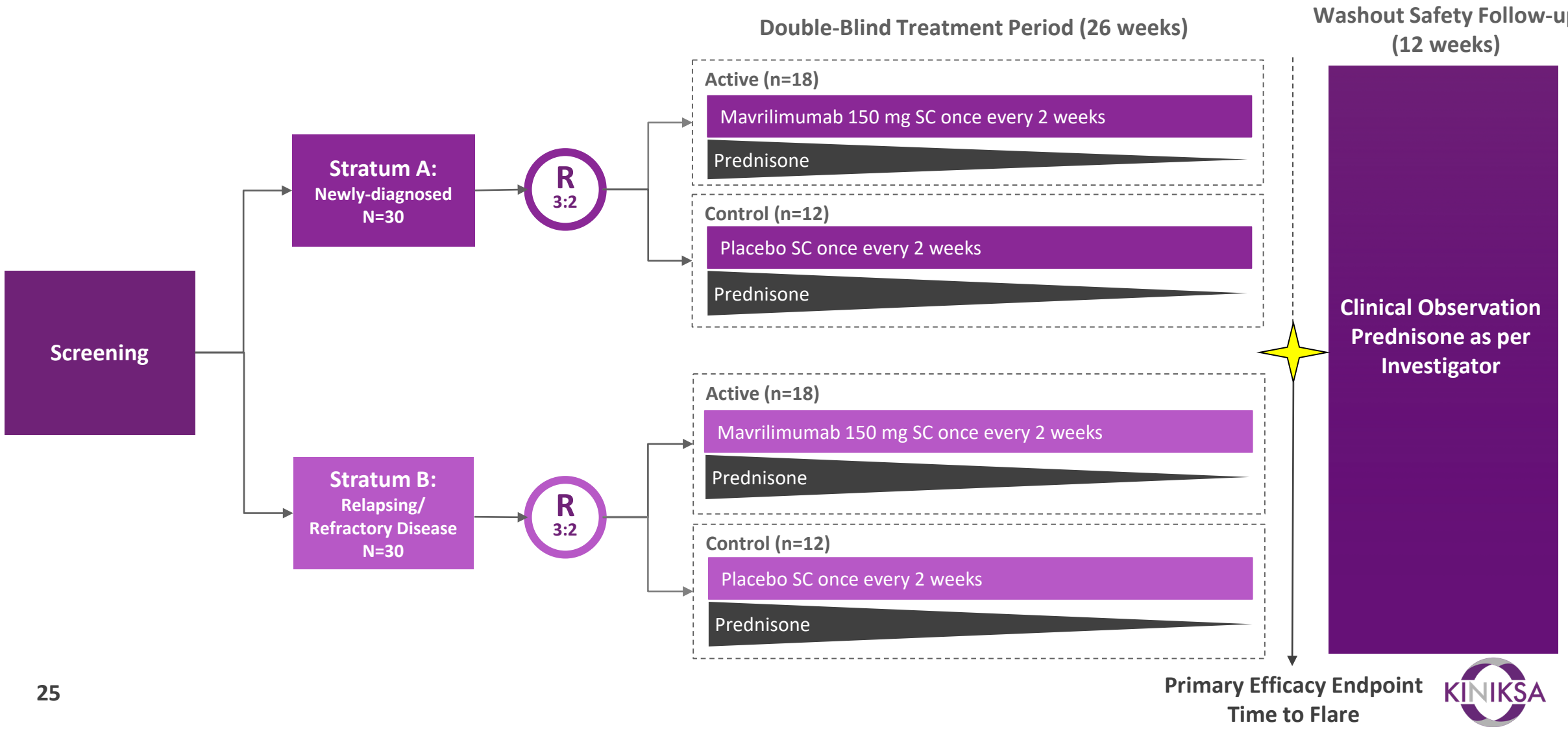


Mavrilimumab suppressed expression of inflammatory genes in artery



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

Phase 2 Clinical Trial of Mavrilimumab in GCA



Mavrilimumab: Potential to Advance Clinical Profile of CAR T Cell Therapy

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	• Treatment related induction of GM-CSF has been identified through clinical, translational and preclinical studies as a potential key signal associated with side effects of chimeric antigen receptor T (CAR T) cell therapy[2]
Preclinical and Clinical Data	• Preclinical data suggest the potential for interruption of GM-CSF signaling to disrupt CAR T cell mediated inflammation without disrupting anti-tumor efficacy[3] • Correlative data from YESCARTA®[4] (axicabtagene ciloleucel) pivotal trials suggest that elevated GM-CSF levels are linked to development of Grade 3+ neurologic events (NEs)[2]
Differentiation	• Mavrilimumab is believed to be the only GM-CSF receptor blocker; other anti-GM-CSF mechanisms 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] • One currently approved treatment of CAR T induced CRS, data suggest that its use as a prophylactic may increase rates of severe NE[8]
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 • Clinical collaboration with Kite, a Gilead Company, to evaluate the investigational combination of Yescarta and mavrilimumab in relapsed or refractory large B-cell lymphoma. The objective of the trial is to evaluate the effect of mavrilimumab on the safety of Yescarta. Expected to commence a Phase 2 trial in the second half of 2020

1) Wicks, Roberts, Nature Review Immunology, 2015; Hamilton, Expert Review of Clinical Immunology, 11:4, 457-465; 2) Neelapu et al., NEJM 2017; Sterner et al., Blood 2019; Roberts ZJ et al., Leukemia Lymphoma 2018 3) Sterner et al., Blood 2019 ; 4) Yescarta® is a registered trademark of Gilead Sciences, Inc., or its related companies; 5) De Alessandris et al., J Leukoc Biol. 2019; 6) Sterner et al., Blood 2019; 7) Guo et al., Rheumatology 2017; 8) Locke et al., Preliminary Results of Prophylactic Tocilizumab After (Axi-cel;KTE-C19) Treatment for Patients with Refractory, Aggressive NHL, Poster 1547; CRS = cytokine release s syndrome; NE = neurologic events

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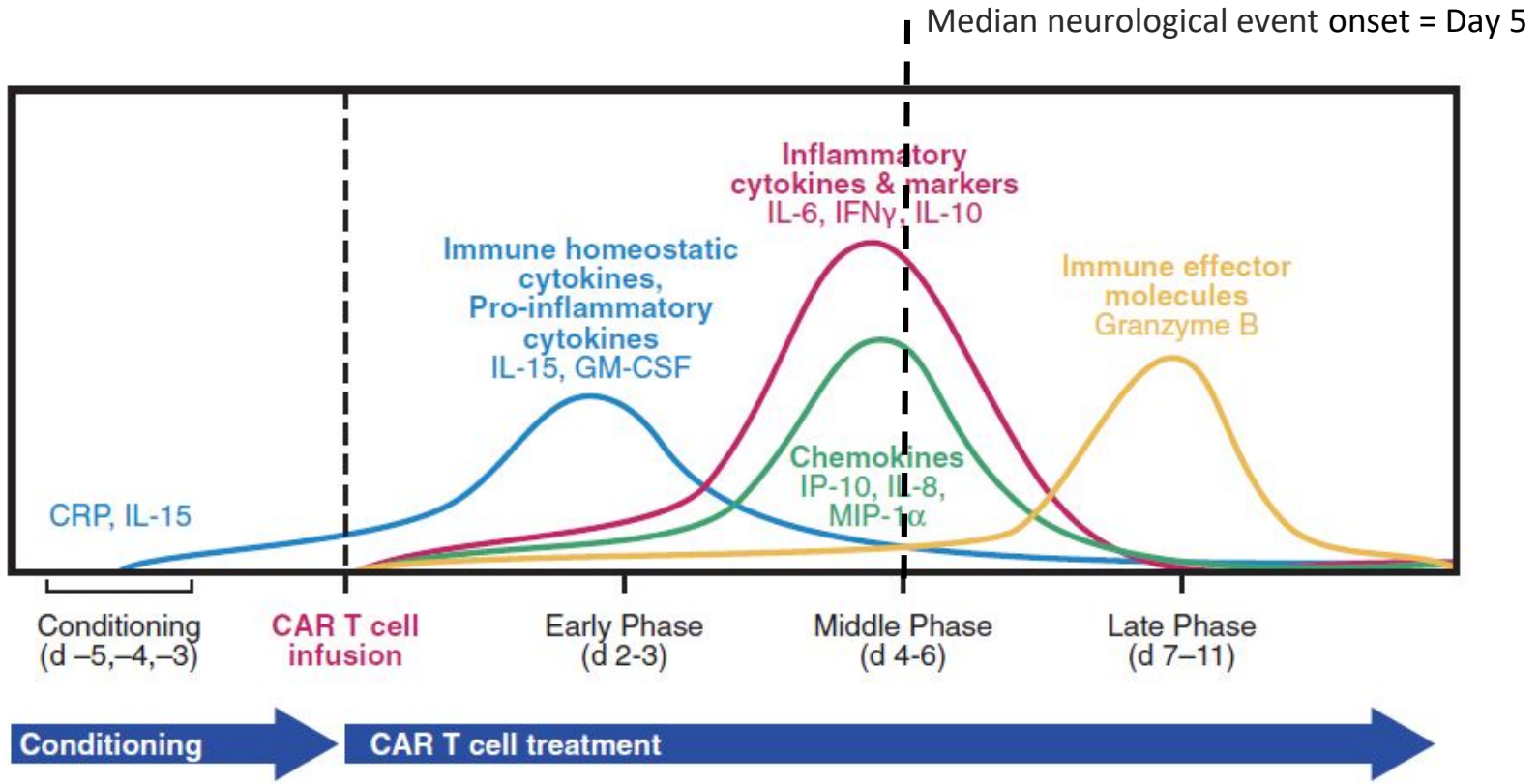
GM-CSF is a Potential Key Signal Associated with Side Effects of CAR T Cell Therapy



Early increases in GM-CSF levels (2-3 days post CAR T cell treatment) is thought to precede and initiate the onset of CRS and NE; therefore prophylactic treatment with mavrilimumab has potential to significantly reduce rates of these severe toxicities[1]

CRS = cytokine release syndrome; NE = neurologic events; 1) Neelapu et al., NEJM 2017; Sterner et al., Blood 2019; Roberts ZJ et al Leukemia Lymphoma 2018

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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]
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 • Active investigational new drug (IND) application with the U.S. Food and Drug Administration (FDA) for a Phase 2/3 clinical trial of mavrilimumab in severe COVID-19 pneumonia and hyperinflammation; placebo-controlled investigator-initiated study in the U.S. enrolling patients

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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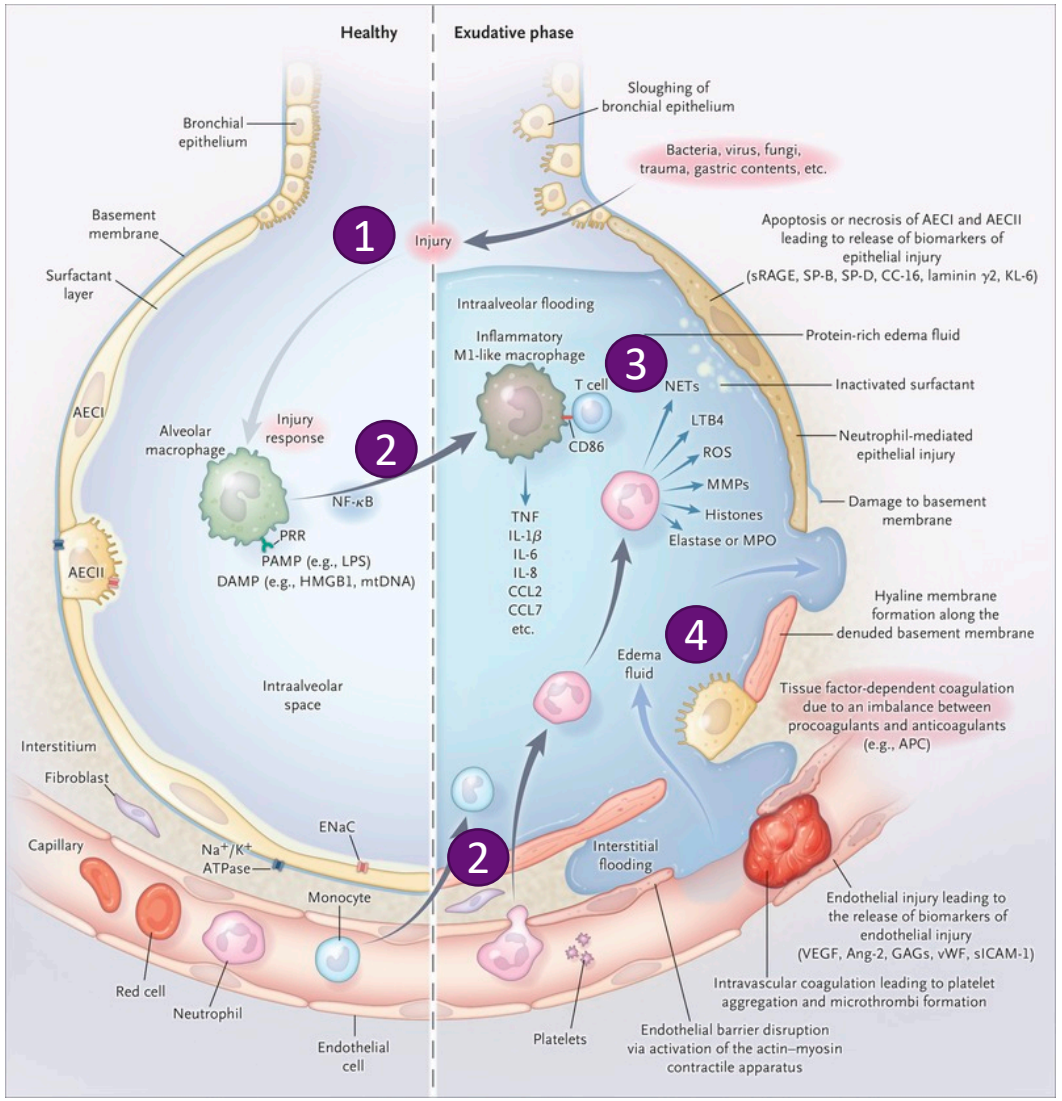
Cytokine Cascade Amplification System in the Pathophysiology of ARDS

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.

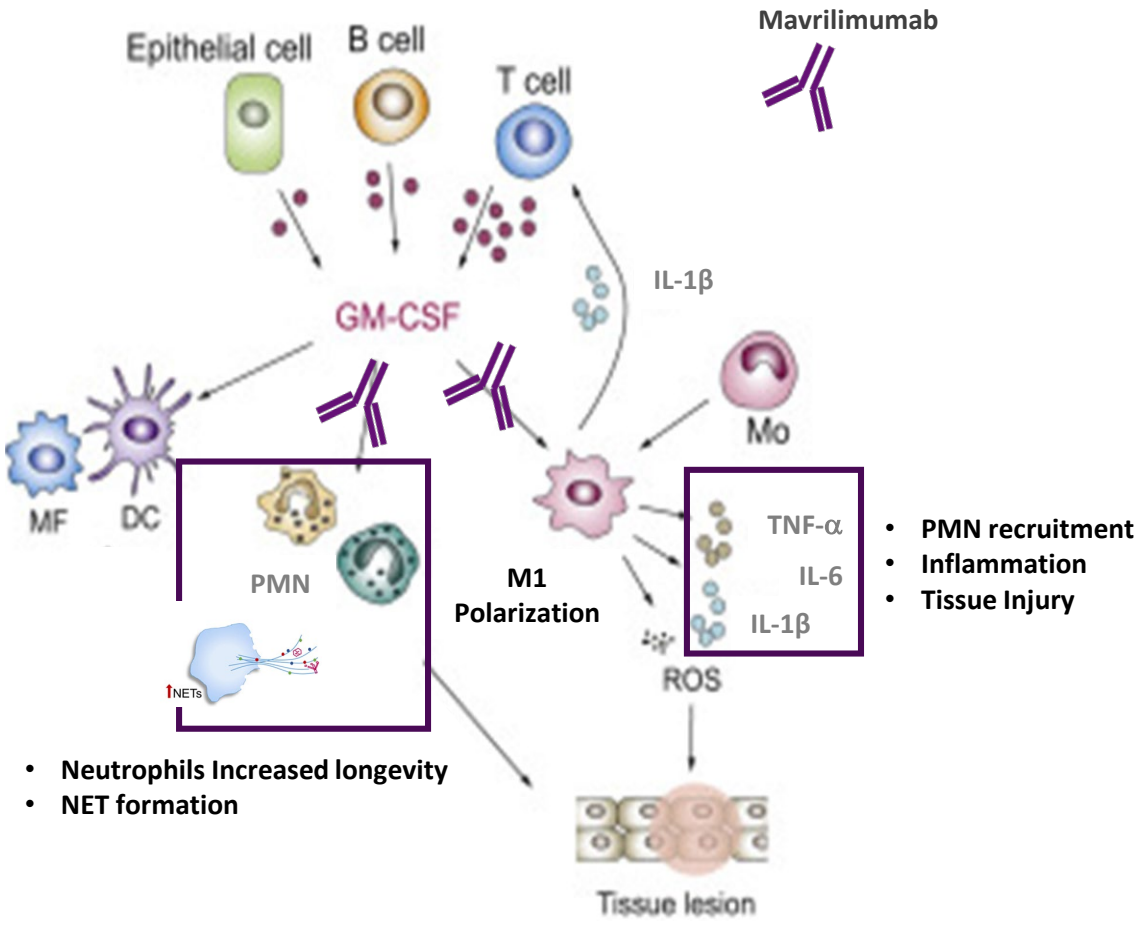
4
- Extensive damage to lung epithelia and endothelia results in an impaired alveolar-capillary barrier.
- Disruption of this barrier allows protein-rich fluid to enter the alveoli causing fluid accumulation in alveolar spaces (pulmonary edema) interfering with gas exchange

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

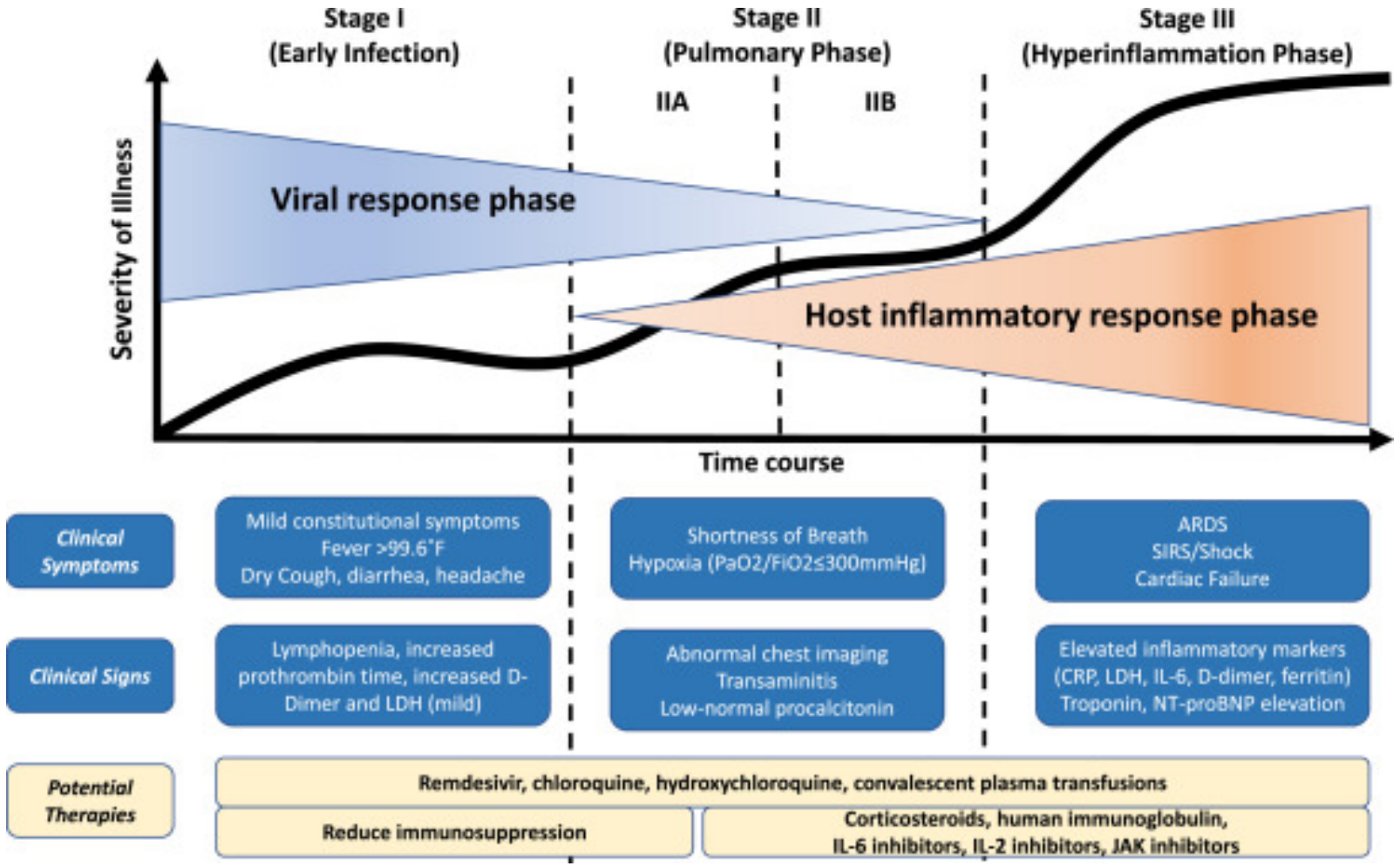
[15] Jones J Infect Dis (2006), [16] Wright Rheumatology (2014), [17] Afford JBC (1992), [18] Biffl JLB (1995), [19] Oh J Exp Med (2011), [20] Yan Sci Rep (2016).

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)

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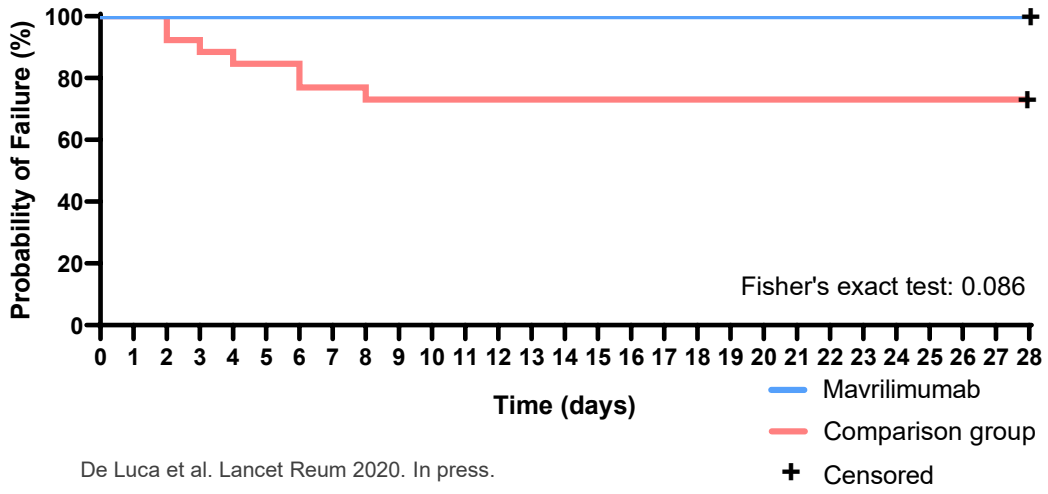
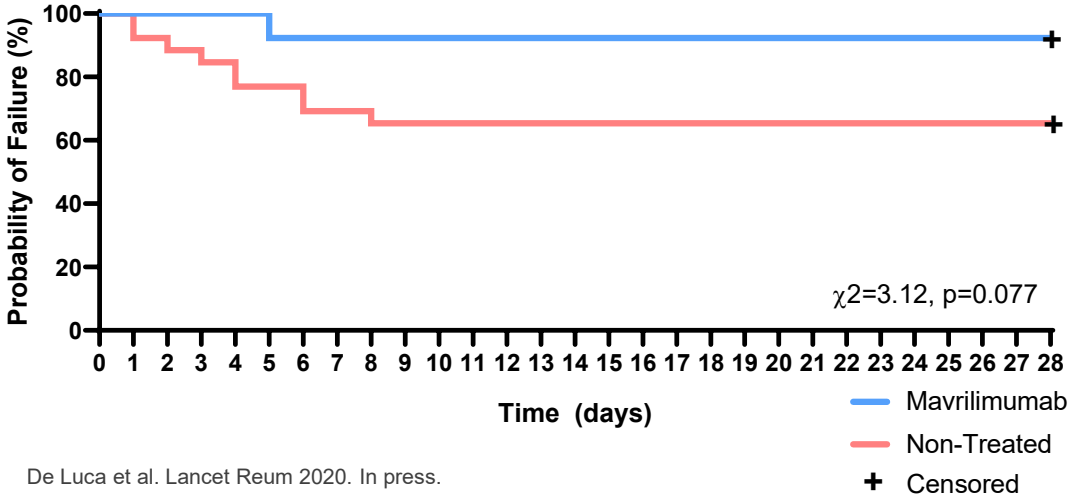
Mavrilimumab Treatment Protocol in Patients with COVID-19 Pneumonia & Hyperinflammation Showed Improved Clinical Outcomes Compared to Matched Contemporaneous Controls[1]



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

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

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



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

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

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

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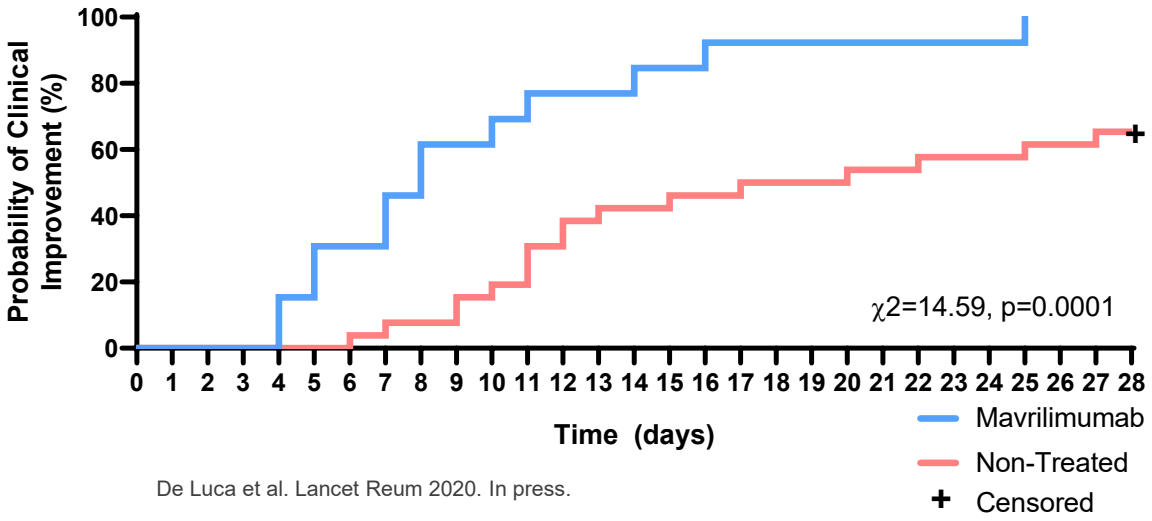
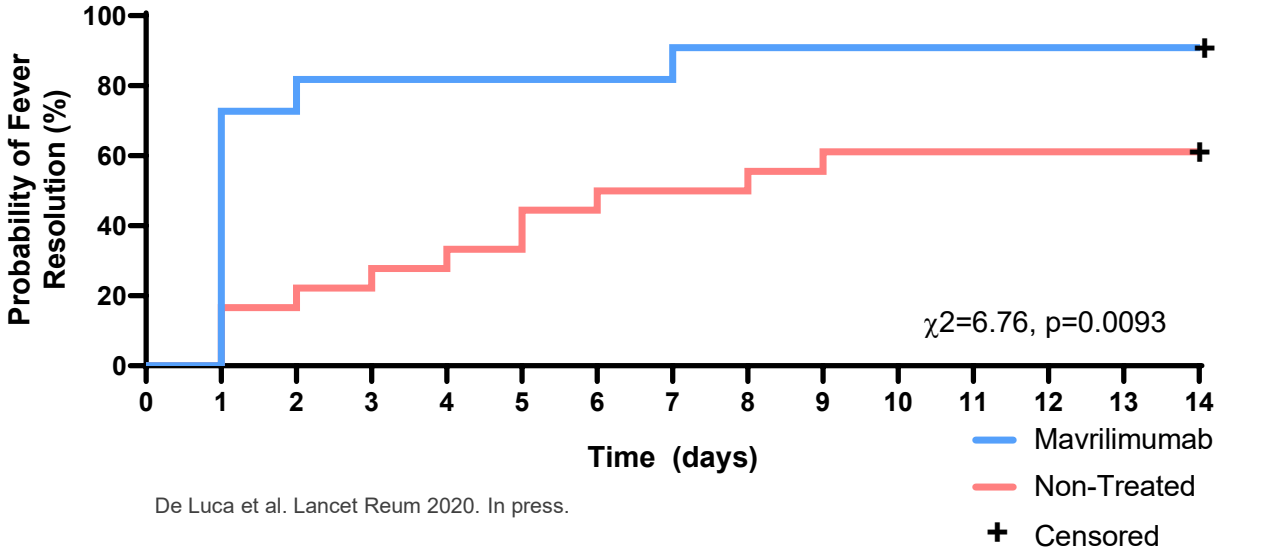
Mavrilimumab Treatment Protocol in Patients with COVID-19 Pneumonia & Hyperinflammation Showed Improved Clinical Outcomes Compared to Matched Contemporaneous Controls[1]



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

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

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



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

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

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

1) 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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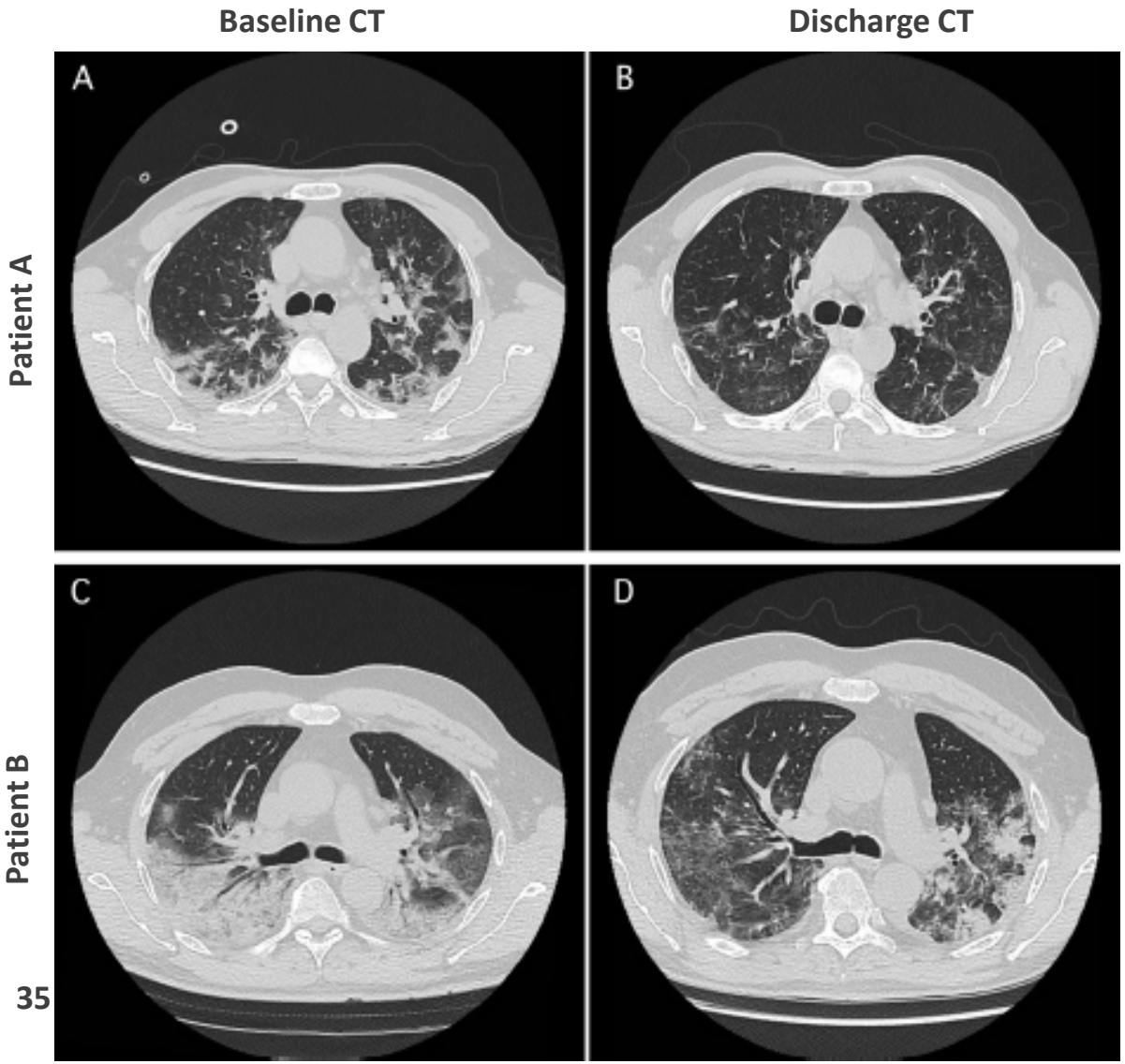
Representative mavrilimumab-treated patients showed significant improvement in lung opacification on computerized tomography (CT) scans, consistent with the overall improvement in their clinical status



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 Reum 2020. In press.

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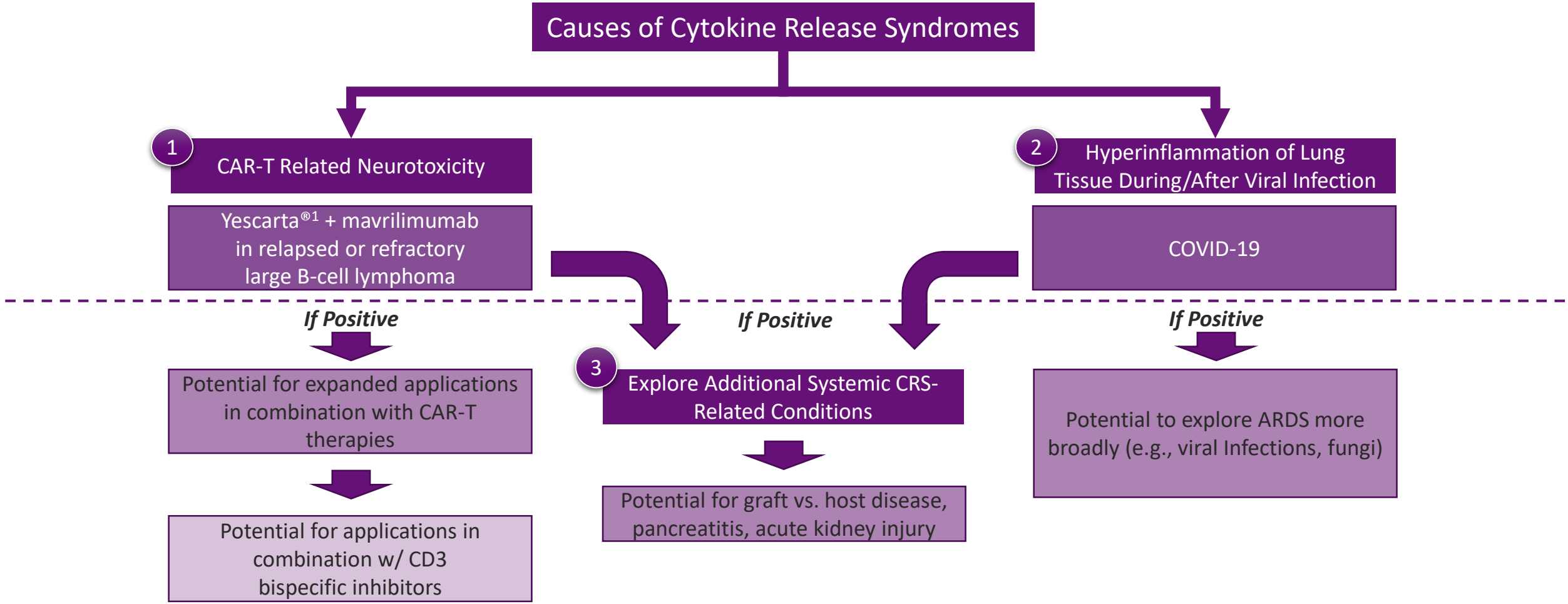
Kiniksa's Development Strategy for Diseases with Cytokine Storm and Hyperinflammation



1) Yescarta® is a registered trademark of Gilead Sciences, Inc., or its related companies; CRS = Cytokine Release Syndrome; Sterner et al., Blood 2019; Mehta et al., The Lancet 2020:https://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736(20)30628-0.pdf

Vixarelimab

Indications	**Prurigo Nodularis (PN):** Chronic inflammatory skin disease with pruritic lesions **Diseases Characterized by Chronic Pruritus:** chronic idiopathic urticaria, chronic idiopathic pruritus, lichen planus, lichen simplex chronicus and plaque psoriasis (PsO)
Mechanism of Action[1]	Monoclonal antibody inhibitor targeting OSMRβ
Scientific Rationale[2,5,6]	OSMRβ is a key receptor subunit shared by IL-31 and OSM; cytokines implicated in chronic pruritic diseases
Prevalence[3]	PN: ~300k prevalent in U.S.
Competition[4]	No FDA-approved therapies for PN
Status[5,6]	Phase 2a data in PN achieved statistical significance in both reduction in weekly-average WI-NRS and attainment of PN-IGA 0/1 score at Week 8[5]; Phase 2 study in diseases characterized by chronic pruritus achieved statistically significant reduction in weekly-average WI-NRS at Week 8 in PsO cohort[6]
Economics	Clinical, regulatory and sales milestones; tiered royalty on annual net sales
Rights	Worldwide

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

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Clinical Development Plan for Vixarelimab

Phase 2a
Prurigo Nodularis

- Evaluating vixarelimab in an 8-week, double-blind, randomized, placebo-controlled clinical trial in subjects with prurigo nodularis
- Primary efficacy endpoint is percent change from baseline in weekly average Worst-Itch Numeric Rating Scale (WI-NRS) at 8 weeks

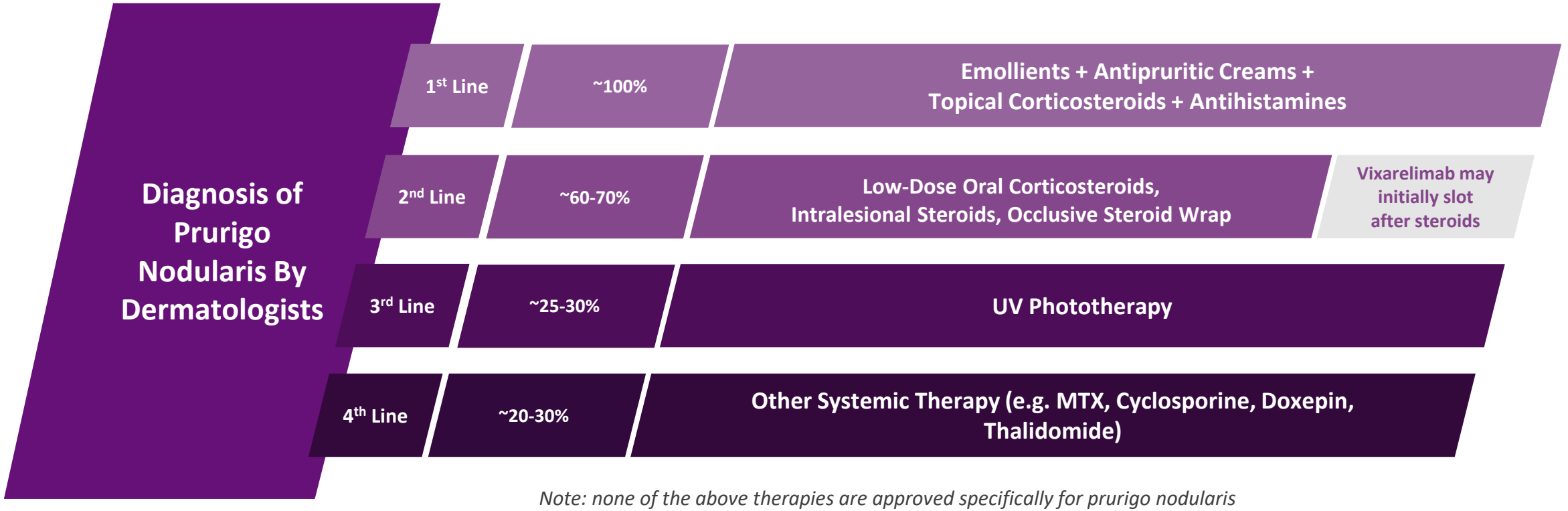
Data Reported in April 2020

Phase 2
Multiple Chronic Pruritic Diseases

- Evaluating vixarelimab in an 8-week, double-blind, randomized, placebo-controlled clinical trial in subjects with chronic idiopathic urticaria, chronic idiopathic pruritus, lichen planus, lichen simplex chronicus and plaque psoriasis
- Primary efficacy endpoint is percent change from baseline in weekly average WI-NRS at 8 weeks

Data Reported in May 2020

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

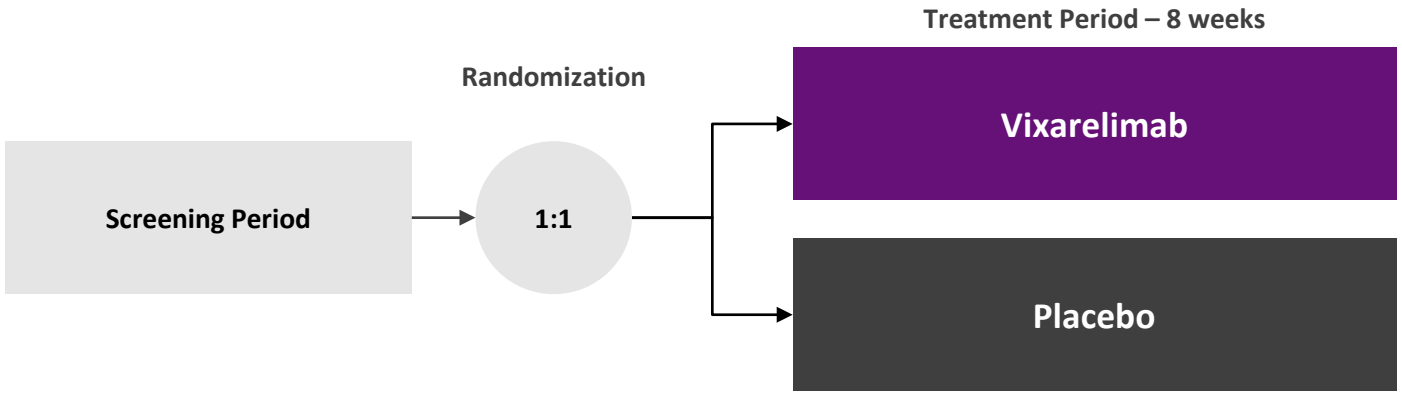
Vixarelimab Phase 2a Study in Prurigo Nodularis

Phase 2a Proof-of-Concept

Objective: Assess pruritus reduction

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

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



Inclusion Criteria

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

Vixarelimab Phase 2a Study Prurigo Nodularis

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

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

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

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

Topline Observations:

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

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

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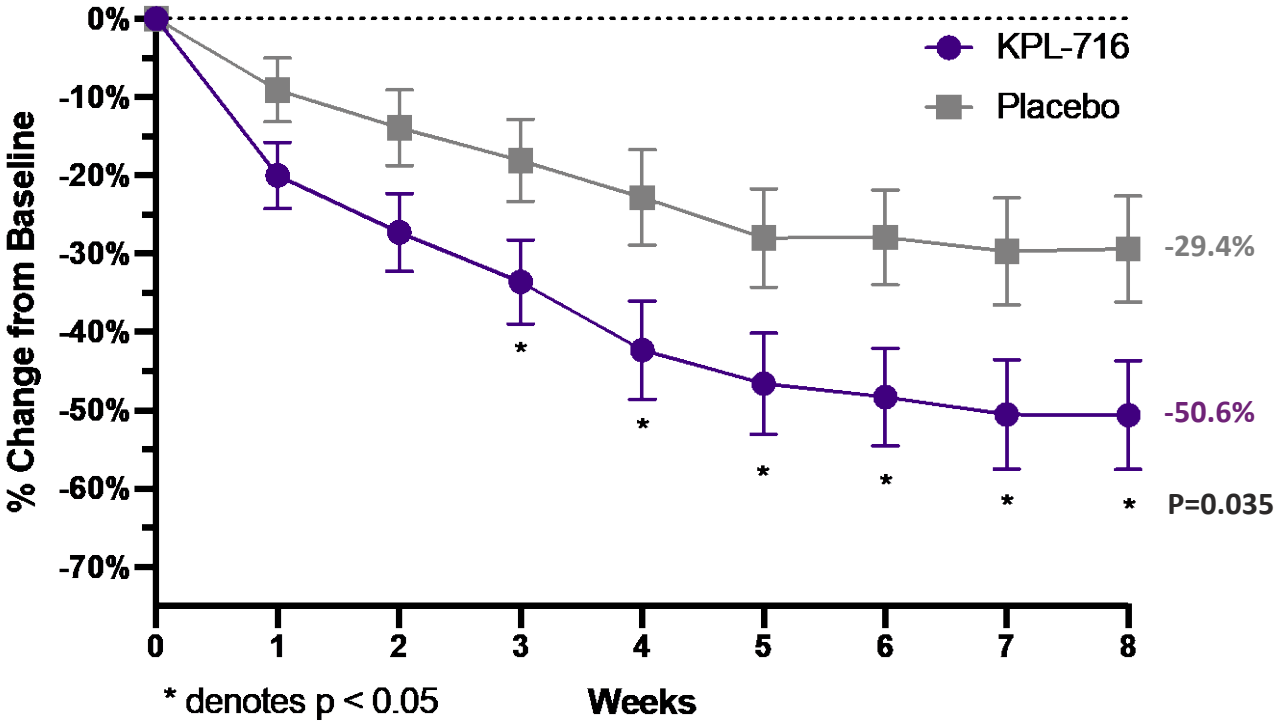
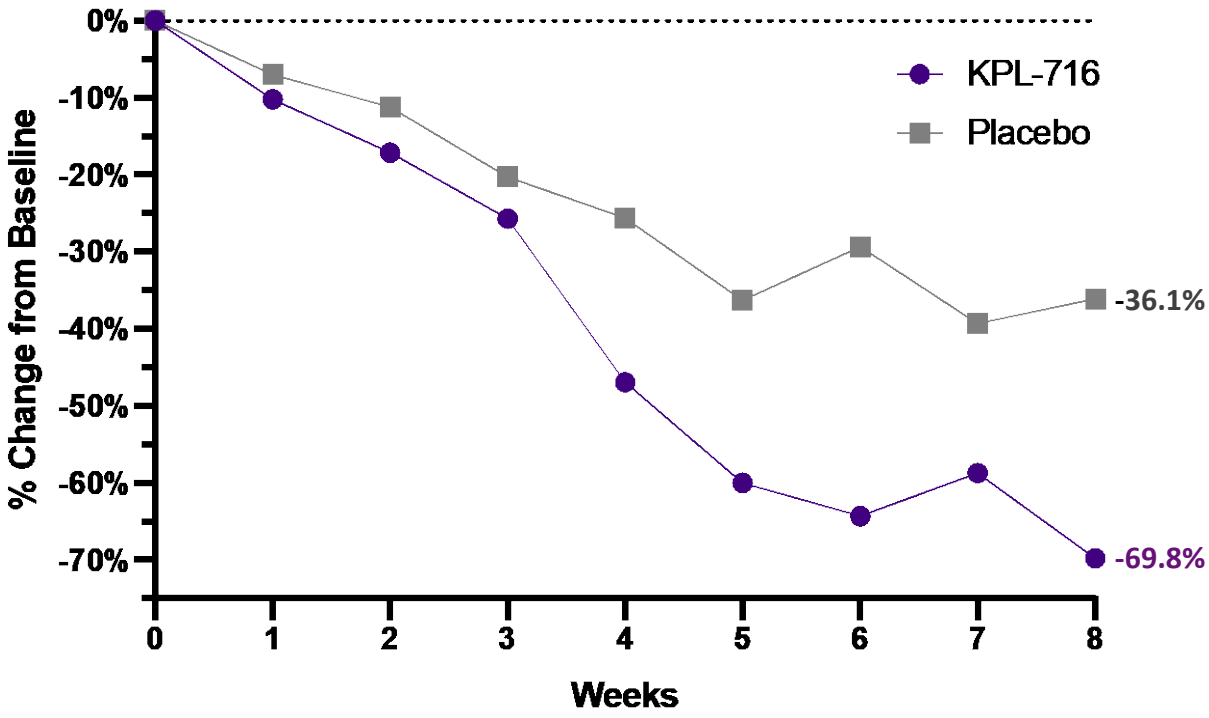
Vixarelimab Phase 2a Study in Prurigo Nodularis: Statistically Significant Primary Efficacy Endpoint of Reduction in Weekly-Average WI-NRS at Week 8

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

LS-Mean % Change in Weekly Average WI-NRS

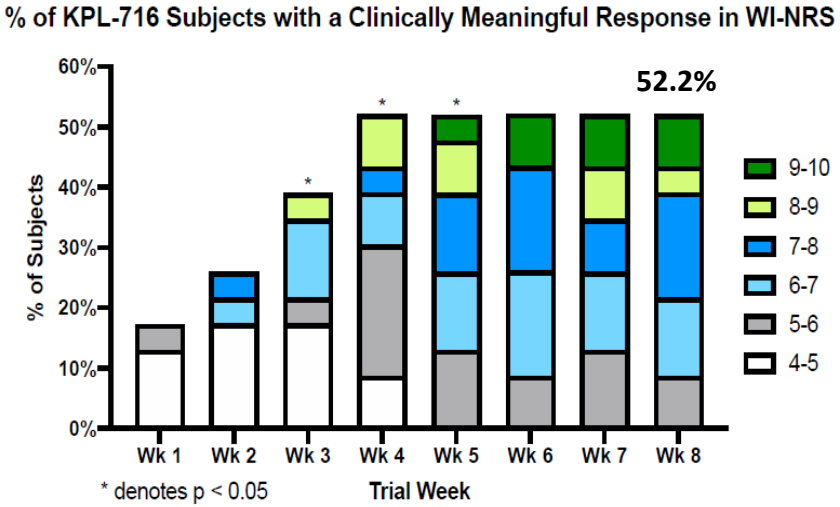


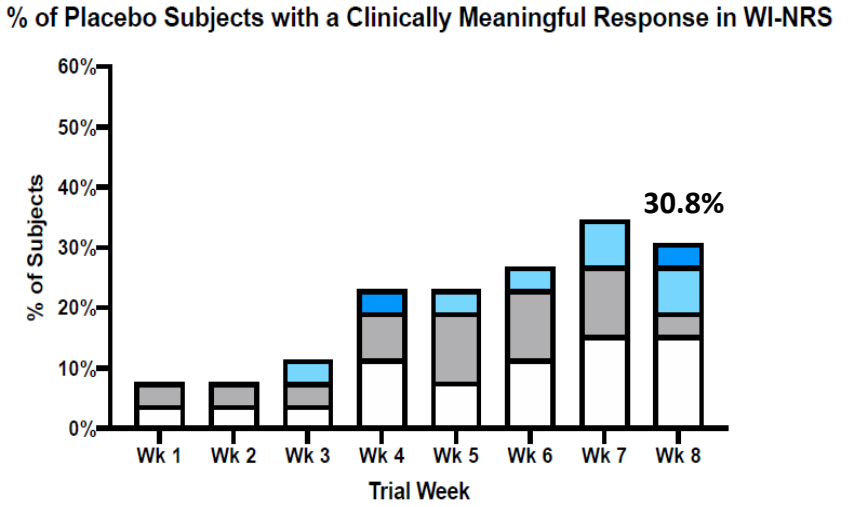
Median % Change in Weekly Average WI-NRS

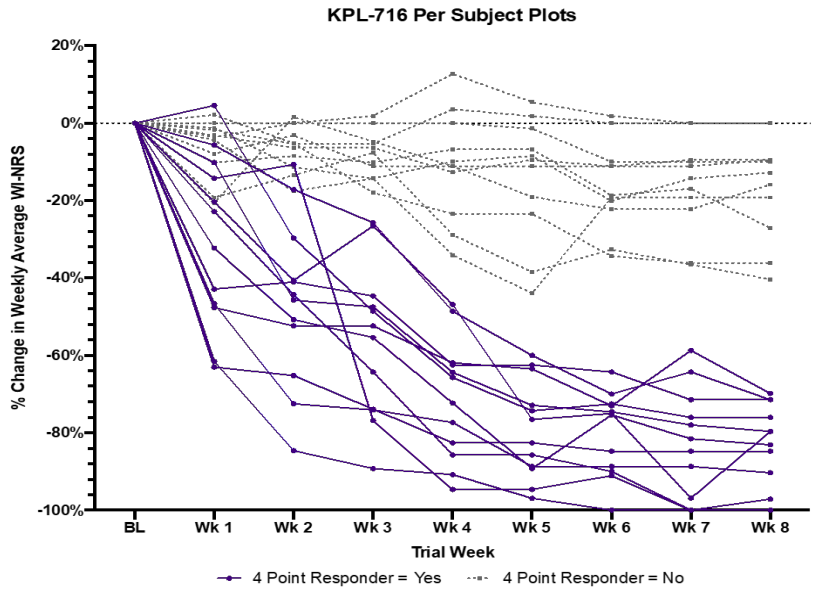


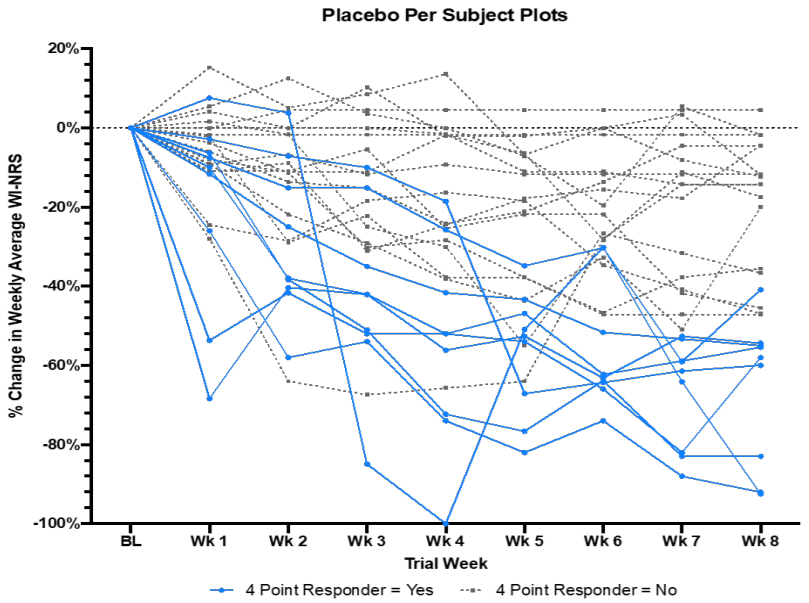
Vixarelimab = KPL-716
WI-NRS = Worst-Itch Numeric Rating Scale
LS = least squares

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





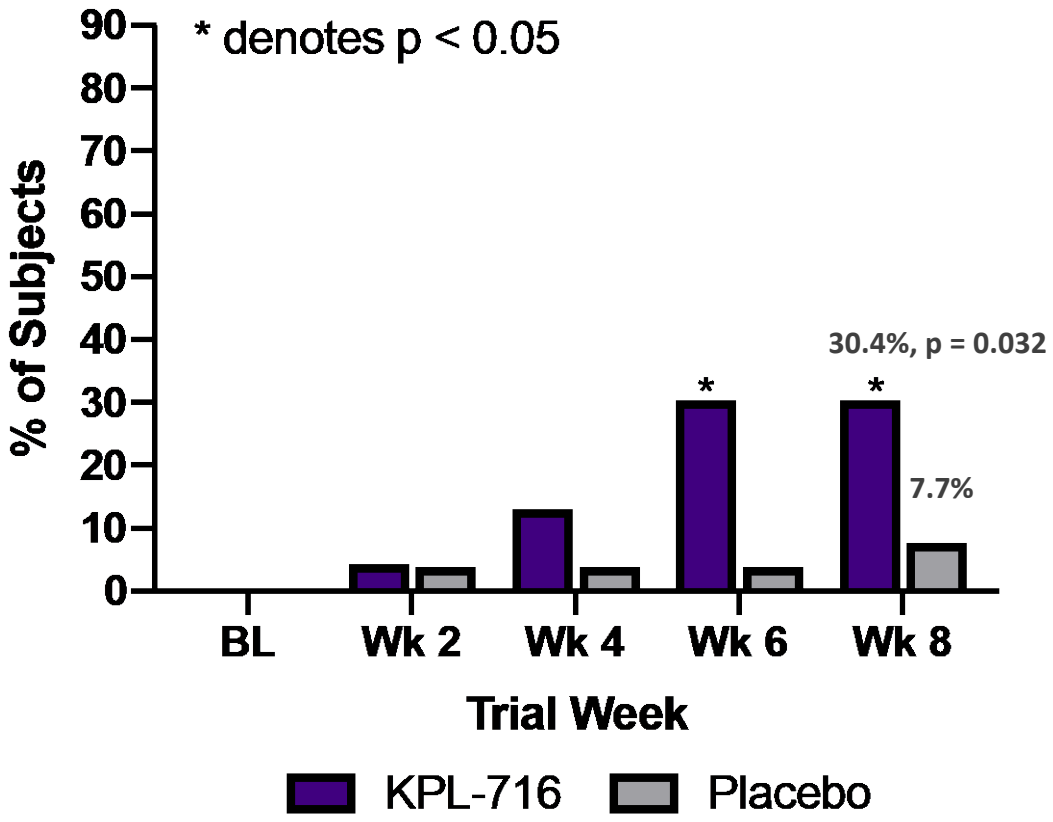




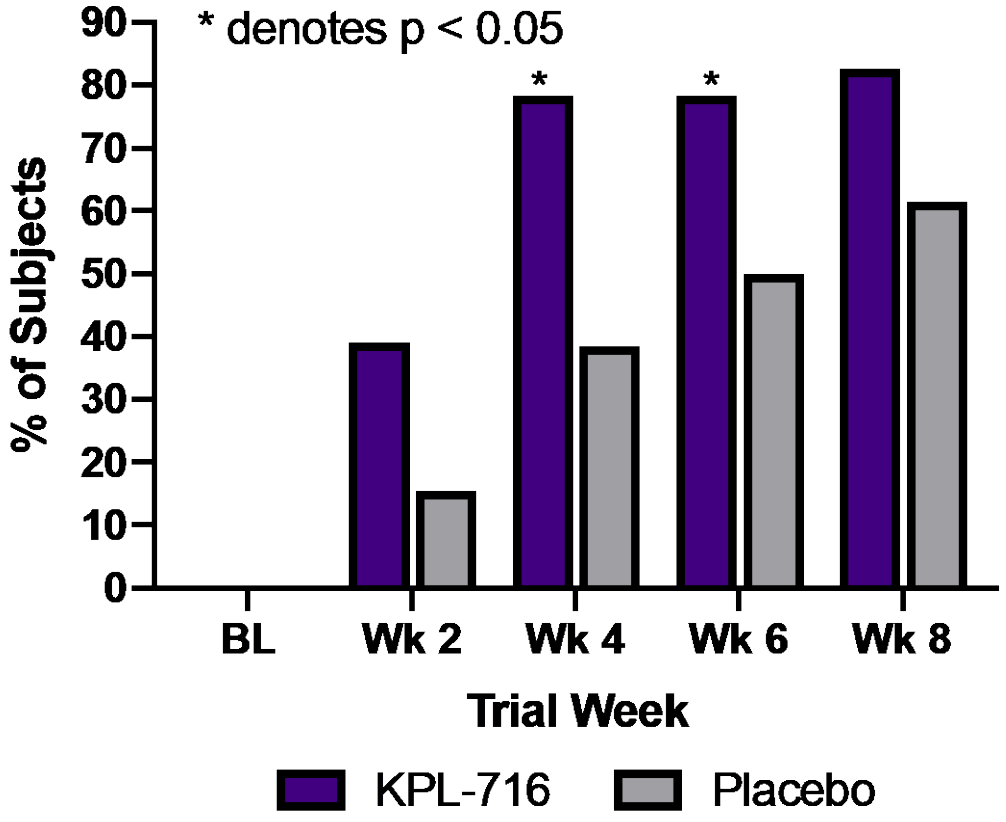
Vixarelimab = KPL-716
WI-NRS = Worst-Itch Numeric Rating Scale

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

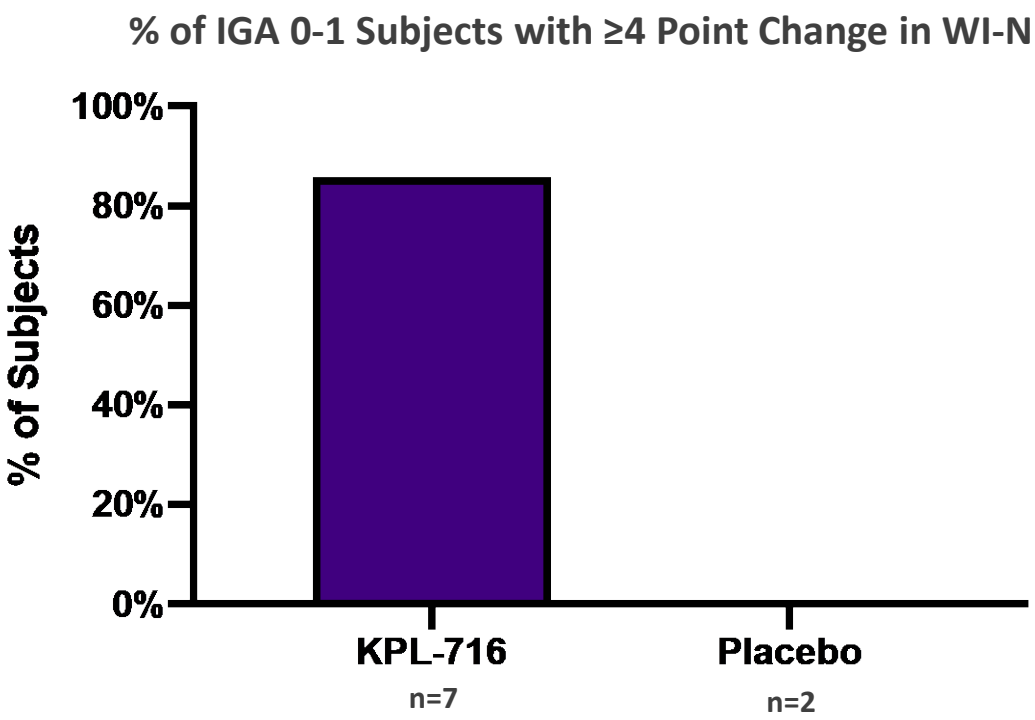


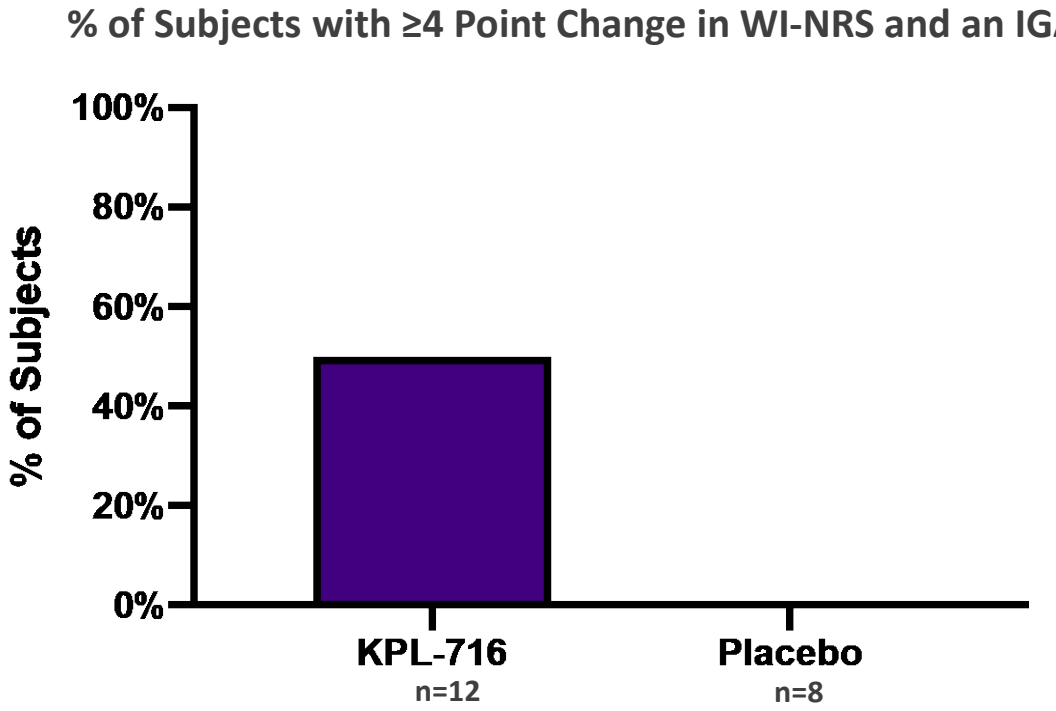
≥1 Point Change in PN-IGA



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



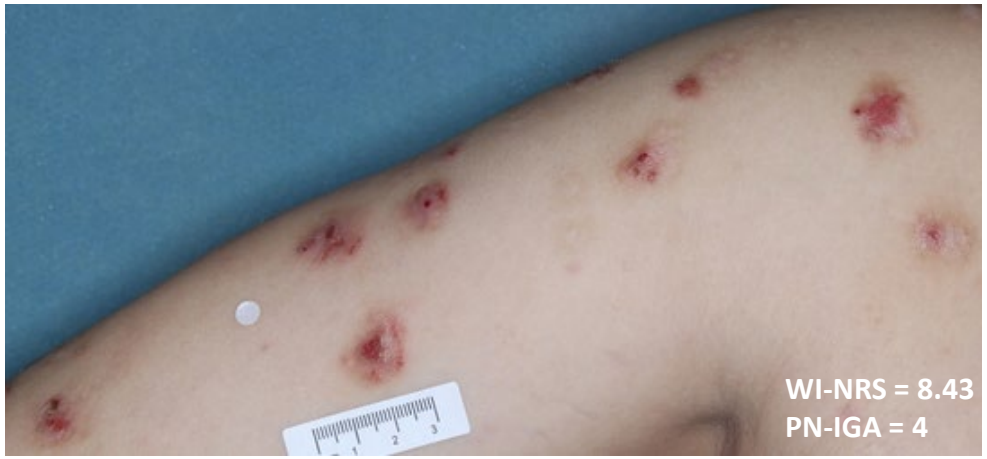
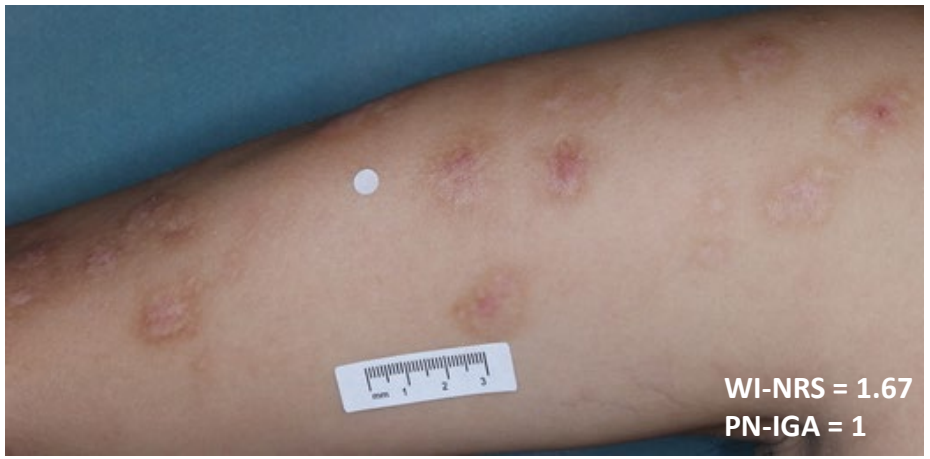
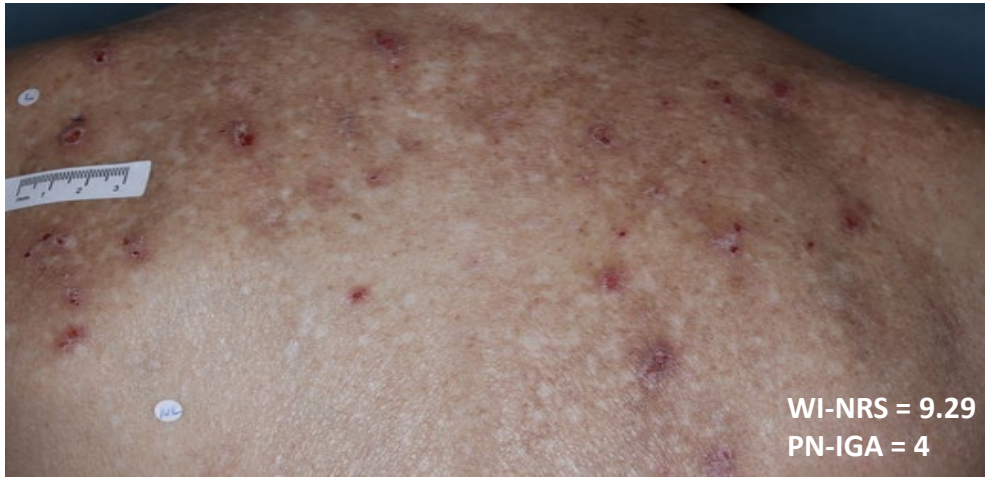
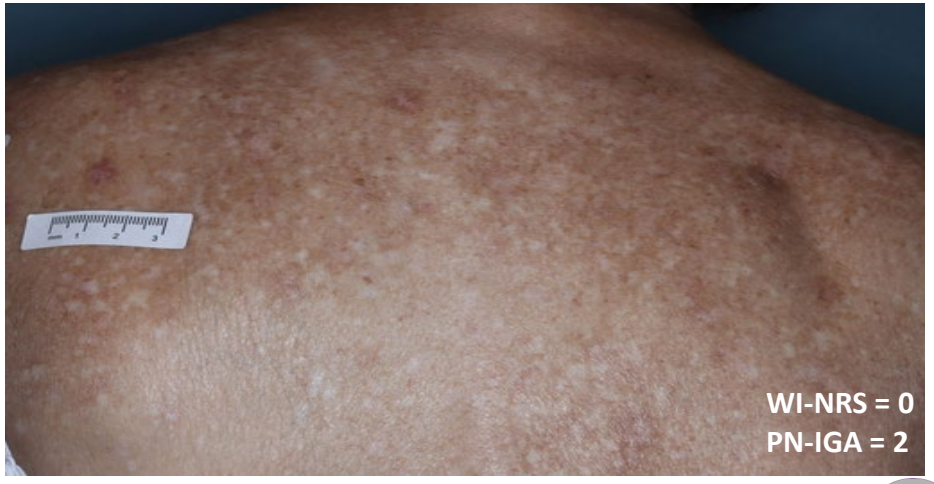


85.7% of the subjects who achieved 0-1 on the PN-IGA scale were also 4-point responders on WI-NRS vs. none for placebo

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

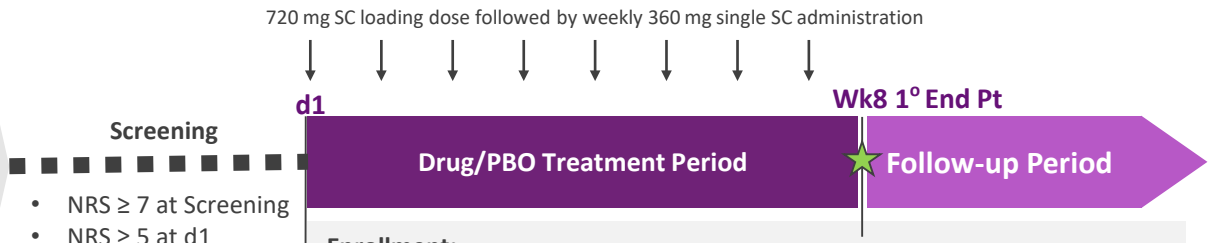
Vixarelimab Exploratory Phase 2 Study in Diseases Characterized by Chronic Pruritus

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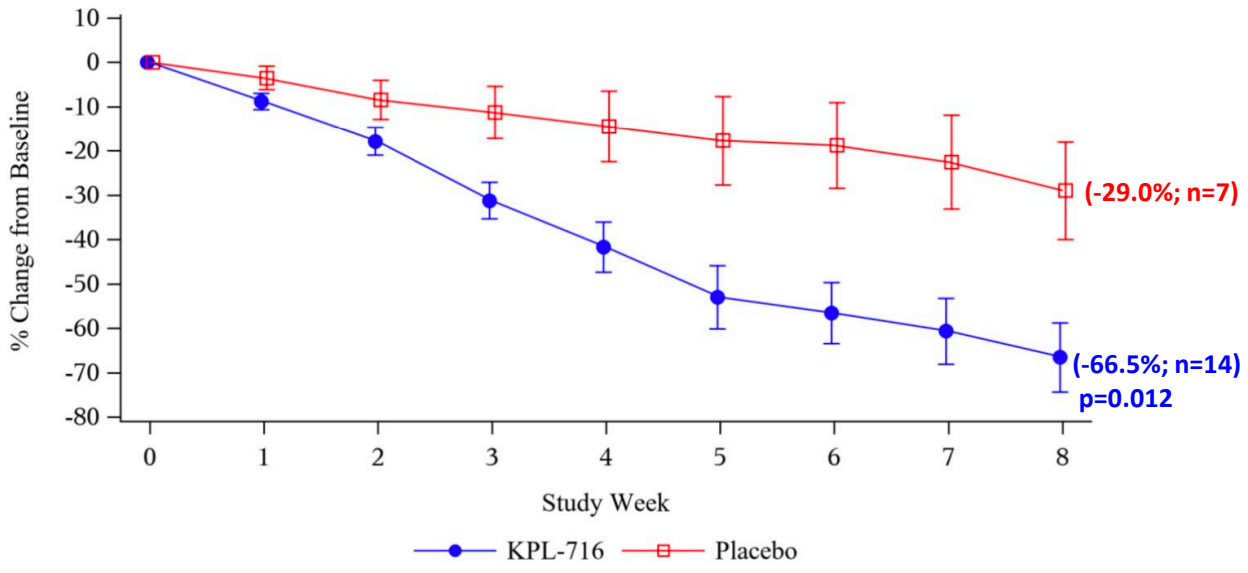
Vixarelimab Exploratory Phase 2 Study in Diseases Characterized by Chronic Pruritus: Reduction in Weekly-Average WI-NRS at Week 8

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

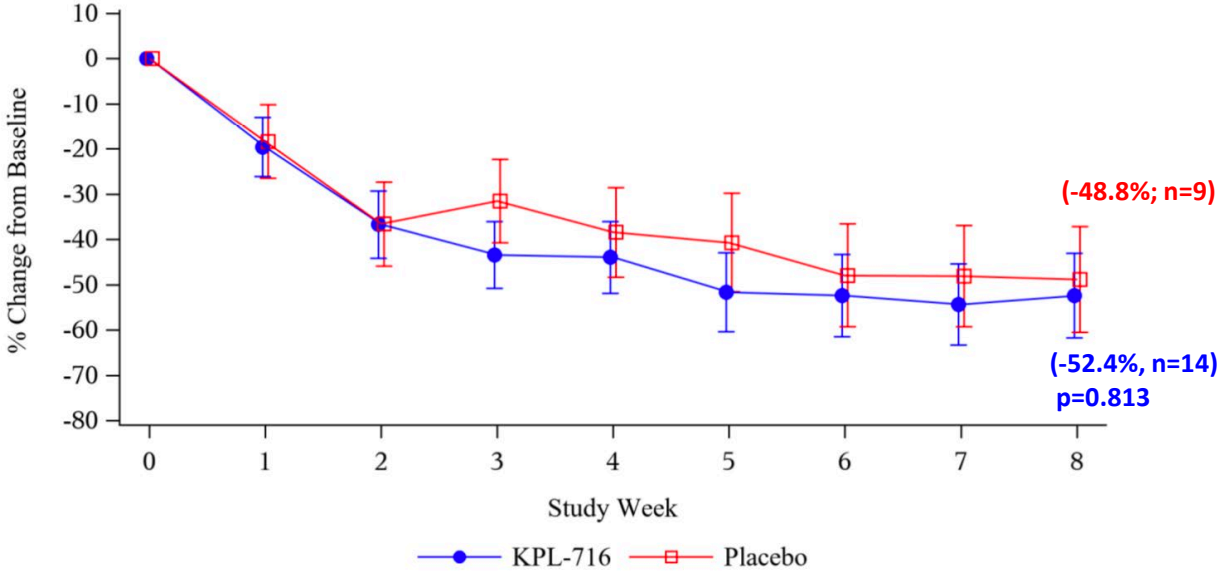
Plaque Psoriasis

LS-Mean % Change in Weekly Average WI-NRS



Chronic Idiopathic Pruritus

LS-Mean % Change in Weekly Average WI-NRS

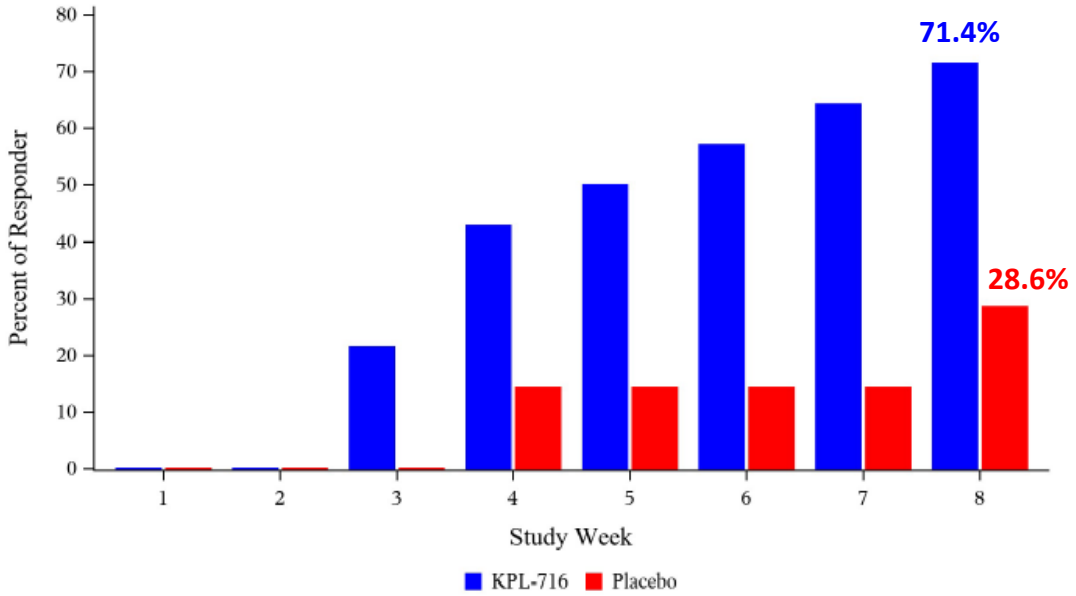


Vixarelimab = KPL-716
WI-NRS = Worst-Itch Numeric Rating Scale
Data as of May 2020

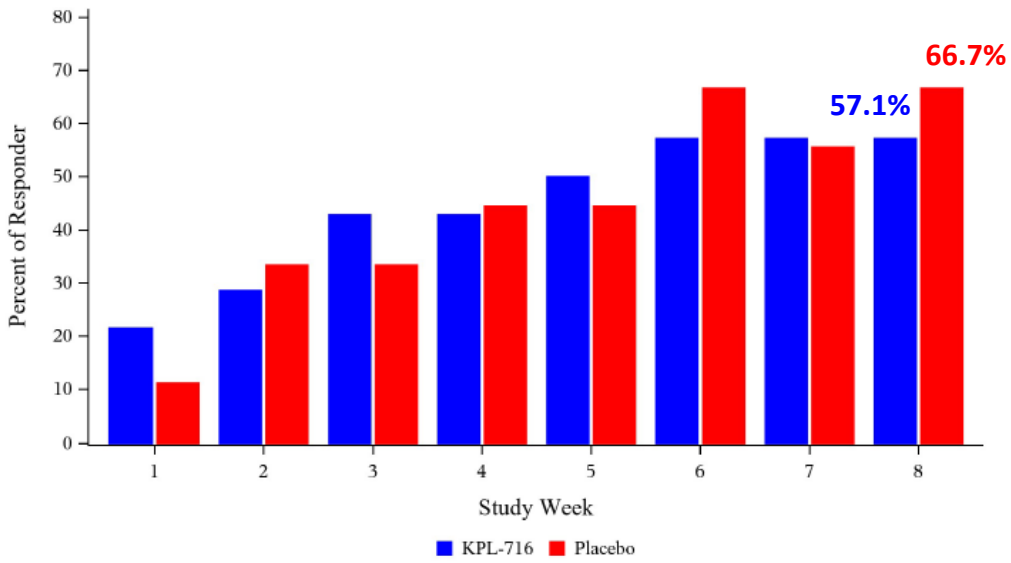
Vixarelimab Exploratory Phase 2 Study in Diseases Characterized by Chronic Pruritus: ≥ 4-Point Weekly-Average WI-NRS Reduction at Week 8

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

Plaque Psoriasis



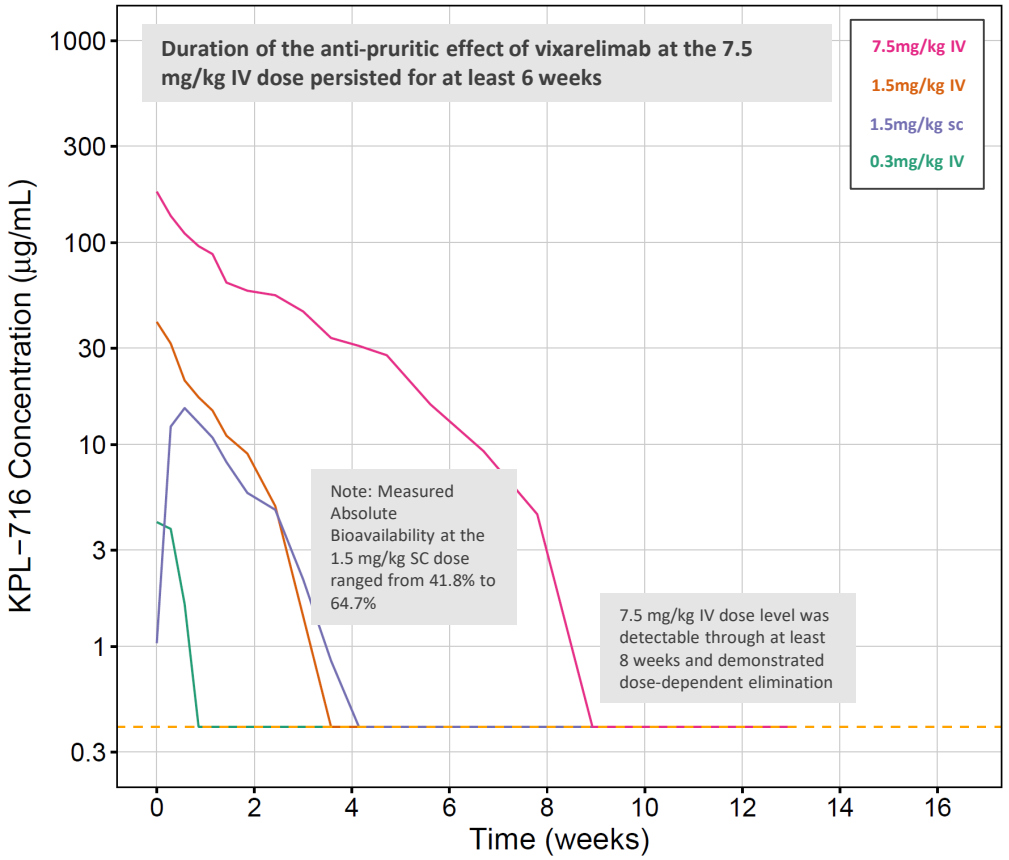
Chronic Idiopathic Pruritus



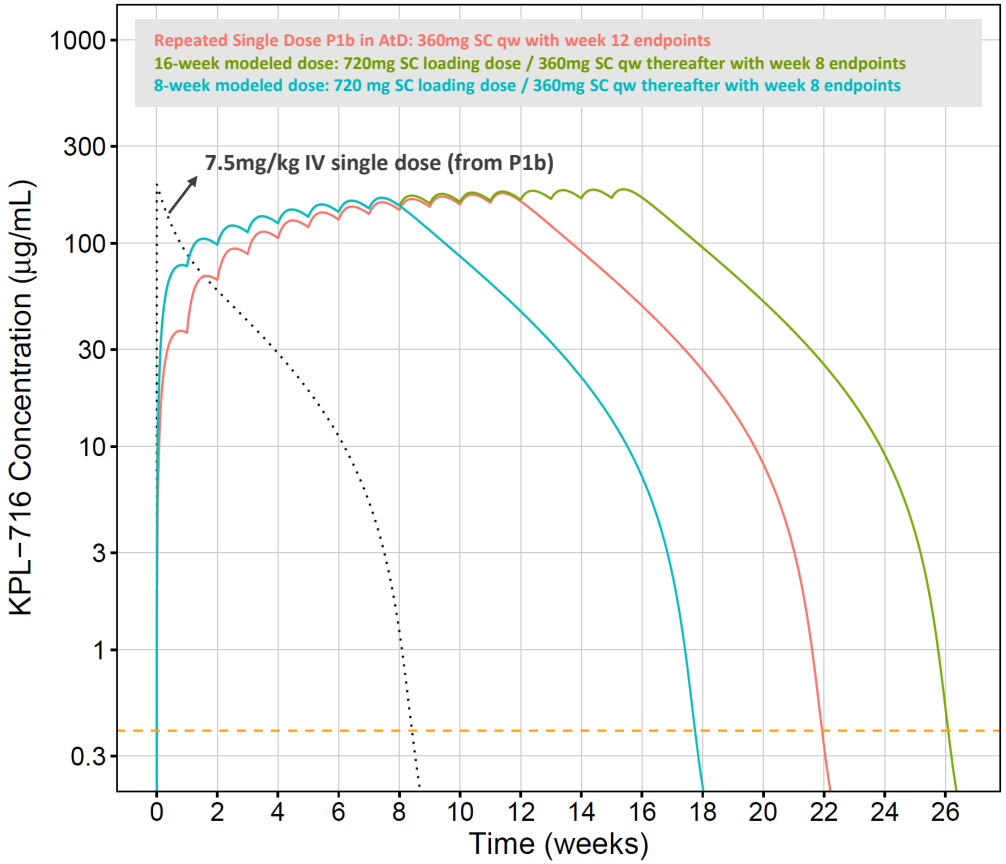
Vixarelimab = KPL-716
WI-NRS = Worst-Itch Numeric Rating Scale
Data as of May 2020

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

Measured Vixarelimab PK From P1b Single Dose



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



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

PK = pharmacokinetic; PD = pharmacodynamic; POC = proof of concept; SC = subcutaneous

KPL-404

Autoimmune Diseases[1]	External proof-of-concept previously established in broad range of autoimmune diseases: Sjogren's disease, systemic lupus, rheumatoid arthritis, solid organ transplant and Graves' disease[1]
Mechanism of Action[2]	Monoclonal antibody inhibitor of CD40-CD40L interaction
Scientific Rationale[3,4]	Attractive target for blocking T-cell dependent, B-cell–mediated autoimmunity
Status	Enrolling first-in-human study with antigen challenge TDAR[5]; Phase 1 data expected in Q4 2020
Economics	Clinical and regulatory milestones and royalty on annual net sales
Rights	Worldwide

1) National Center for Biotechnology Information - Targeting the CD40-CD154 Signaling Pathway for Treatment of Autoimmune Arthritis: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6721639/; 2) 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; 3) Elgueta, et al. Immunol Rev 2009, 229 (1), 152-172; 4) Peters, et al. Semin Immunol 2009, 21 (5) 293-300; 5) TDAR, T-cell Dependent Antibody Response

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

Mechanism	**Humanized mAb inhibitor of CD40-CD40L interaction[1]**	• Designed to inhibit CD40-CD40L, a T-cell co-stimulatory pathway critical for B-cell maturation and immunoglobulin class switching
Rationale	**External POC for CD40-CD40L inhibition observed in a range of autoimmune diseases[2,3]**	• **Published Positive Class-Related Clinical Data**: Sjogren's syndrome, systemic lupus erythematosus, solid organ transplant, rheumatoid arthritis, Graves' disease • **Ongoing Class-Related Studies**: type 1 diabetes, ulcerative colitis, lupus nephritis, hidradenitis suppurativa, kidney transplant and focal segmental glomerulosclerosis
Preclinical Data	**Robust preclinical package supports development potential**	• Favorable pharmacokinetic and pharmacodynamic findings, including engagement of CD40 target and block of antigen-specific primary and secondary antibody responses in a T-cell dependent antibody response cynomolgus monkey model
Competition	**Potential differentiation**	• KPL-404 at 10mg/kg achieved/maintained ~100% receptor occupancy in 7/7 non-human primates (NHP) through 4 weeks • KPL-404 10mg/kg suppressed T-cell dependent antibody responses (TDAR) in NHP model to tetanus toxoid (TT) and keyhole limpet hemocyanin (KLH) for >4 weeks
Status	**Enrolling first-in-human study**	• Enrolling a single-ascending-dose Phase 1 study in healthy volunteers which will provide safety data and pharmacokinetics as well as receptor occupancy and TDAR • Top-line data are expected in 4Q 2020

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; TDAR, T-cell Dependent Antibody Response

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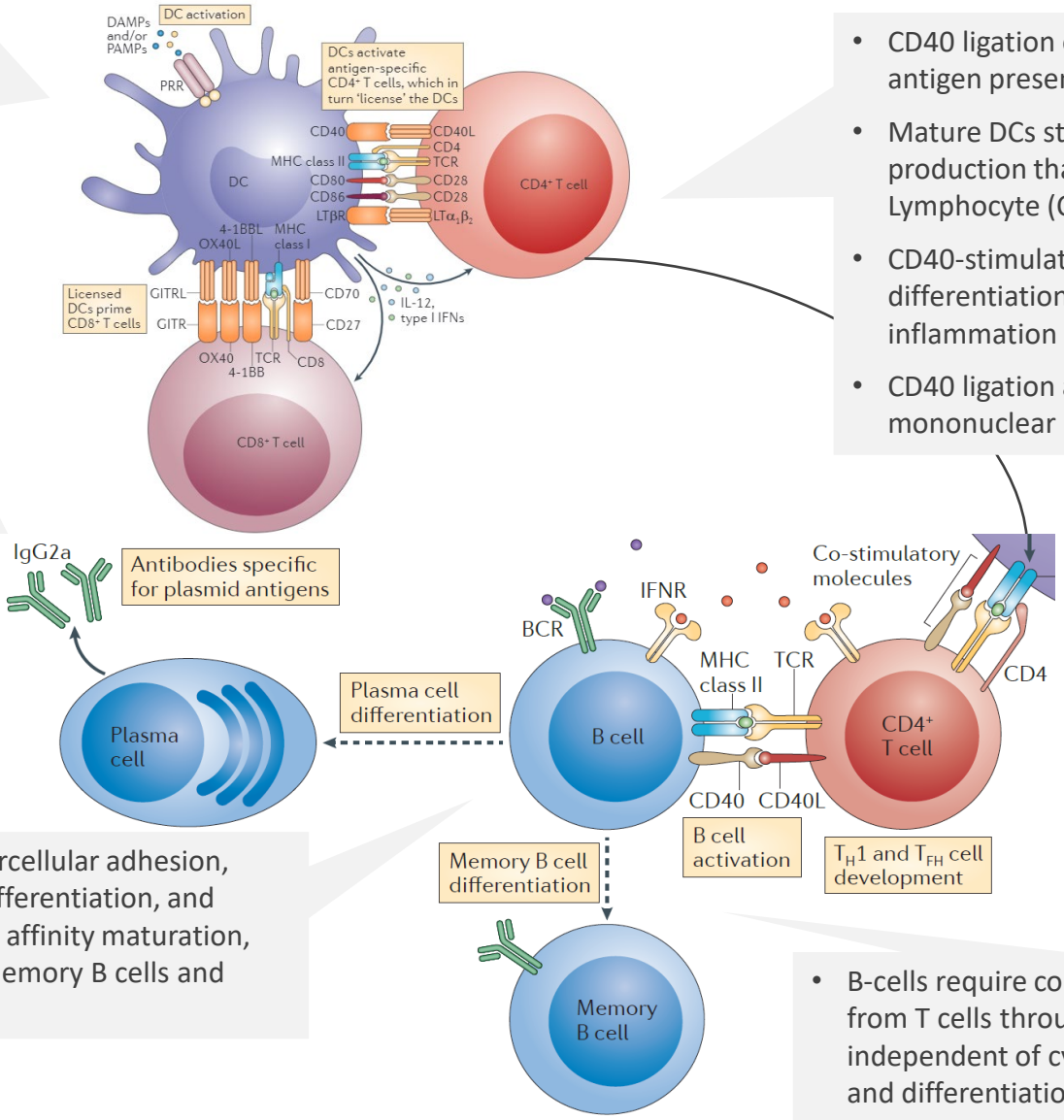
CD40/CD40L is an Essential Immune Pathway for T-Cell Priming and T-Cell Dependent B-Cell Responses

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



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

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

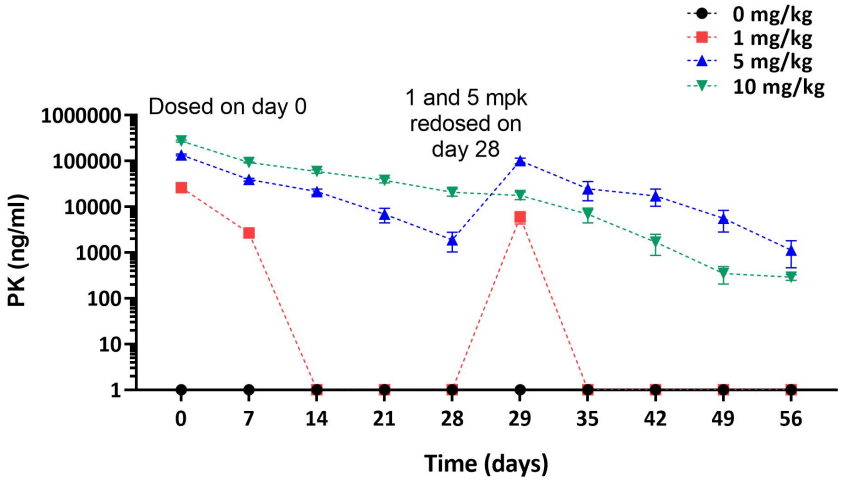
- CD40 engagement triggers B-cell intercellular adhesion, sustained proliferation, expansion, differentiation, and antibody isotype switching leading to affinity maturation, which is essential for generation of memory B cells and long-lived plasma cells

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

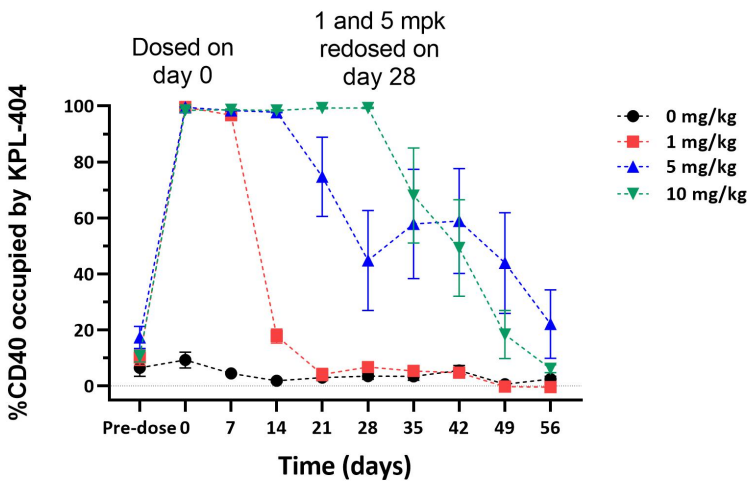
Sources: Elgueta et al., Immunol Rev, 2009; Peters et al., Semin Immunol, 2009; Kambayashi et al., Nature Reviews: Immunology, 14, 2014; Desmet et al., Nature Reviews: Immunology, 12, 2012

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

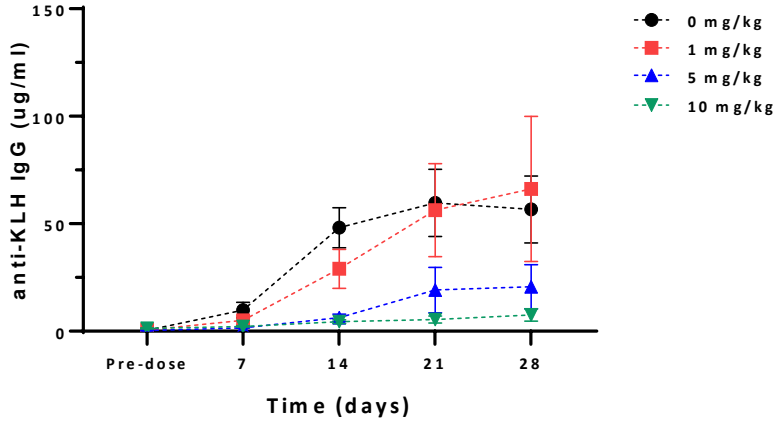
Mean KPL-404 PK



Mean KPL-404 Receptor Occupancy (RO)



Mean KLH IgG



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

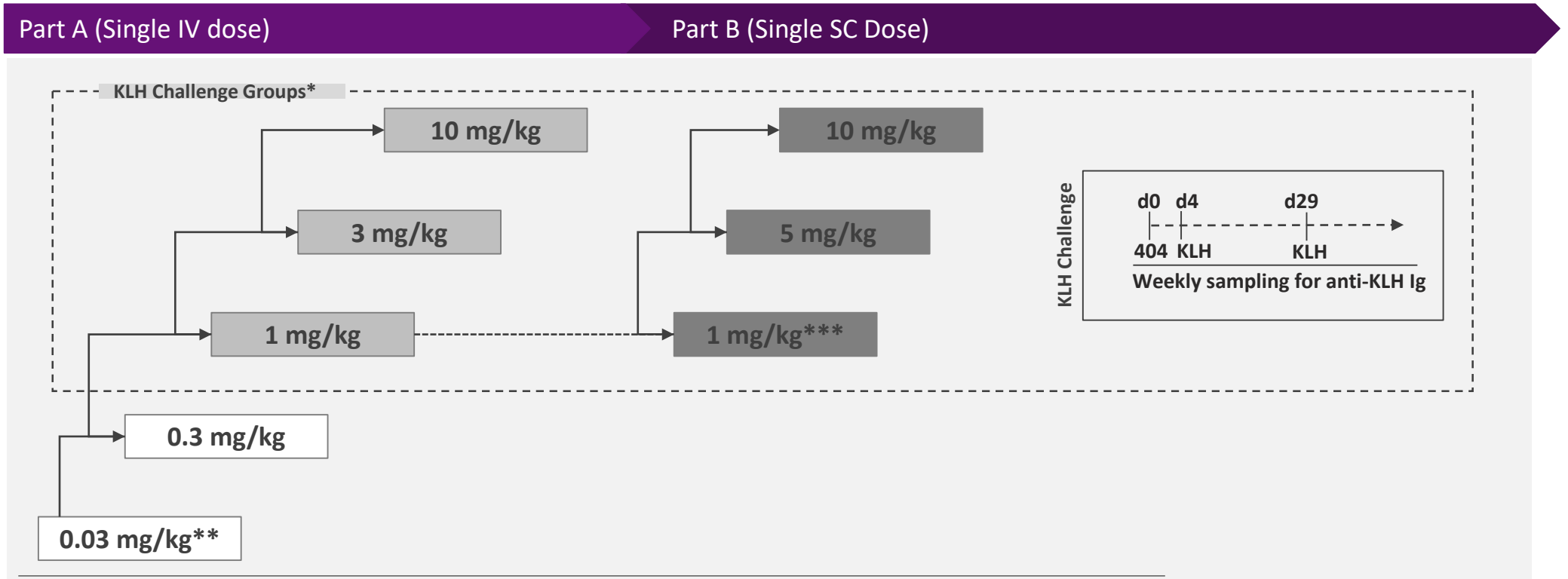
Complete suppression of primary T-cell dependent antigen response correlated with 100% receptor occupancy

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

KPL-404 Single-Ascending-Dose Phase 1 Study

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

Phase 1 SAD Study Design (n=60 NHV)



- **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; *** The 1 mg/kg SC dose arm will enroll after review of the 1 mg/kg IV SMC

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

Immune-Modulating Product Candidates

Validated Mechanisms or **Strong Biologic Rationale**

Debilitating Diseases with **Unmet Medical Need**

~$279M Proforma Cash Reserves* **Extend into 2H 2021**

Multiple **Clinical Data Readouts** Expected in **2H 2020**

*Our proforma cash reserves includes ~$204 million of cash, cash equivalents and short-term investments as of 3/31/2020 and ~$75 million of estimated net proceeds from our follow-on public offering, including underwriters' exercise of the overallotment option in full, and concurrent private placement as though we had closed on these financings in Q1 2020. As such our proforma cash reserves is not prepared in accordance with GAAP.

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Appendix

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Appendix – Rilonacept

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

Pericarditis is chest pain caused by pericardial inflammation

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

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

Often Idiopathic Etiology:

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

Recurrent Pericarditis:

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

Involvement of IL-1 in Idiopathic Recurrent Pericarditis:

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

Recurrent pericarditis causes significant impairment of quality of life

Recurrent Disease Creates Burden on QoL:

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

Complications Are Rare but Severe:

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

1) Maish et al European Heart Journal 2004, 25, 587-610; 2) Alder et Al. European Heart Journal, 2015 ESC guidelines

Phase 2 Rilonacept Data

Baseline demographics and clinical characteristics

Baseline Demographics

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

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

Clinical Characteristics

	Idiopathic RP			PPS	
Disease Status:	Active[a]	Active[b]	CS-dep[c]	Active[d]	CS-dep[e]
CRP requirement (mg/dL):	>1	≤1	N/A	>1	N/A
N:	12	3	6	1	3
Mean NRS[f] (SD)	4.6 (1.7)	4.7 (3.1)	1.2 (0.8)	4.0 (N/A)	2.0 (2.7)
Mean CRP (SD), mg/dL	4.9 (5.8)	0.5 (0.4)	0.2 (0.1)	1.1 (N/A)	0.1 (0.1)

[a]Part 1; [b]Part 2; [c]Part 3; [d]Part 4; [e]Part 5; [f]11-point numeric scale, ranging from zero (0, no pain) to ten (10, pain as bad as possible); CRP, C-reactive protein; CS-dep, corticosteroid-dependent; NRS, numeric rating scale; PPS, post-pericardiotomy syndrome

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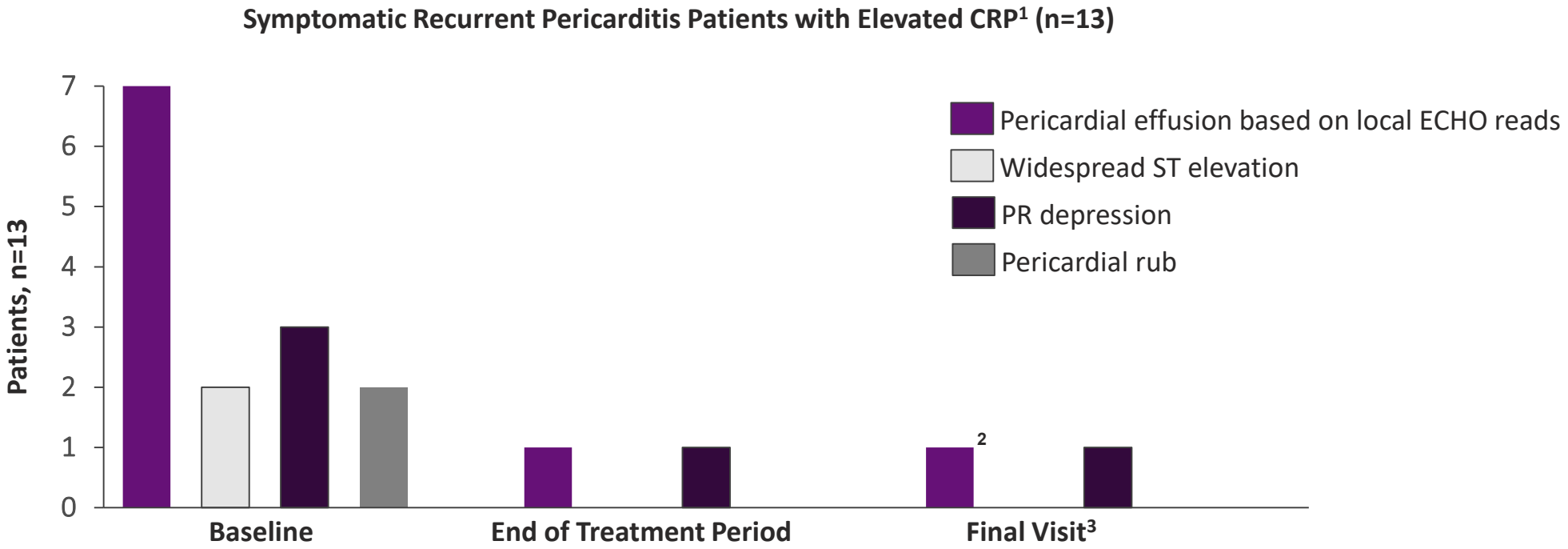
Phase 2 Rilonacept Data

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

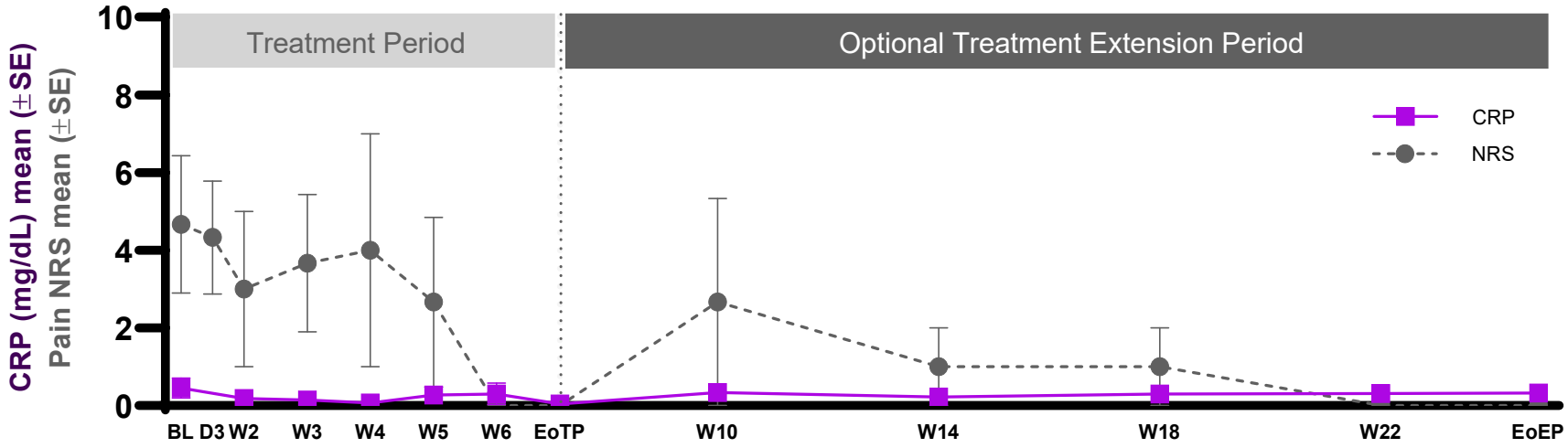


1) Patients with elevated CRP and symptomatic disease (Parts 1 and 4) are most representative of real-world recurrent pericarditis. Inclusion and exclusion criteria for the ongoing Phase 3 study RHAPSODY align with this patient population (clinicaltrials.gov/NCT03737110); 2) patient with effusion at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

Phase 2 Rilonacept Data

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

Symptomatic Recurrent Pericarditis Patients (CRP ≤1mg/dL + MRI inflammation) (n=3)



		BL D3	W2	W3	W4	W5	W6	EoTP	W10	W14	W18	W22	EoEP
CRP	# of Patients	3		3	3	2	3	2	1	3	3	3	3	3
	CRP Mean	.46		.18	.15	0.08	.28	.31	.05	.33	.23	.30	.31	.32
Pain NRS	# of Patients	3	3	3	3	2	3	2	2	3	3	3	3	3
	Pain Mean	4.7	4.3	3.0	3.7	4.0	2.7	0	0	2.7	1.0	1.0	0	0

EoTP = end of treatment period; EoEP = end of extension period; CRP = C-Reactive Protein; NRS = Numeric Rating Scale; MRI = magnetic resonance imaging

Phase 2 Rilonacept Data

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

Corticosteroid-Dependent Patients (Parts 3 and 5): Pericarditis Medications During TP and EP Combined

	Medications					
n/N (%)	At least 1	Analgesics	Aspirin	NSAIDs	Colchicine	CS
Dose stopped	7/8 (87.5)	0/0	0/1	2/5 (40.0)	1/7 (14.3)	7/8 (87.5)
Dose decreased	4/8 (50)	0/0	1/1 (100)	2/5 (40)	1/7 (14.3)	1/8 (12.5)
Dose increased	0/8	0/0	0/1	0/5	0/7	0/8
Starting new	0/8	0/8	0/8	0/8	0/8	0/8

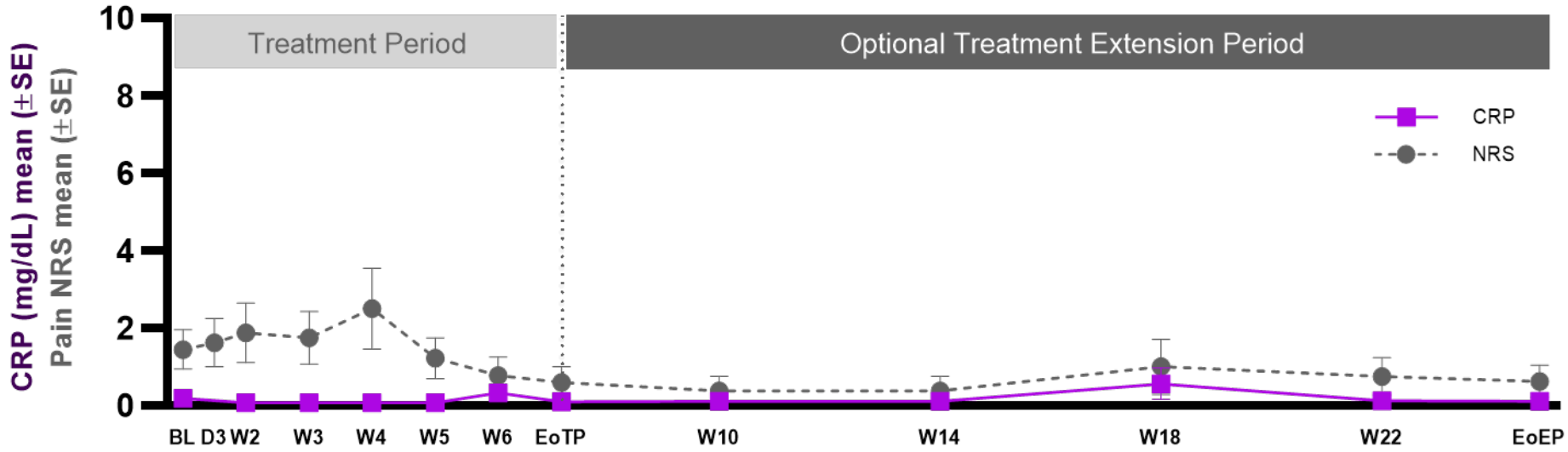
CS, corticosteroid; **NSAID**, nonsteroidal anti-inflammatory drugs

TP = treatment period; EP = extension period;
Rilonacept in Recurrent Pericarditis is for Investigational Use Only; Clinicaltrials.gov: NCT03980522
Klein A. Et al. Circulation. 2019;140:A12851 | AHA Scientific Sessions 2019: Poster SA1094

Phase 2 Rilonacept Data

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

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



		BL	D3	W2	W3	W4	W5	W6	EoTP	W10	W14	W18	W22	EoEP
CRP	# of Patients	9		8	9	5	9	5	9	7	8	4	8	8
	CRP Mean	0.19		0.07	0.07	0.07	0.07	0.33	0.09	0.10	0.11	0.56	0.12	0.12
Pain (NRS)	# of Patients	9	8	8	8	4	9	9	5	8	8	4	8	8
	Pain Mean	1.4	1.6	1.9	1.8	2.5	1.2	0.8	0.6	0.4	0.4	1.0	0.8	0.6

TP = treatment period; EP = extension period; EoTP = end of treatment period; EoEP = end of extension period; CRP = C-Reactive Protein; NRS = Numeric Rating Scale
Rilonacept in Recurrent Pericarditis is for Investigational Use Only; Clinicaltrials.gov: NCT03980522
Klein A. Et al. Circulation. 2019;140:A12851 | AHA Scientific Sessions 2019: Poster SA1094

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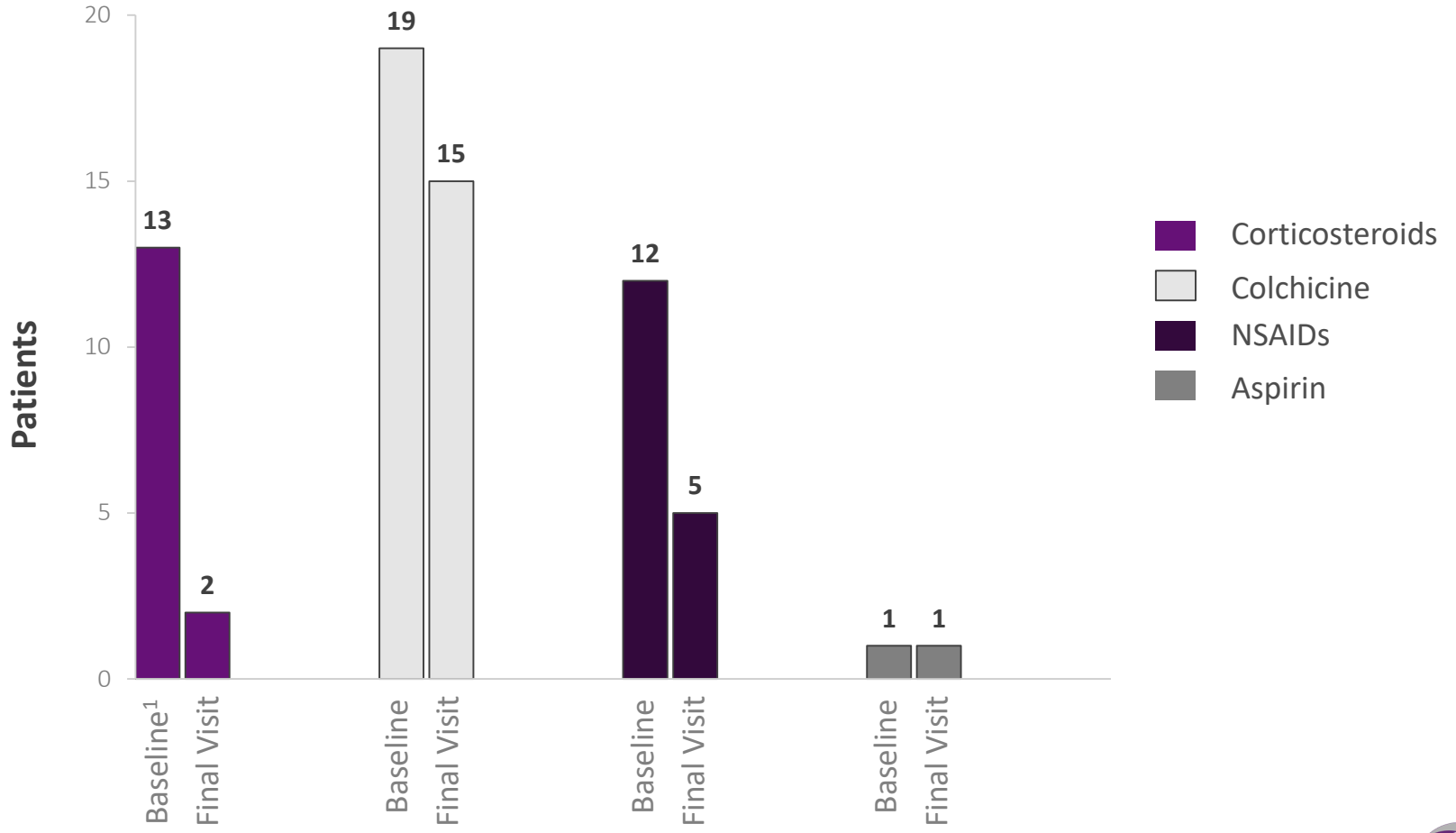
Phase 2 Rilonacept Data

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

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



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

Phase 2 Rilonacept Data

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

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

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

Phase 2 Rilonacept Data

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

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

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

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Phase 2 Rilonacept Data

Rilonacept treatment resulted in improvement of quality of life scores[1]

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

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

Phase 2 Rilonacept Data

Summary of adverse events

	Idiopathic			PPS		Idiopathic or PPS		
Disease Status:	Active[1]	Active[2]	CS-dep[3]	Active[4]	CS-dep[5]	Active[1,2,4]	CS-dep[3.5]	All[1-5]
CRP requirement (mg/dL):	>1	≤1	N/A	>1	N/A	N/A	N/A	N/A
N:	12	3	6	1	3	16	9	25
≥1 TEAE, n (%)	12 (100)	3 (100)	6 (100)	1 (100)	3 (100)	16 (100)	9 (100)	25 (100)
≥1 treatment-related TEAE, n (%)	9 (75)	2 (66.7)	3 (50)	1 (100)	2 (66.7)	12 (75)	5 (55.6)	17 (68)
≥1 serious TEAE, n (%)	2 (16.7)	0	0	0	0	2 (12.5)	0	2 (8)
≥1 treatment-related serious TEAE, n (%)	1 (8.3)	0	0	0	0	1 (6.3)	0	1 (4)
≥1 TEAE leading to treatment discontinuation, n (%)	1 (8.3)	0	0	0	0	1 (6.3)	0	1 (4)
≥1 TEAE leading to death, n (%)	0	0	0	0	0	0	0	0
TEAEs by severity, n (%)								
Mild	9 (75)	3 (100)	4 (66.7)	1 (100)	2 (66.7)	13 (81.3)	6 (66.7)	19 (76)
Moderate	2 (16.7)	0	2 (33.3)	0	0	2 (12.5)	2 (22.2)	4 (16)
Severe	1 (8.3)	0	0	0	1 (33.3)	1 (6.3)	1 (11.1)	2 (8)
Reactions at injection site[6], n (%)	5 (41.7)	1 (33.3)	3 (50)	1 (100)	2 (66.7)	7 (43.8)	5 (55.6)	12 (48)

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

1) Part 1; 2) Part 2; 3) Part 3; 4) Part 4; 5) Part 5; 6) Includes injection site bruising, erythema, pain, reaction, joint warmth, and application site bruising and erythema; CRP = C-reactive protein; CS-dep = corticosteroid-dependent; PPS = post-pericardiotomy syndrome

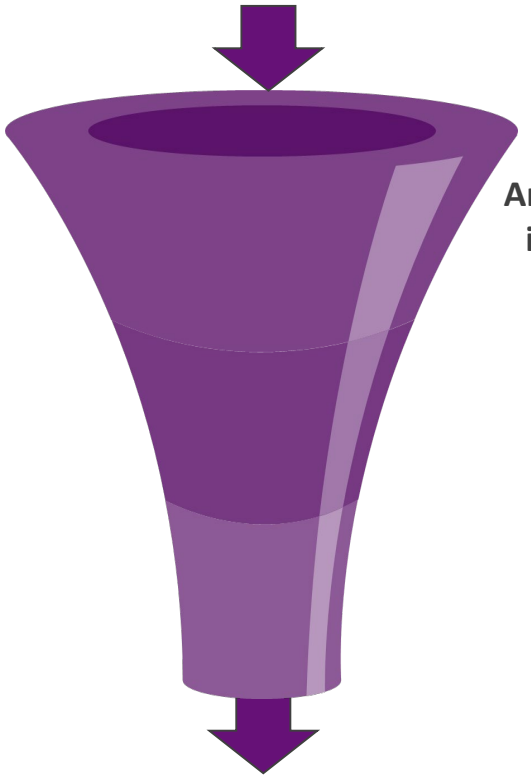
Case Study: Treatment/Retreatment of Recurrent Pericarditis with Rilonacept

- **Patient**
  - 50-year-old female with idiopathic pericarditis and 1 prior recurrence, enrolled in Part 1 during her third episode (pain NRS 6/10; CRP 8.85 mg/dL; pericardial effusion on echocardiography) while receiving colchicine 0.6 mg bid.
- **Pain and CRP Reduction During the Study**
  - Addition of rilonacept to colchicine background rapidly reduced pain (week 2 pain NRS 1/10; week 24 pain NRS 0/10), decreased CRP (week 2 CRP 0.66 mg/dL; week 24 CRP 0.09 mg/dL), and resolved pericardial effusion.
- **Safety**
  - Mild, transient injection site reactions occurred for 21 of 24 rilonacept injections; the patient also had reported mild AEs of heartburn, common cold, worsening of elevated LFTs, elevated cholesterol, elevated HDL, intermittent chest discomfort and elevated CK
- **After Completing the EP**
  - Approximately 8 weeks after rilonacept discontinuation, while continuing on colchicine 0.6 mg bid, the patient presented with pericarditis symptoms requiring addition of celecoxib 200 mg/day. Ten weeks later the patient developed frank pericarditis recurrence (pain NRS 7/10; CRP 23.1 mg/dL) and cardiac tamponade requiring pericardiocentesis. The patient was re-enrolled in the study.
- **Pain and CRP Normalized and Pericardial Effusion Resolved with Rilonacept Retreatment**
  - Rapid improvements in pain and CRP were observed after the first rilonacept administration (week 2 pain NRS 0/10; CRP 0.57 mg/dL). At the week 7 visit, NRS pain was 1/10, CRP was 0.09 mg/dL, and there was no evidence of pericardial effusion on echocardiography. At the last study evaluation available (1 month EP), NRS pain was 0/10 and CRP remained normal (0.08 mg/dL). At the Final Visit NRS pain was 0/10 and CRP remained normal (0.14 mg/dL).
- **Safety**
  - Mild, transient injection site reactions occurred in 17 out of 24 rilonacept administrations; the patient also developed mild AEs of hypokalemia, decreased WBC count, and increased lipids.

NRS = numeric rating scale; CRP = C-reactive protein; LFT= liver function test; CK = creatine kinase; HDL = high-density lipoprotein; WBC = white blood count

Addressable U.S. Opportunity of Rilonacept 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

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Appendix – Mavrilimumab

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

1

Chronic inflammation of medium-to-large arteries

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

2

If left untreated, GCA can cause serious complications

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

3

GCA variants associated with unique presentations

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

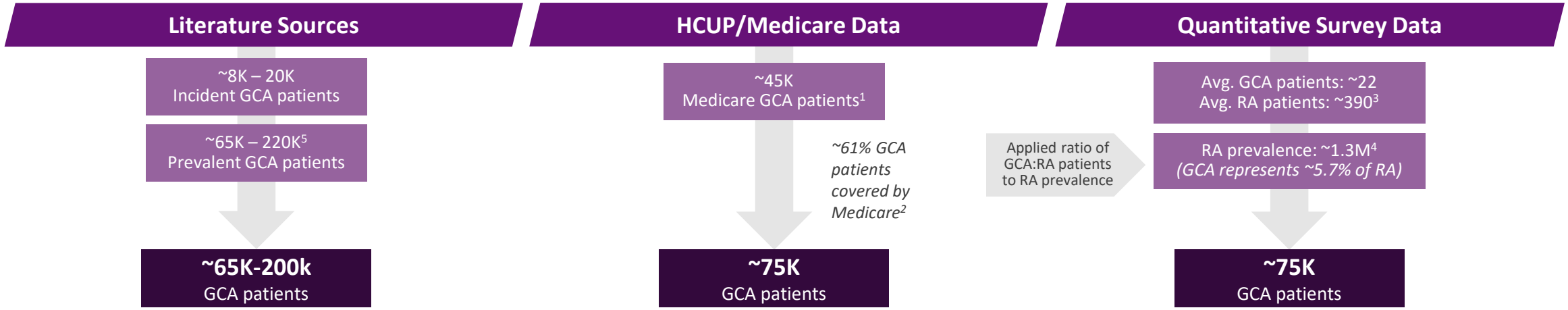
"There is an urgency of treatment with these patients, compared to other conditions it's serious."
– Rheumatologist

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

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

Sources: Medcape; Trinity Partners primary market research

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

GM-CSF is a Key Growth Factor Believed to be Involved in the Pathology of GCA

1	**GM-CSF and GM-CSFRα are overexpressed in GCA lesions**	• Both the receptor[1] and the GM-CSF[2] are expressed in the lesion vs. normal healthy controls
2	**GCA Lesions are heavily comprised of giant cells & non-classical macrophages**	• GM-CSF signaling plays a role in the generation and maturation of giant cells[3] and non-classical macrophages (CD16+)[4] • GM-CSF has been shown to induce endothelial cell migration and proliferation[5] • Inhibition of GM-CSF signaling by mavrilimumab could reduce the number and/or activity of these cells in the vessel wall
3	**Multiple key cytokines driving GCA are downstream of GM-CSF signaling**	• Relevant downstream cytokines in GCA are IL-6, IFNγ and IL-17/23[86] • Inhibiting GM-CSF signaling with mavrilimumab could reduce the relevant pathways involved in both new-onset disease and refractory disease maintenance
4	**Mavrilimumab P2 Trial Underway**	• First-in-class mechanism with the potential to treat both newly diagnosed and refractory patient subsets • Global, P2 proof-of-concept trial ongoing with strata for both patient populations

1) Unpublished Kiniksa Data; 2) Weyand et al., Ann. Int. Med. 1994; 3) Yoshihara et al., Immunology 2003; 4) van Sleen et al., Sci Reports, 2017; 5) Bussolino et al., Letters to Nature 1989; 6) Samson et al Autoimm. Rev. 2017

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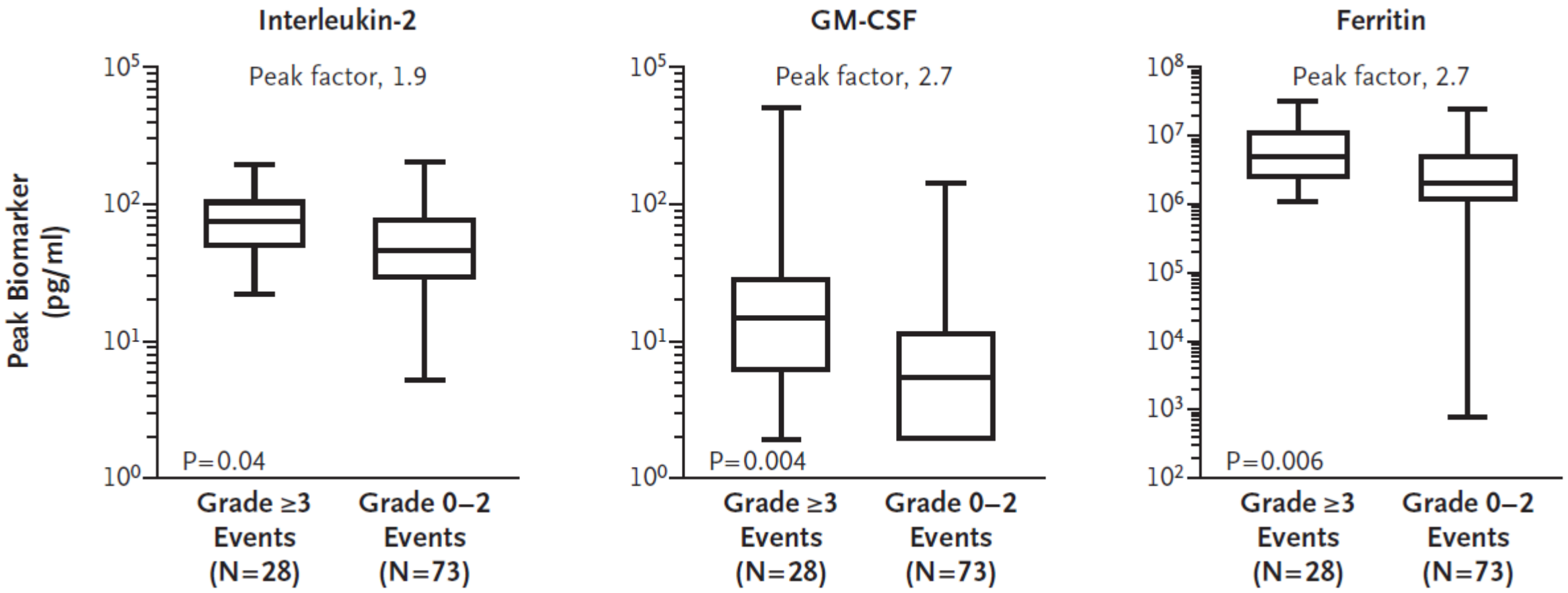
In the ZUMA-1 Trial, Elevated GM-CSF was Most Significantly Associated With the Presence of Severe Neurologic Events in the Biomarkers Explored[1,2]



AUC = area under the curve
CRS = cytokine release syndrome
NE = neurologic events

1) Neelapu et al., Axicabtagene Ciloleucel CAR T-Cell Therapy in Refractory Large B-Cell Lymphoma, NEJM 2017

2) Peak cytokine levels were used in the comparison. These findings were also applicable to cumulative levels across first 28 days after axi-cel infusion (AUC). Adjusted *P* values are calculated from Holm's procedure after multiple testing using the Wilcoxon rank sum test.

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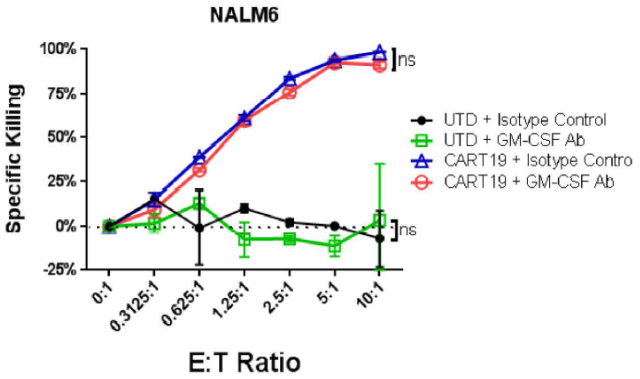
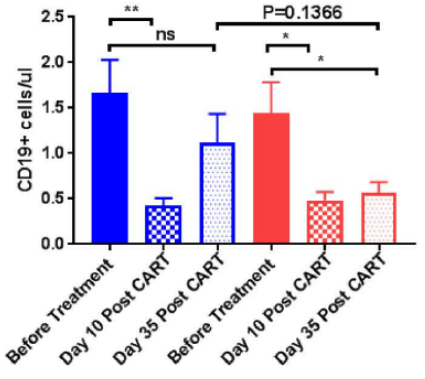
Blockade of GM-CSF signaling attenuated both Cytokine Release Syndrome and Neurologic Events, as well as enhanced CAR T effector function in Preclinical Xenograft Models

GM-CSF Blockade Shows No Negative Effect on CAR T Effector Function

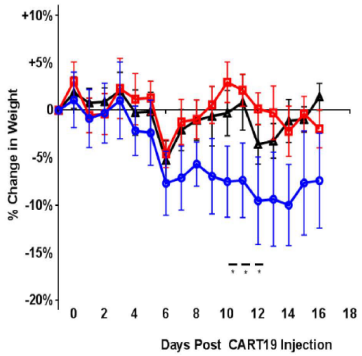




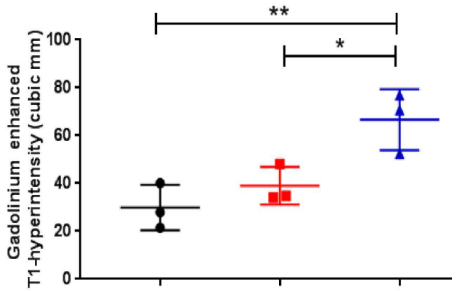
CART19 + anti-GM-CSF showed a more sustained anti-tumor effect than CART19 + control

GM-CSF Blockade Attenuates CRS and Neurological Events

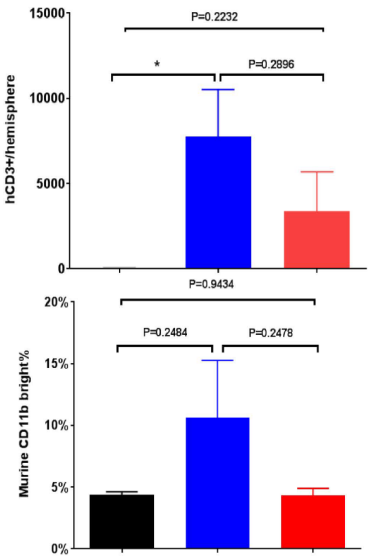
CRS as Measured by Weight Change

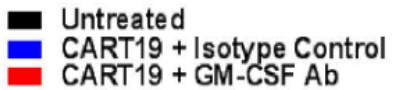


NRS as Measured by Neuroinflammation



NRS as Measured by Cellular Infiltrates

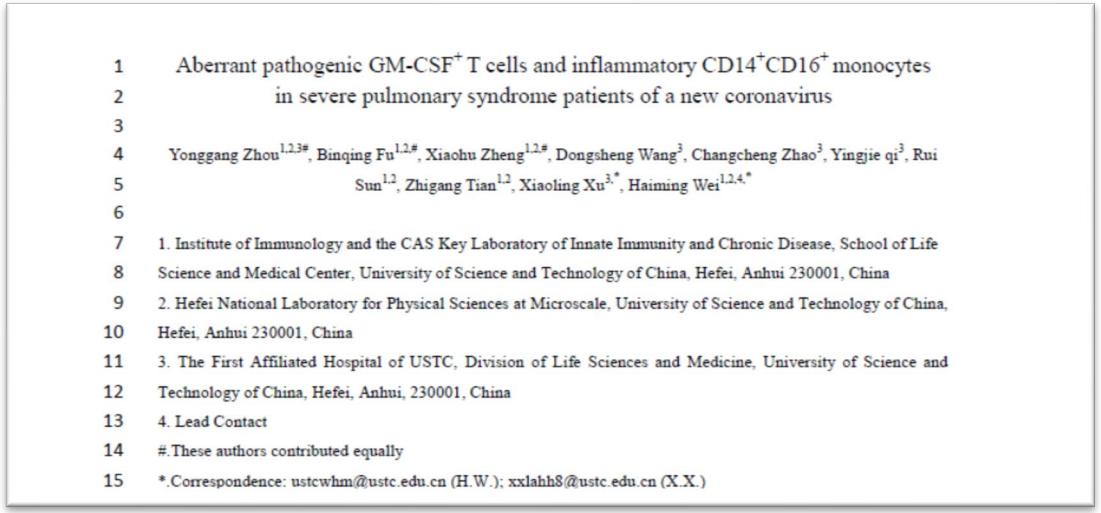




CART19 + anti-GM-CSF treated animals showed reduced CRS (as measured by % change in weight) and NE (as measured by reduction in T1 enhancement and infiltration of T-cells and macrophages)

CRS = cytokine release syndrome
NE = neurologic events
Neelapu et al., NEJM 2017; Sterner et al., Blood 2019

Emerging Literature Support Rationale for Mavrilimumab in COVID-19



Aberrant pathogenic GM-CSF$^+$ T cells and inflammatory CD14$^+$CD16$^+$ monocytes in severe pulmonary syndrome patients of a new coronavirus

Yonggang Zhou[1,2,3#], Binqing Fu[1,2,#], Xiaohu Zheng[1,2,#], Dongsheng Wang[3], Changcheng Zhao[3], Yingjie qi[3], Rui Sun[1,2], Zhigang Tian[1,2], Xiaoling Xu[3,*], Haiming Wei[1,2,4,*]

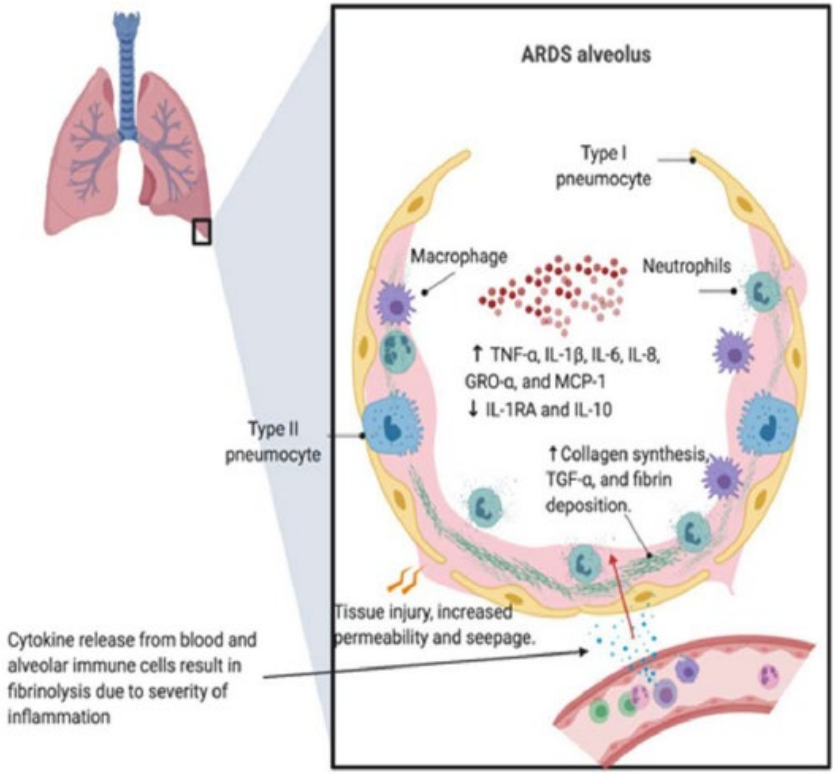
1. Institute of Immunology and the CAS Key Laboratory of Innate Immunity and Chronic Disease, School of Life Science and Medical Center, University of Science and Technology of China, Hefei, Anhui 230001, China
2. Hefei National Laboratory for Physical Sciences at Microscale, University of Science and Technology of China, Hefei, Anhui 230001, China
3. The First Affiliated Hospital of USTC, Division of Life Sciences and Medicine, University of Science and Technology of China, Hefei, Anhui, 230001, China
4. Lead Contact
#.These authors contributed equally
*.Correspondence: ustcwhm@ustc.edu.cn (H.W.); xxlahh8@ustc.edu.cn (X.X.)

- Recent data provide scientific rationale implicating GM-CSF in the mechanism of excessive and aberrant immune cell infiltration and activation in the lungs thought to contribute significantly to mortality in the disease.
- The emerging data indicate that patients with COVID-19 have elevated serum levels of pro-inflammatory cytokines, including GM-CSF, and interferon-gamma, which are thought to be drivers of a cytokine storm that plays a significant role in clinical complications and acute lung injury.
- Infiltration of immune cells in the lungs of COVID-19 patients, as part of an exaggerated immune response despite falling viral loads, results in severe lung complications.
- These data suggest that it may be the excessive, non-effective host immune response by pathogenic T cells and inflammatory monocytes that causes the severe lung pathology most often associated with mortality.

Zhou et al. bioRxiv. 2020

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



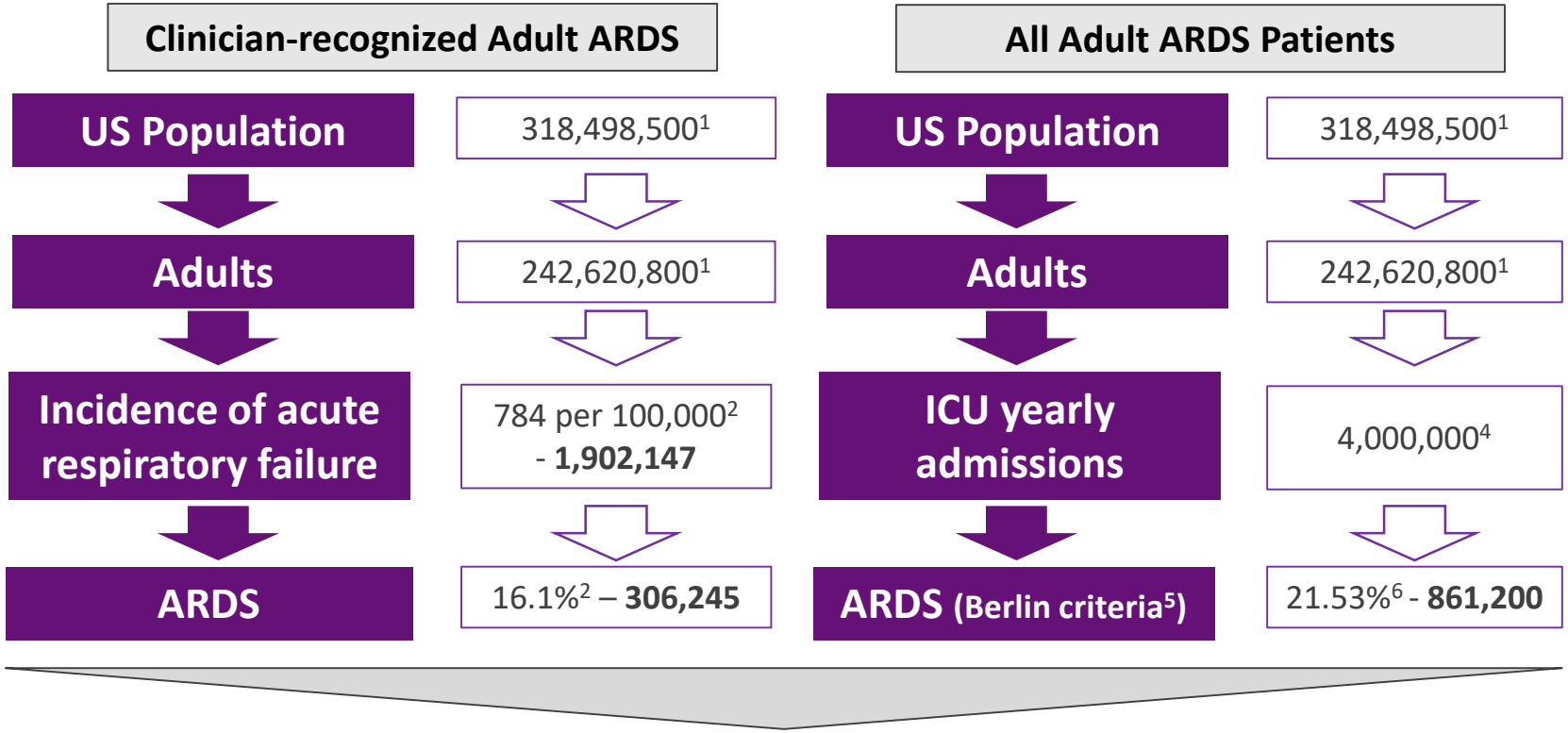
McGonagle, et al., Autoimmunity Reviews (2020), https://doi.org/10.1016/j.autrev.2020.102537

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

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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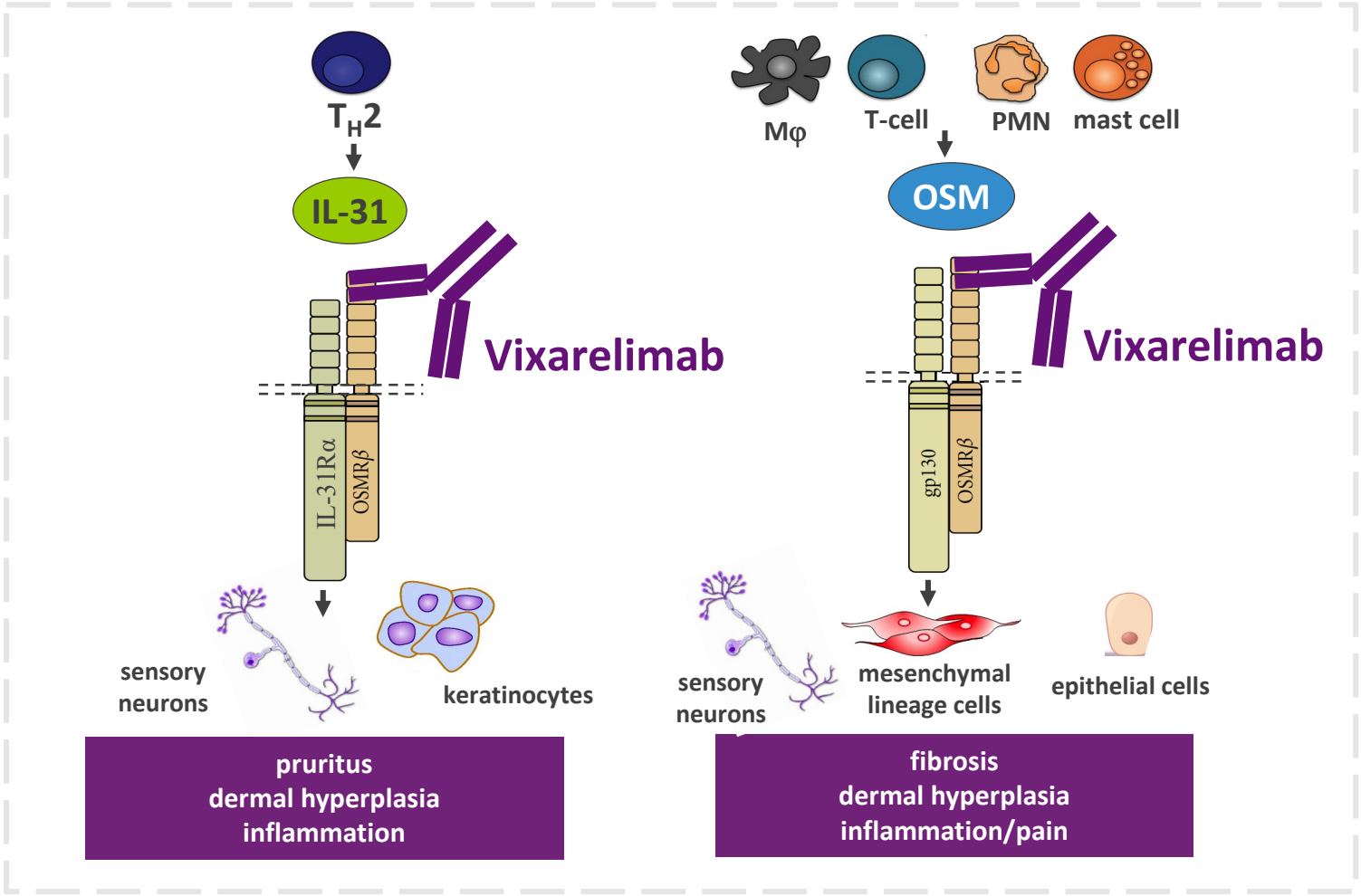
Every Second Counts!™

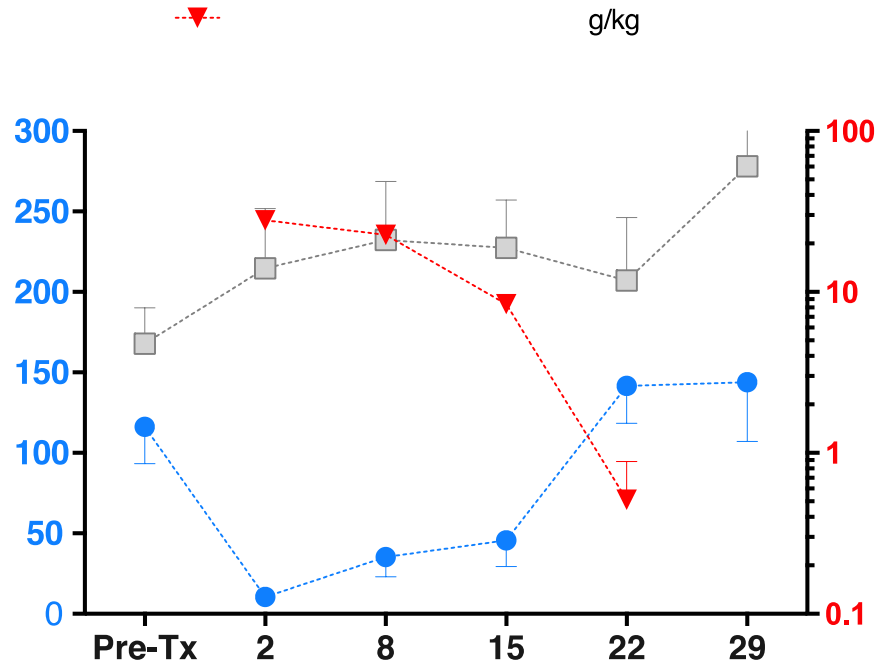
Appendix – Vixarelimab (KPL-716)

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



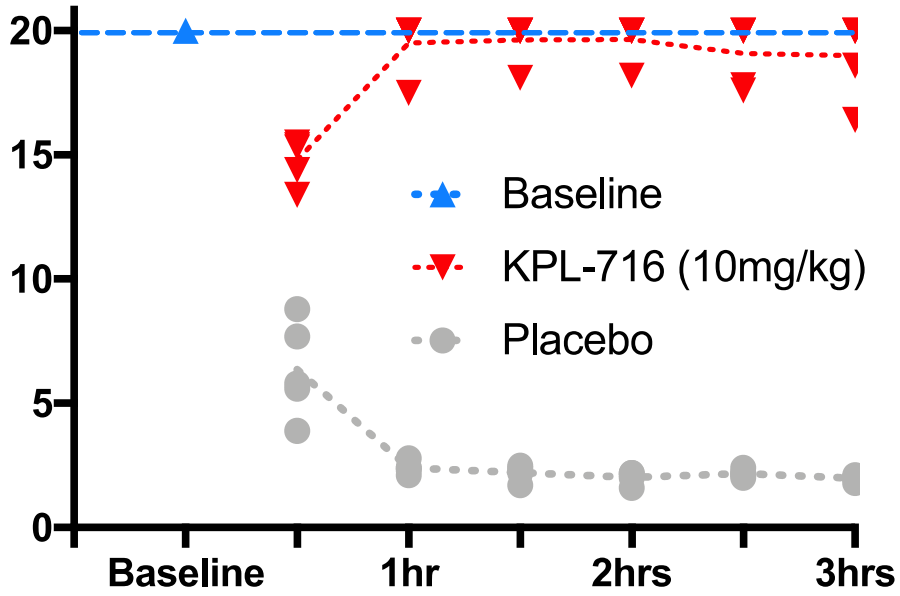
Vixarelimab Inhibited Pruritic Response and Pain Reflex in Two Validated Non-Human Primate Models of Pruritus and Inflammation After a Single Dose

NHP Model of Pruritus*



A single dose of KPL-716 at 3mg/kg inhibited pruritic response driven by supraphysiologic levels of IL-31 for over 2 weeks

NHP Model of Inflammation*

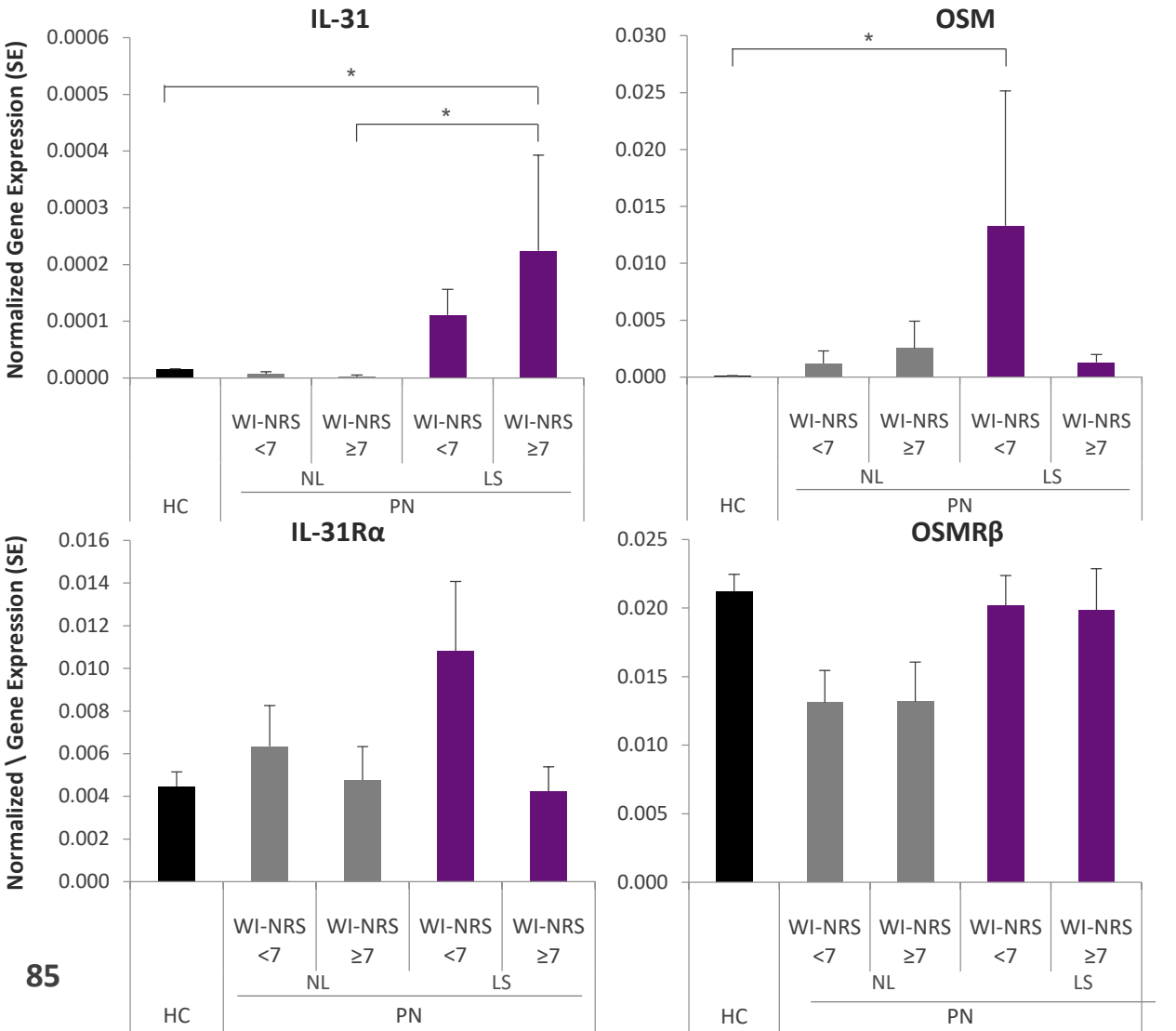


A single dose of KPL-716 at 10mg/kg increased tail withdrawal latency; implicates OSMRβ in the inflammatory response

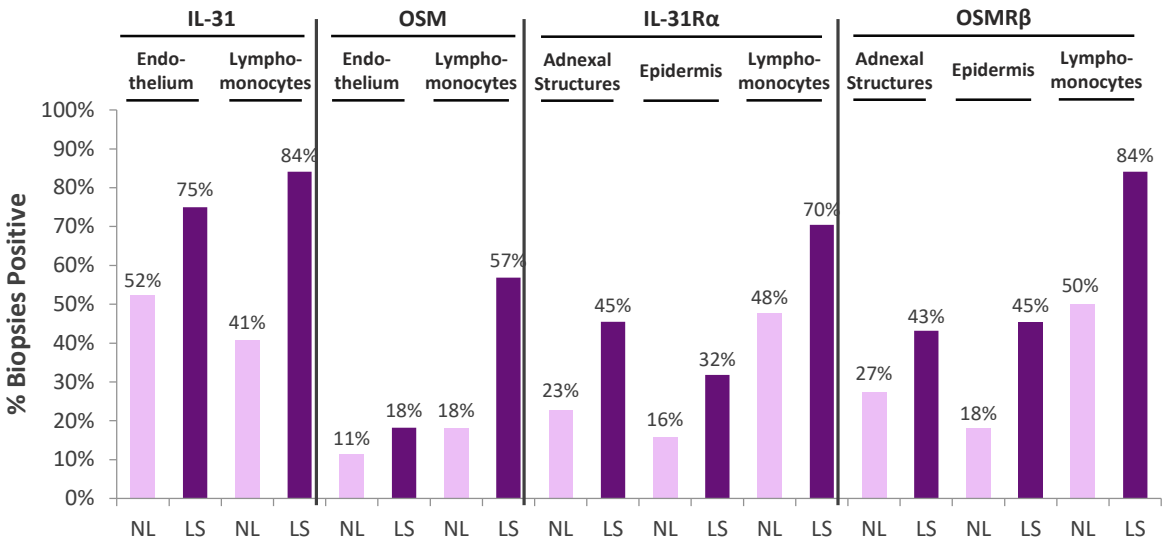
* Unpublished data: not to be reproduced without Kiniksa's express permission; Vixarelimab = KPL-716

All Components of the Type II OSMRβ Signaling Complex Show Upregulation in Lesional Skin of PN Patients; IL-31 is More Highly Expressed in Those Reporting Severe Pruritus

Levels of Gene Expression in PN and HC Skin Biopsies



Presence of Type II OSMRβ Signaling Complex Protein in PN Skin Biopsies*



IHC scores each biopsy on a 1-4 scale; 1=negative, 2=questionably present; 3=present; 4= strongly present; biopsies scored 3 or 4 are considered positive

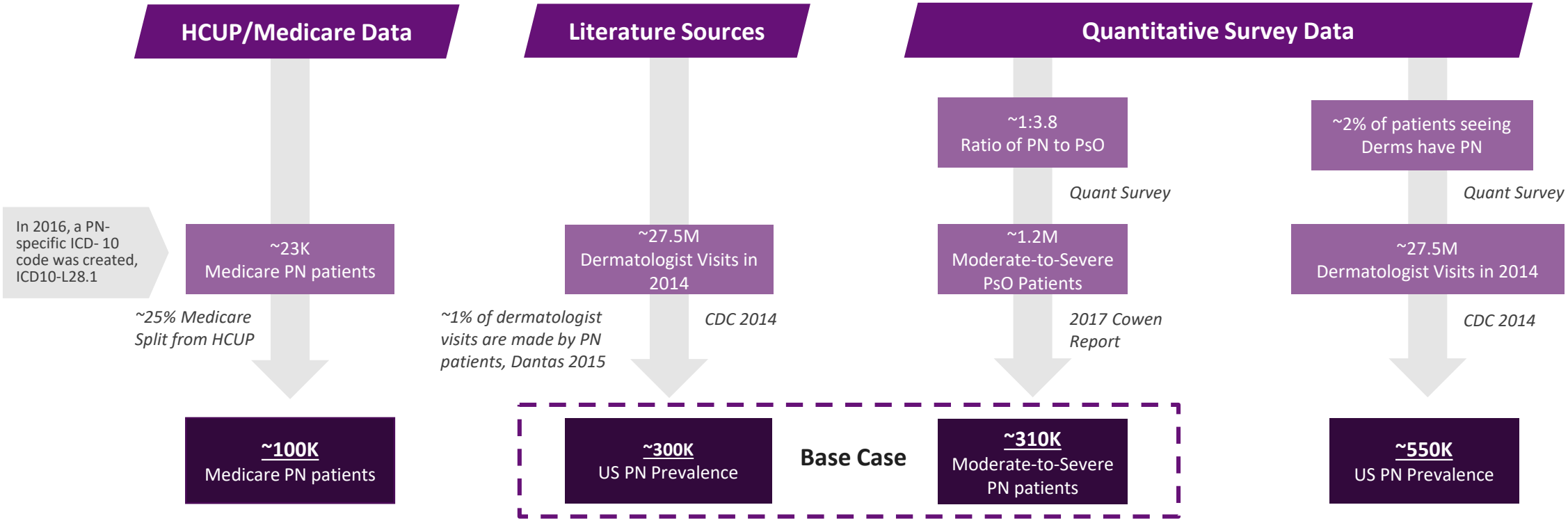
- OSM, OSMRβ, IL-31, and IL-31Rα mRNA expression was higher in lesional (LS) PN biopsies compared with non-lesional (NL) biopsies; all components except for OSMRβ, which is known to be constitutively expressed, showed elevation compared to healthy controls (HC)
  - LS samples from PN patients with WI-NRS≥7 expressed higher levels of IL-31 mRNA compared with HC samples ($p<0.05$) and NL samples
- Protein, analyzed through immunohistochemistry (IHC), for each of the Type II OSMRβ signaling proteins shows upregulation in LS vs NL biopsies of PN patients' skin

These data suggest a role for the OSMRβ axis (IL-31, OSM, IL-31Rα, OSMRβ) in the pathogenesis of PN given its prevalent expression in PN lesional skin

HC, healthy volunteers; IL-31Rα, interleukin 31 receptor α; LS, lesional; NL, non-lesional; SE, standard error; WI-NRS, Worst Itch Numeric Rating Scale. WI-NRS ranges from 0 ("no itch") to 10 ("worst imaginable itch"). *$P<0.05$

*Key tissue compartments for each component included; data for additional tissue compartments available

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

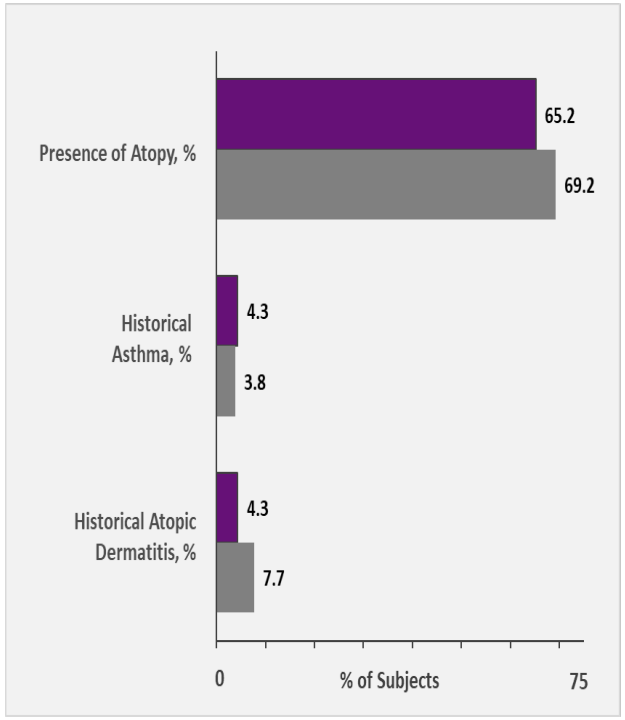


Sources: CDC 2014: National Ambulatory Medical Care Survey: 2014 State and National Summary Tables <https://www.cdc.gov/nchs/data/ahcd/namcs_summary/2014_namcs_web_tables.pdf>; Cowen and Company, Therapeutic Categories Outlook: Comprehensive Study September 2017; Primary Market Research; 3. Dantas, 2015,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

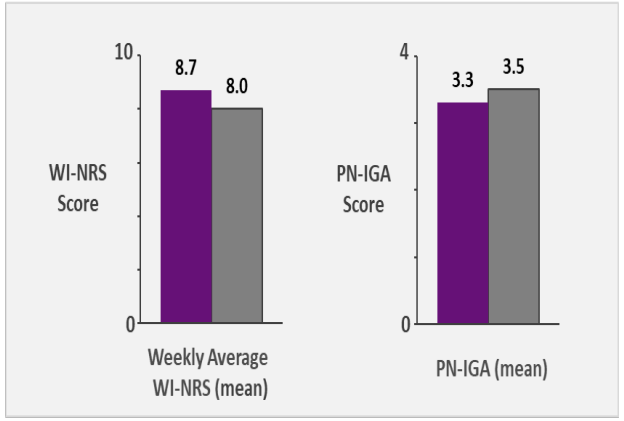
Vixarelimab Phase 2a Study in Prurigo Nodularis: Baseline Characteristics

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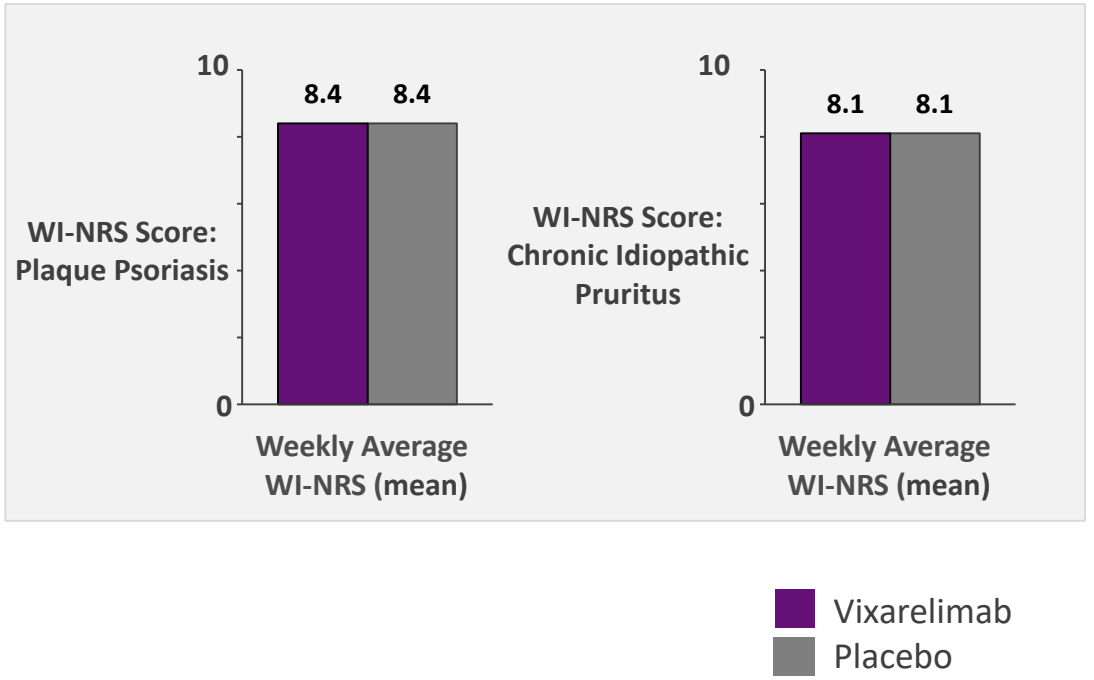
Vixarelimab Exploratory Phase 2 Study in Diseases Characterized by Chronic Pruritus: Baseline Characteristics

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

Vixarelimab was Well-Tolerated in Exploratory Phase 2 Trial

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

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)
Skin and Subcutaneous Tissue Disorders	26.1% (6)	15.4% (4)
Eczema Nummular	4.3% (1)	3.8% (1)
Pruritus	4.3% (1)	3.8% (1)
Dermatitis Allergic	4.3% (1)	0
Idiopathic Angioedema	4.3% (1)	0
Night Sweats	4.3% (1)	0
Urticaria	4.3% (1)	0
Skin Burning Sensation	0	7.7% (2)
Neurodermatitis	0	3.8% (1)

Vixarelimab Placebo-Controlled, Single-Ascending-Dose Phase 1a/1b Study Design

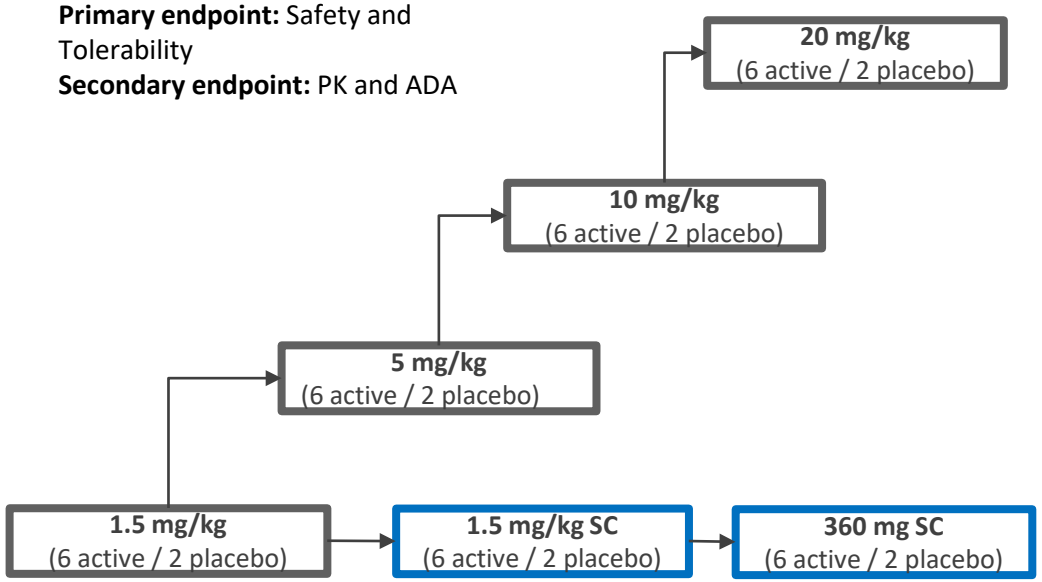
Phase 1a: Normal Healthy Volunteer (n=50)

Dose Groups

Single IV Dose

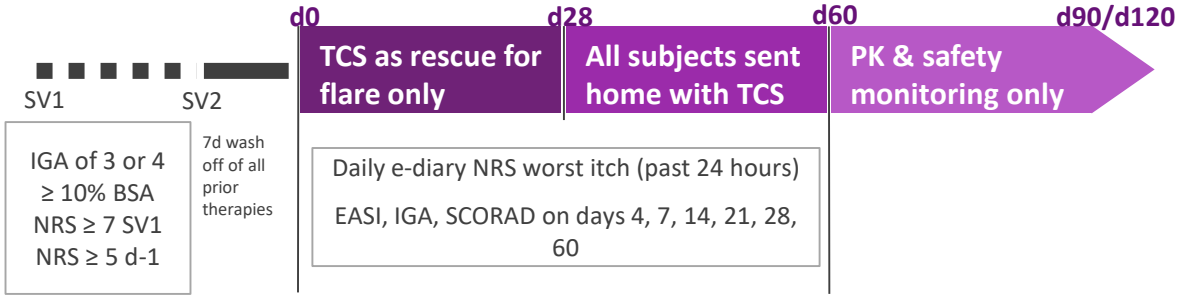
Single SC Dose

Primary endpoint: Safety and Tolerability
Secondary endpoint: PK and ADA



Phase 1b: Subjects with Atopic Dermatitis (n=32)

Patient Experience

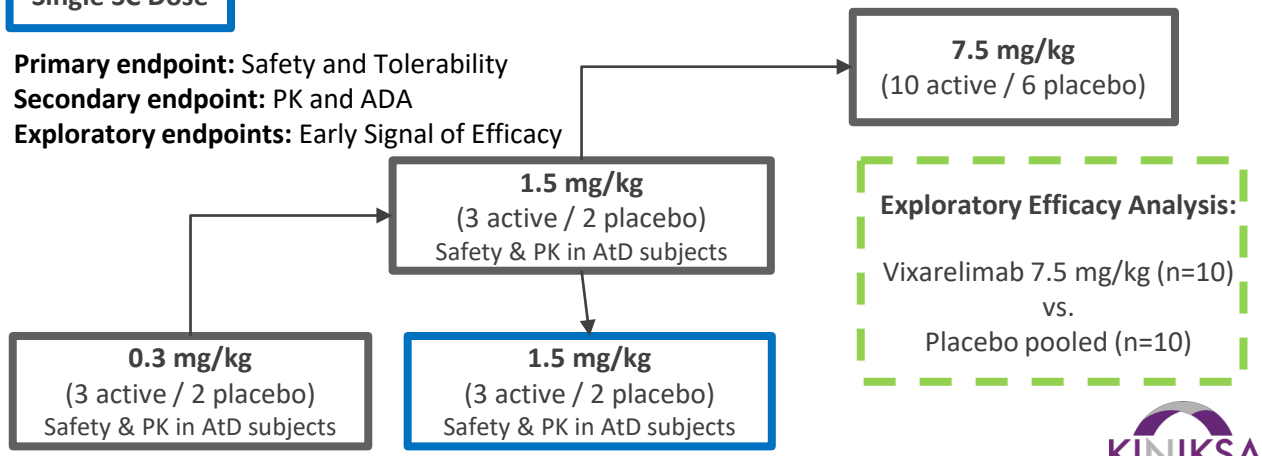


Dose Groups

Single IV Dose

Single SC Dose

Primary endpoint: Safety and Tolerability
Secondary endpoint: PK and ADA
Exploratory endpoints: Early Signal of Efficacy



Vixarelimab was Well-Tolerated in Single-Dose Phase 1a/1b Study

- No Deaths
- No SAEs
- No Discontinuations due to AEs
- No Infusion Reactions
- No Injection Site Reactions
- No Thrombocytopenia
- No Peripheral Edema
- No Conjunctivitis
- Drug-Related Treatment Emergent Adverse Events (DR-TEAEs) infrequent and not related to dose
- All resolved without sequalae

Normal Healthy Volunteers

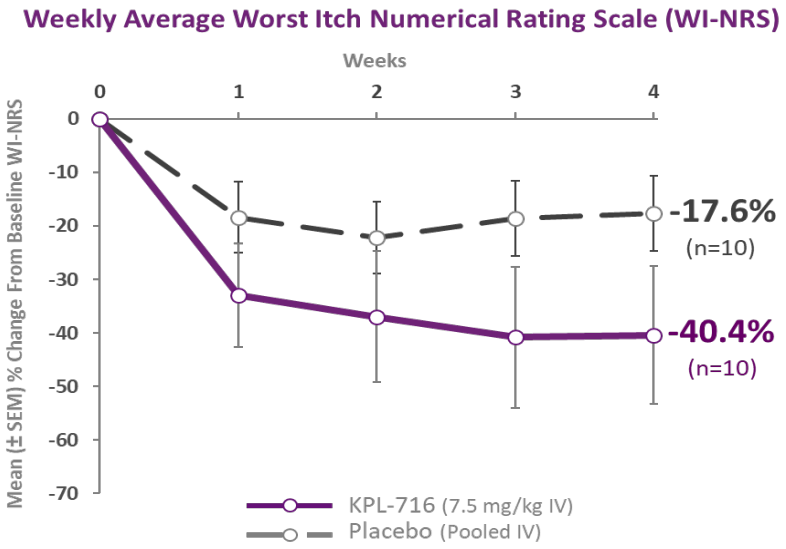
AE	Vixarelimab (IV)				Placebo (IV)	Vixarelimab (SC)		Placebo (SC)
	1.5 mg/kg n=6	5 mg/kg n=6	10 mg/kg n=6	20 mg/kg n=6	Pooled n=8	1.5 mg/kg n=6	360 mg n=7	Pooled n=5
DR-TEAE	0	Mild headache (n=1)	0	0	0	Mild flushing (n=1)	Mild anemia (n=1)	0

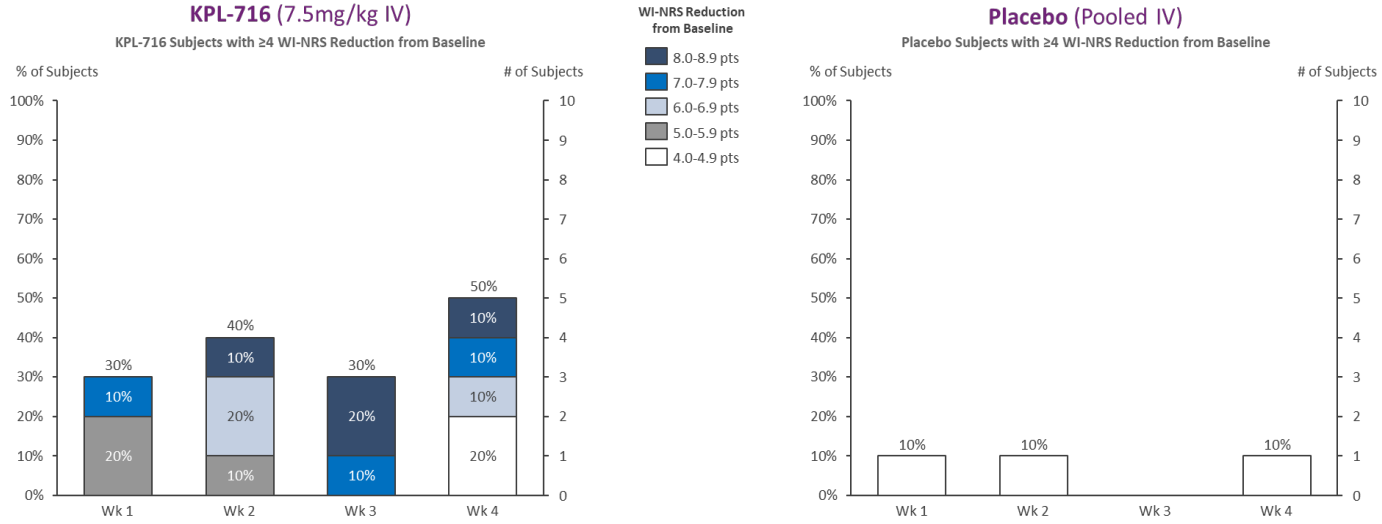
Subjects with Atopic Dermatitis

AE	Vixarelimab (IV)			Placebo (IV)	Vixarelimab (SC)	Placebo (SC)
	0.3 mg/kg n=3	1.5 mg/kg n=3	7.5 mg/kg n=10	Pooled n=10	1.5 mg/kg n=4	Pooled n=2
DR-TEAE*	0	Mild headache (n=1), Decreased appetite (n=1)	Moderate dizziness (n=1)	Mild somnolence (n=1)	Mild dizziness (n=1)	0
AD flare	1	0	2	3	0	0
Study day of AD flare	7	N/A	14, 20	1, 5, 45	N/A	N/A

* The only moderate DR-TEAE occurred after a protocol violation.

Single Doses of Vixarelimab Provided Early Evidence Indicative of Target Engagement and Showed Reduction in Pruritus Over 28-Day Monotherapy Period[1]





Mean % change in WI-NRS decreased by 40.4% in vixarelimab recipients compared to 17.6% decrease in placebo recipients at Day 28 in the absence of concomitant TCS

50% of vixarelimab recipients demonstrated a ≥ 4-point reduction in WI-NRS compared to 10% of placebo recipients at Day 28 in the absence of TCS

1) Oral presentation at the 27th European Academy of Dermatology and Venereology (EADV) Congress: *First-In-Human Study of KPL-716, Anti-Oncostatin M Receptor Beta Monoclonal Antibody, in Healthy Volunteers and Subjects with Atopic Dermatitis;* TCS = topial corticosteroids; vixarelimab = KPL-716

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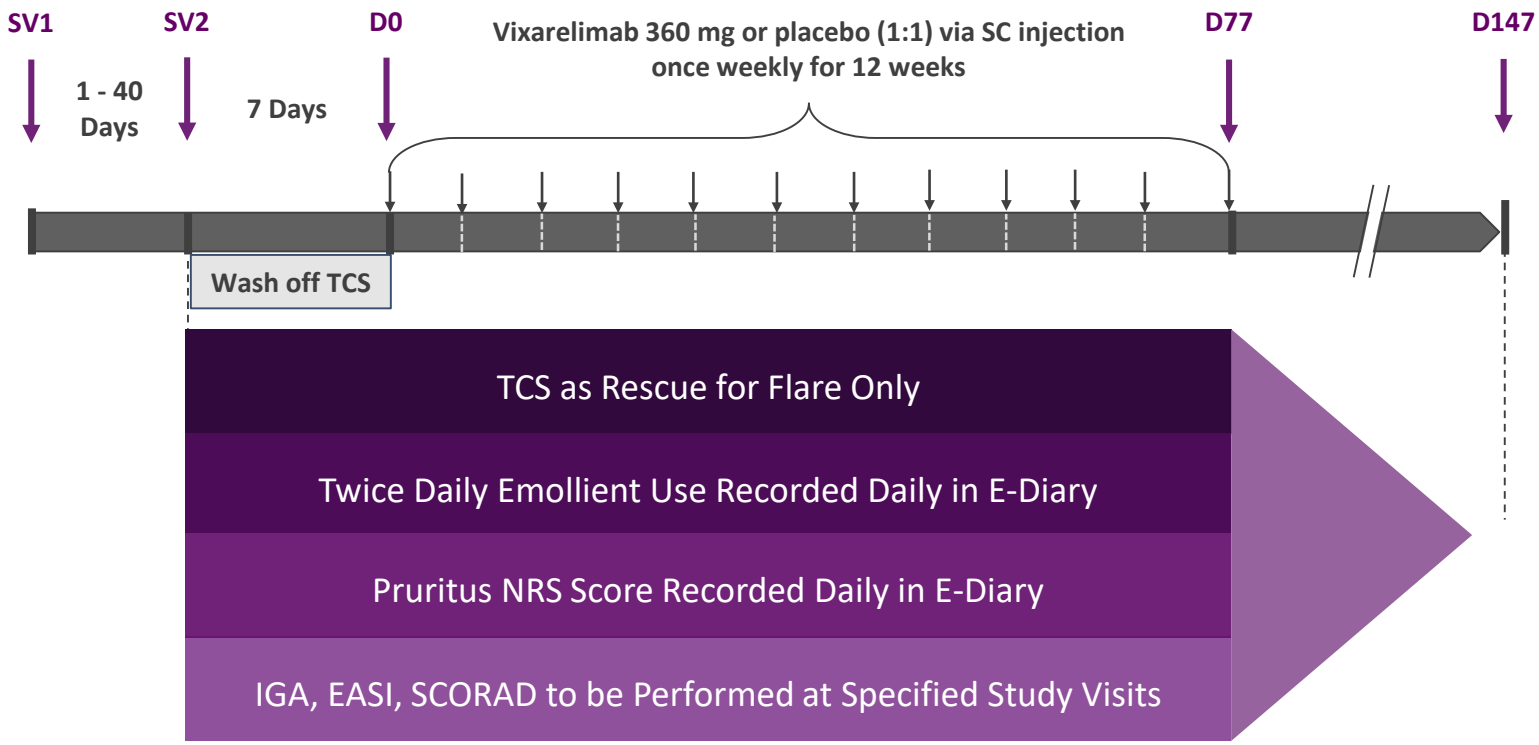
Vixarelimab Placebo-Controlled Repeated-Single-Dose Phase 1b Study Design in Patients with Moderate-to-Severe Atopic Dermatitis

Key Inclusion Criteria:

- IGA of 3 or 4
- BSA ≥ 10%
- EASI ≥ 12
- NRS ≥7 at SV1
- NRS ≥5 at d0



Summary of Interim Vixarelimab Phase 1b Repeated-Single-Dose Data

Enrolled 43 Subjects with Moderate-to-Severe Atopic Dermatitis Experiencing Moderate-to-Severe Pruritus

- Randomized 1:1 between weekly subcutaneous (SC) injections of either placebo or 360mg of vixarelimab for 12 weeks
- Interim data includes all subjects through the 12-week treatment period

Primary Endpoint: safety and tolerability of vixarelimab

Exploratory Endpoints

- Worst-Itch Numerical Rating Score (WI-NRS) as recorded in a daily e-diary
- Measures of atopic dermatitis disease severity

Topline Observations

- Vixarelimab showed rapid and sustained reductions in pruritus versus placebo for the duration of the treatment period
    - The mean change from baseline in weekly-average WI-NRS at Week 1 was -28.1% in vixarelimab recipients compared to -6.8% in placebo recipients
    - The mean change from baseline in weekly-average WI-NRS at Week 12 was -55.0% in vixarelimab recipients compared to -30.9% in placebo recipients
    - 52.6% of vixarelimab recipients demonstrated a ≥ 4-point reduction in weekly-average WI-NRS at Week 12 compared to 26.3% of placebo recipients
- There were no meaningful benefits of repeated-single-doses of vixarelimab on other efficacy endpoints specific to atopic dermatitis, including Eczema Area and Severity Index (EASI) and Scoring Atopic Dermatitis (SCORAD)
- There were no serious adverse events. However, there were more atopic dermatitis flares in vixarelimab recipients compared to placebo recipients (47.6% for the vixarelimab arm vs. 4.5% for the placebo arm) through the 12-week treatment period. Vixarelimab was otherwise well-tolerated

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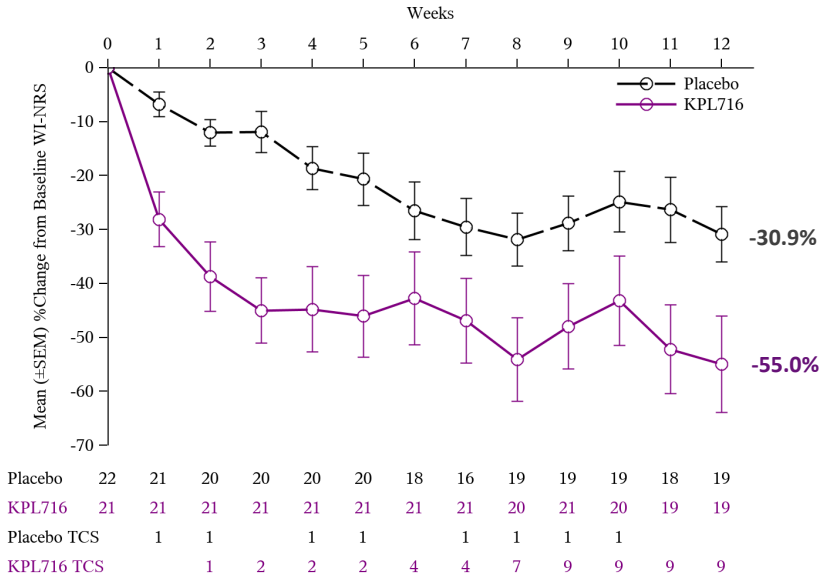
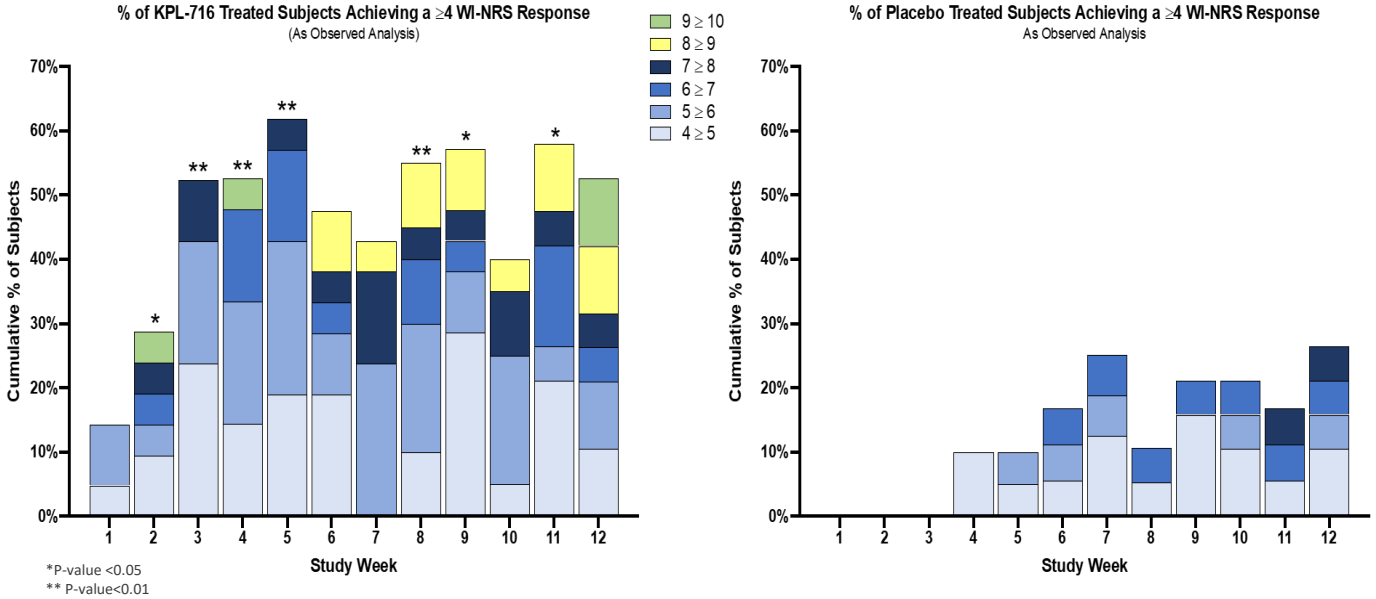
Repeated-Single-Doses of Vixarelimab Showed Rapid and Sustained Reduction in Pruritus Versus Placebo[1]



Mean % change in WI-NRS decreased by 55.0% in vixarelimab recipients compared to 30.9% decrease in placebo recipients at Week 12



A larger percentage of subjects in the vixarelimab arm achieved a ≥4-point change in weekly average WI-NRS versus placebo

1) Interim data results 8/12/19 – available through Investors & Media section of Kiniksa's website at www.kinksa.com; vixarelimab = KPL-716

Overview of Treatment-Emergent Adverse Events (TEAE) Through 12-Week Treatment Period

	Placebo (N=22)	Vixarelimab (N=21)
Any TEAE	12 (54.5%)	18 (85.7%)
Any Drug-Related TEAE	4 (18.2%)	8 (38.1%)
Any Moderate or Severe TEAE	6 (27.3%)	11 (52.4%)
Any Drug-Related Moderate or Severe TEAE	0	2 (9.5%)
Any Treatment-Emergent Serious AE	0	0
Any Drug-Related Serious TEAE	0	0
Any Atopic Dermatitis Flare-Related TEAE	1 (4.5%)	10 (47.6%)
Any Injection Site Reaction	2 (9.1%)	3 (14.3%)
Any TEAE Led to Dose Interruptions	1 (4.5%)	2 (9.5%)
Any TEAE Led to Study Drug Discontinuation	0	2 (9.5%)
Any TEAE Led to Death	0	0

Moderate / Severe Drug-Related TEAE

	Placebo (N=22)	Vixarelimab (N=21)
Subjects with At Least 1 Drug-related Moderate or Severe TEAE	0	2 (9.5%)
Infections and infestations	0	1 (4.8%)
Eczema impetiginous	0	1 (4.8%)
Psychiatric disorders	0	1 (4.8%)
Depression	0	1 (4.8%)
Skin and subcutaneous tissue disorders	0	1 (4.8%)
Dermatitis atopic	0	1 (4.8%)

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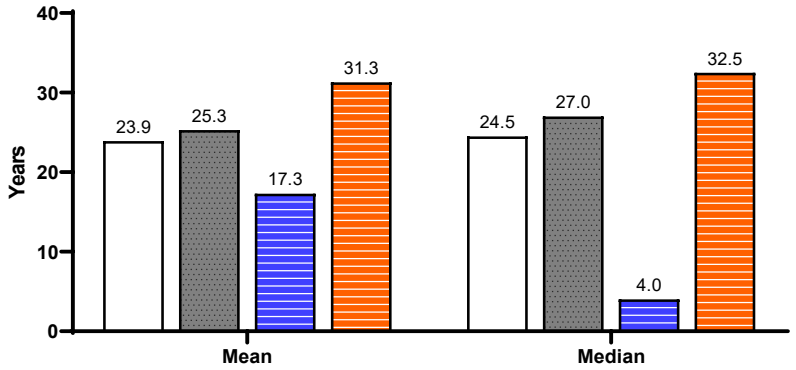
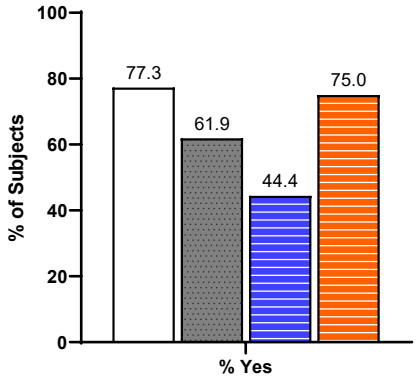
Baseline Subject Characteristics and Retrospective Groupings

PBO (All)
716 (All)
KPL-716 (Subjects Who Did NOT Flare)
KPL-716 (Experienced a Flare)

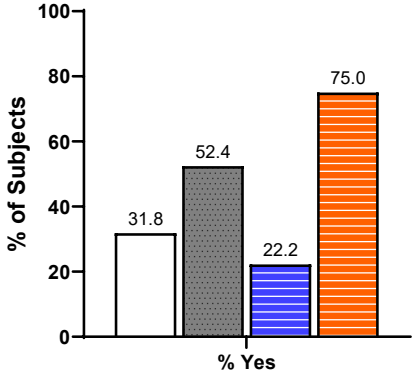
Disease Duration at Baseline



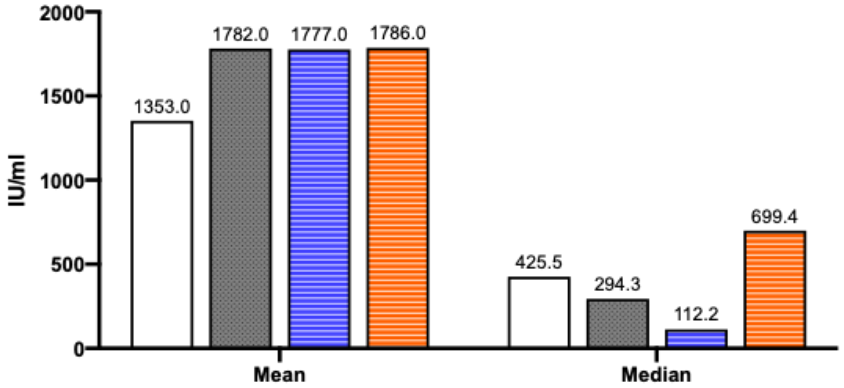
Subjects with History of Allergy



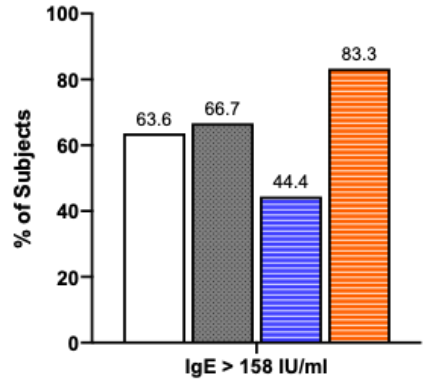
Subjects with Prior TCS Use



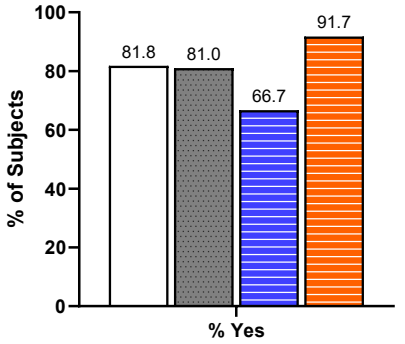
IgE Levels at Baseline



Subjects with IgE > ULN



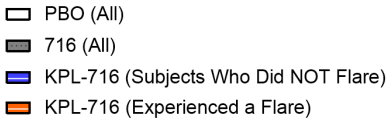
Subjects with Atopy

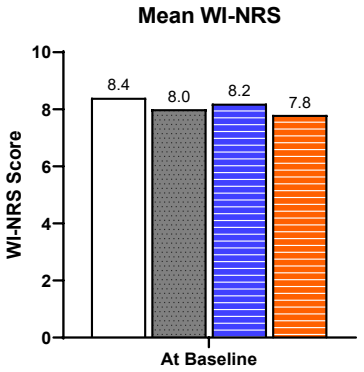


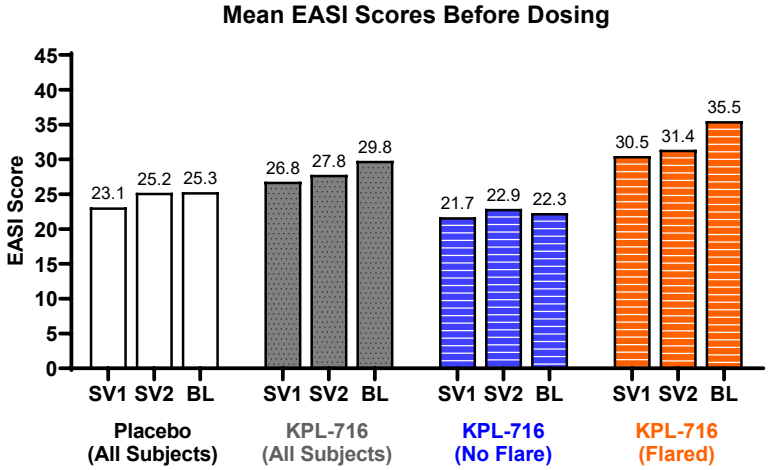
Note: Based on full interim data set as of 1st database lock

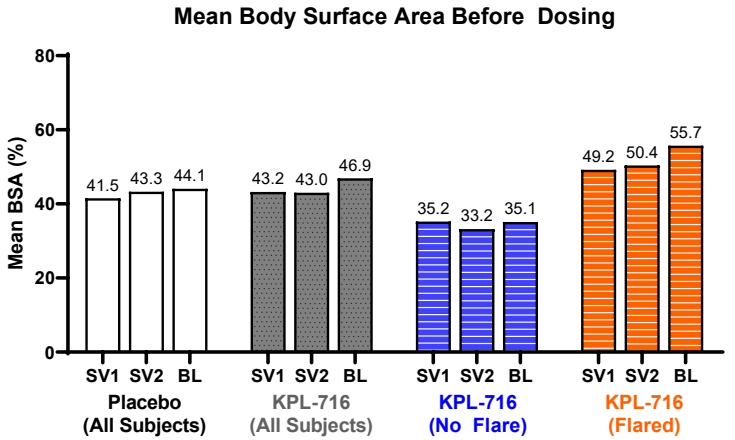
ULN: Upper Limit of Normal; **PBO**: Placebo; **TCS:** Topical corticosteroid

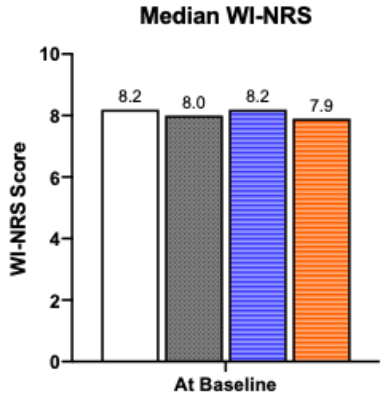
Disease Characteristics at Baseline and Retrospective Groupings

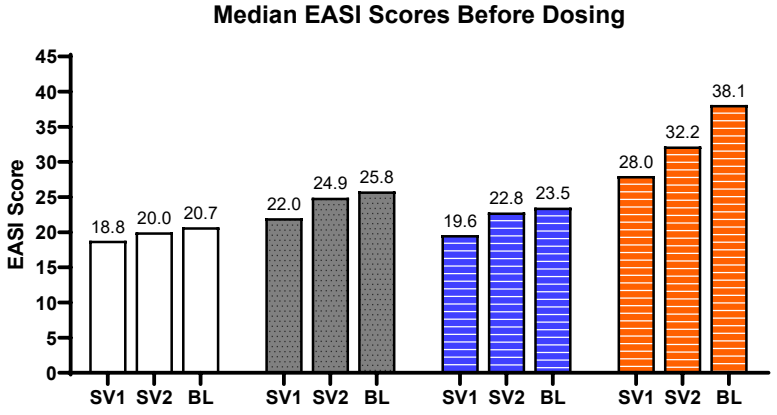


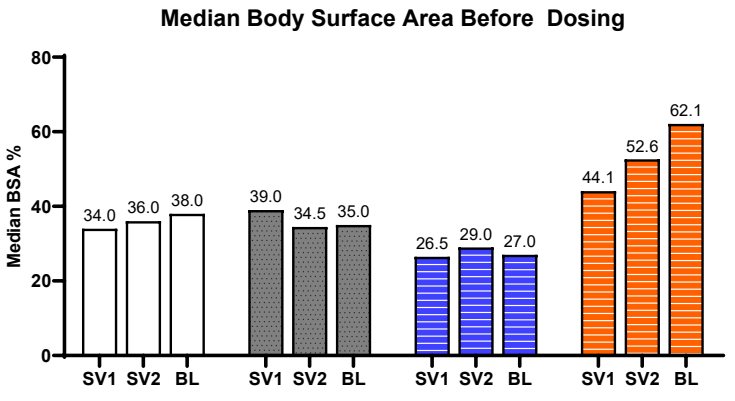






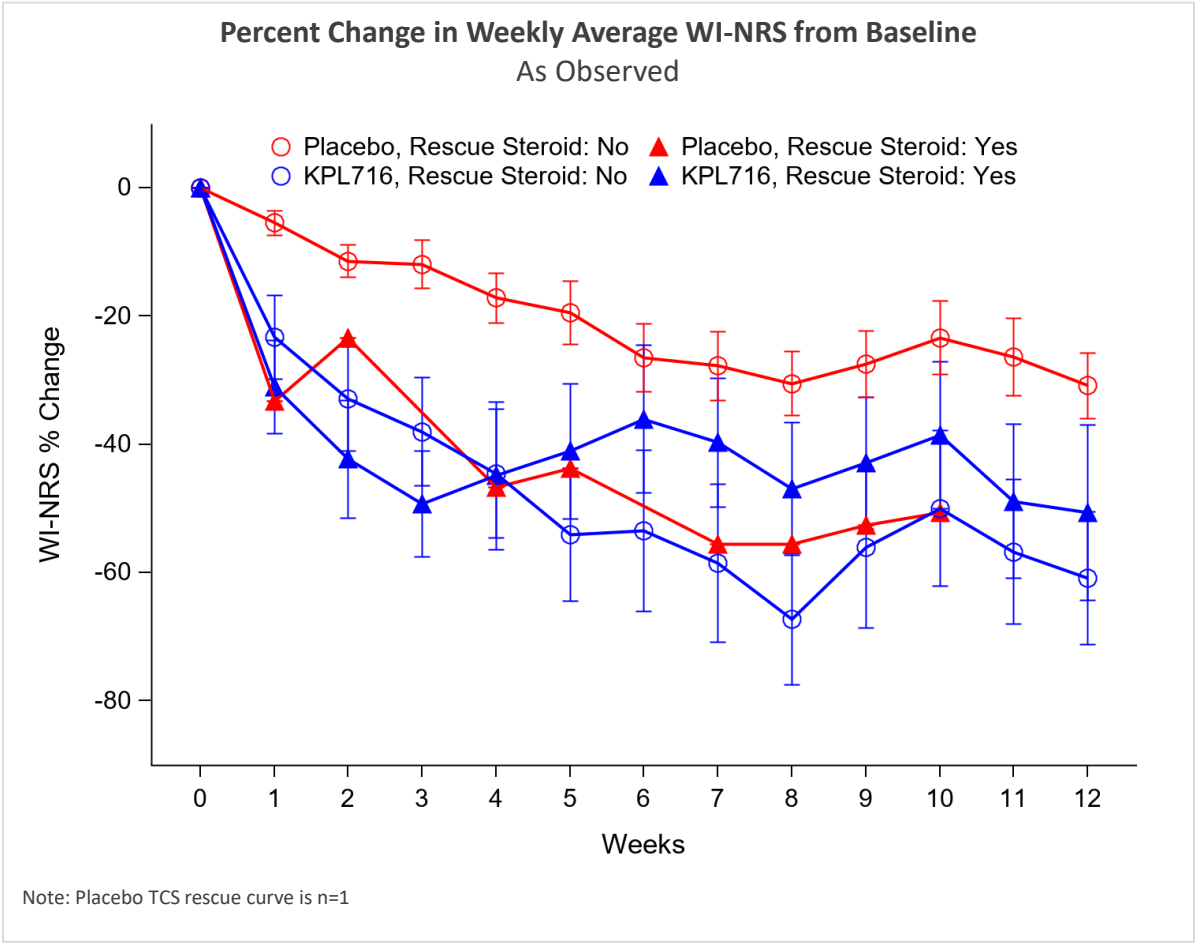






Note: Based on full interim data set as of 1st database lock **SV1**: Screening Visit 1; **SV2**: Screening Visit 2; **BL**: Baseline on Day 0 before first dose of KPL-716; **TCS**: Topical Corticosteroid; **PBO:** Placebo

Vixarelimab Showed Rapid and Sustained Reduction in Pruritus in Patients Who Did Not Receive Topical Corticosteroid Rescue[1]



Note: Placebo TCS rescue curve is n=1

1) Interim data results 8/12/19 – available through Investors & Media section of Kiniksa's website at www.kinksa.com; vixarelimab = KPL-716

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Every Second Counts!™