Every Second Counts™

January 2019

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 subsidiary, together, unless context otherwise requires, "Kiniksa," "we" 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 and corporate goals, potential acquisitions and collaborations, product development activities, clinical trials and other studies, regulatory and other applicable authority submissions, applications and approvals, our pre-commercial efforts, potential value drivers for the company, potential market opportunities and competitive position, and plans for 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 the important factors discussed under the caption "Risk Factors" in the registration statement on Form S-1 filed with the Securities and Exchange Commission (the "SEC") on January 28, 2019 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.

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This presentation does not constitute an offer to sell or the solicitation of an offer to buy any of our securities.

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- ✓ Passionate Employees
- ✓ Sequential Pipeline
- ✓ Rare and Specialty Diseases
- ✓ Strong Biologic Rationale or Validated Mechanisms
- ✓ Potential for Multiple Indications

Building a fully-integrated global biopharmaceutical company

Discovering, acquiring, developing and commercializing life-changing therapies for debilitating diseases

DATA-DRIVEN CAPITAL ALLOCATION

Pipeline of 5 product candidates across various stages of development

	Program & Target	Indication	Preclinical / Phase 1 / Phase 2 / Phase 3	Status	Rights
1	**Rilonacept**[1] IL-1α & IL-1β	Recurrent Pericarditis		• Enrolling single, pivotal Phase 3 trial	Worldwide (excluding MENA)
2	**Mavrilimumab** GM-CSFRα	Giant Cell Arteritis (GCA)		• Enrolling global Phase 2 proof-of-concept trial	Worldwide
3	**KPL-716** OSMRβ	Prurigo Nodularis (PN)		• Plan to initiate adaptive design Phase 2a/2b trial in PN in 1H 2019	Worldwide
		Chronic Idiopathic Pruritus, Chronic Idiopathic Urticaria, Plaque Psoriasis, Lichen Simplex Chronicus, Lichen Planus		• Plan to initiate Phase 2 exploratory pilot study in multiple diseases characterized by chronic pruritus in 1H 2019	
		Atopic Dermatitis (AD)		• Enrolling repeated-single-dose Phase 1b trial	
4	**KPL-045**[2] CD30L	Autoimmune		• Plan to file IND in 2H 2019	Worldwide
5	**KPL-404**[2,3] CD40	Autoimmune		• Plan to file IND in 2H 2019	Worldwide

1) Rilonacept (ARCALYST®) is approved and marketed for cryopyrin-associated periodic syndrome, in the United States by Regeneron Pharmaceuticals, Inc. We will assume the rights to this indication upon receiving approval for rilonacept in the recurrent pericarditis indication; 2) We are planning IND-enabling studies for both KPL-045 and KPL-404 in T-cell-dependent, B-cell-mediated diseases, such as pemphigus/pemphigoid, myasthenia gravis, or graft versus host disease; 3) Subject to closing our acquisition of Primatope.

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Strong execution produced transformational 2018

2018 Goals	2019 Goals
✓ **Rilonacept** Report interim Phase 2 data Start Phase 3 clinical trial	☐ **Rilonacept** Enroll in the pivotal Phase 3 clinical trial Present Phase 2 data at ACC
✓ **Mavrilimumab** U.S. IND and global regulatory submissions Start global Phase 2 clinical trial (GCA)	☐ **Mavrilimumab** Enroll in the global Phase 2 clinical trial (GCA) Announce additional indication
✓ **KPL-716** Report Phase 1a/1b data Start repeated-single-dose Phase 1b clinical trial	☐ **KPL-716** Advance into multiple chronic pruritic diseases Report repeated-single-dose-data
✓ **KPL-045** IND enabling studies	☐ **KPL-045** File IND
✓ **KPL-404** IND enabling studies	☐ **KPL-404** File IND

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1 Rilonacept – Phase 3

(IL-1α and IL-1β cytokine trap)

RHAPSODY

Rilonacept Mavrilimumab KPL-716 KPL-045 KPL-404

Opportunity in an inflammatory cardiovascular disease with no currently-approved therapies

Mechanism of Action[1]	IL-1α and IL-1β cytokine trap
Lead Indication	Recurrent Pericarditis (approved in the U.S. for CAPS, a rare autoinflammatory disease)
Addressable Population[2]	~14k patients in the U.S. (~3k refractory, ~6k poorly-controlled or steroid-dependent, ~5K steroid-intolerant)
Competition[3]	No currently-approved therapies for recurrent pericarditis; differentiated from other marketed IL-1 agents
Clinical Development	Enrolling a global, pivotal Phase 3 trial (RHAPSODY); Presenting data from ongoing Phase 2 trial at ACC
Rights	Worldwide (excluding MENA); BLA transfers to Kiniksa upon approval in recurrent pericarditis

1) Brucato et al. JAMA. 2016, 316 (18): 1906-1912; Arcalyst Prescribing Information; 2) 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; 3) 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 is a debilitating disease with no currently 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 and PR depression); (3) Pericardial effusion

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

Involvement of IL-1 in Recurrent Idiopathic Pericarditis:

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

Recurrent pericarditis causes significant impairment of quality of life

Acute Episodes Have Favorable Prognosis:

- For most patients, acute pericarditis episodes last less than a few weeks and resolve on their own

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 surgery

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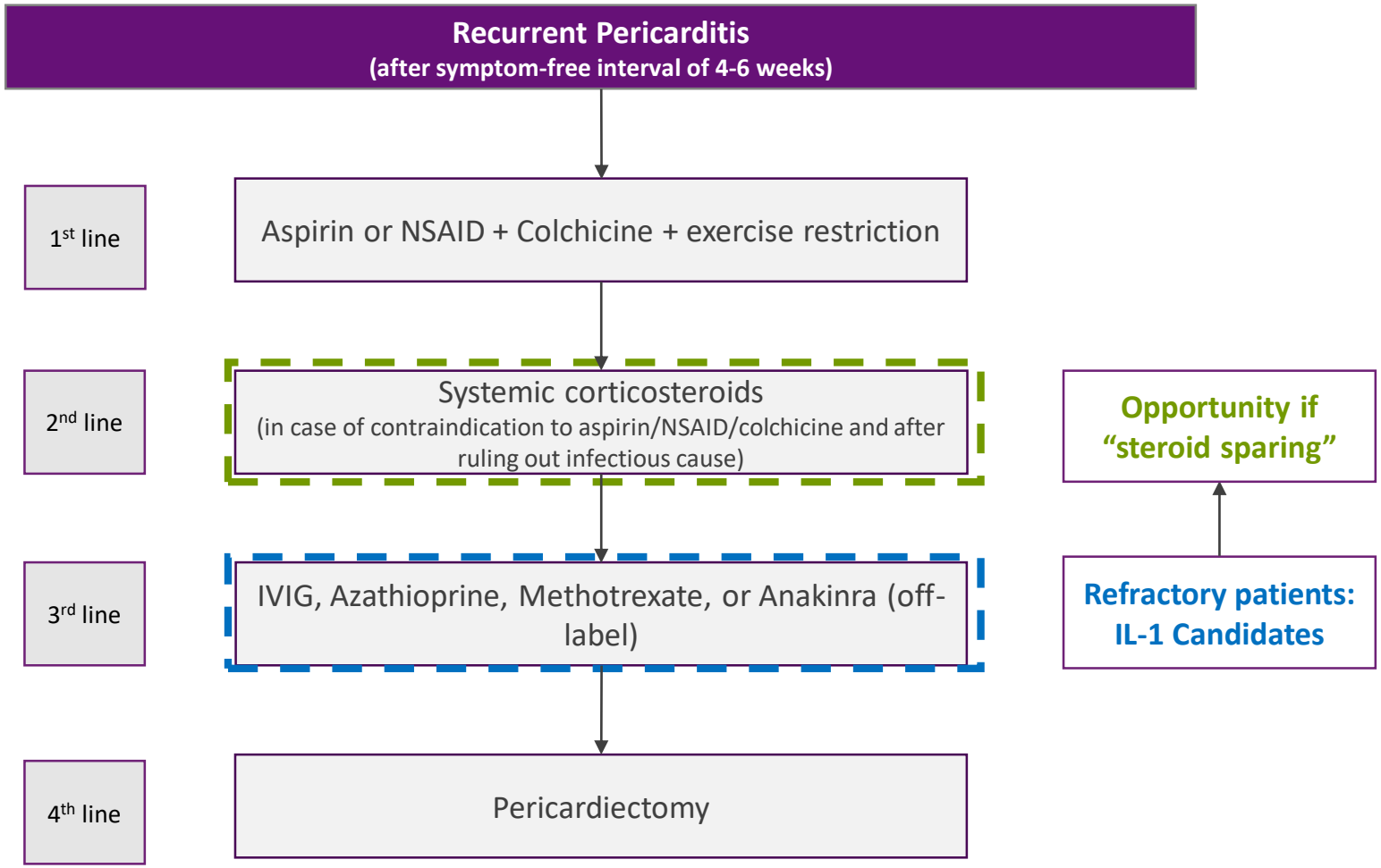
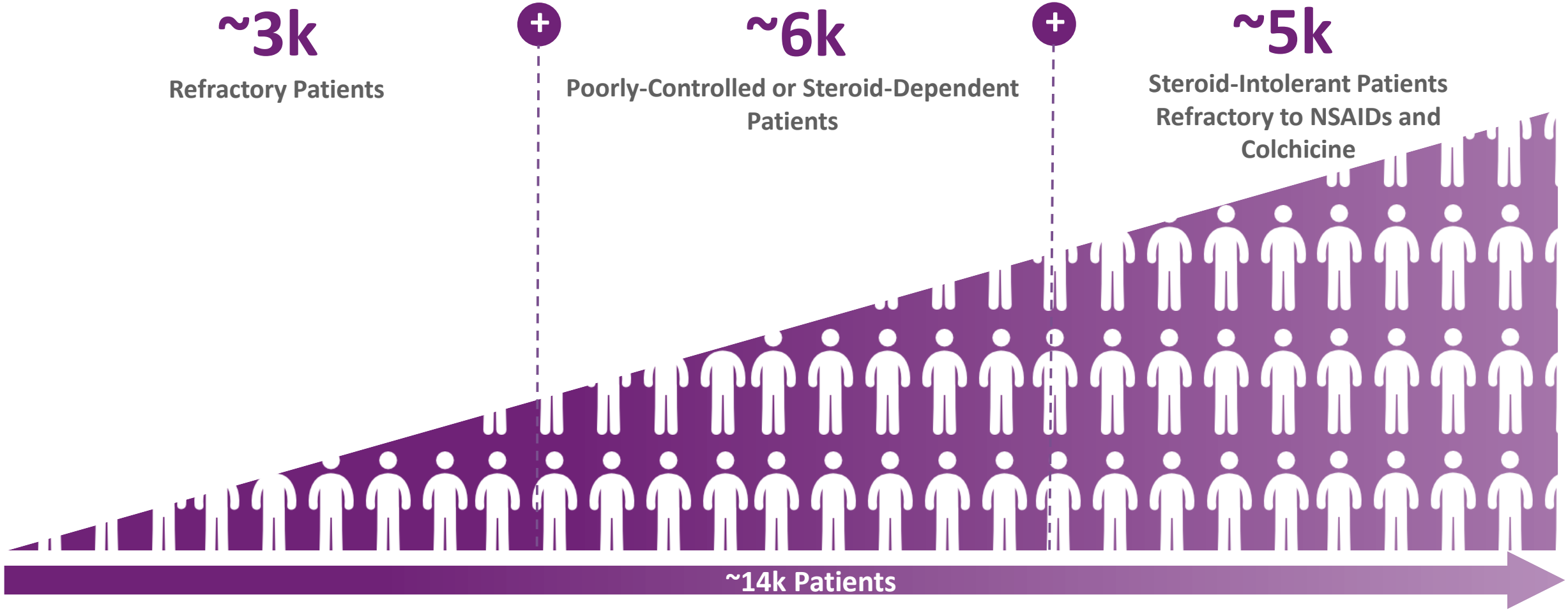
Refractory patients are left with few treatment options and rilonacept could mitigate the dangers of long-term steroid use



Sources: UptoDate, Trinity Partners, Kiniksa Analysis

Recurrent pericarditis prevalence in the U.S. estimated to be ~40k patients*

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



Based on multiple claims data

* Estimates based upon the diagnosed and treated patients in the healthcare system per IQVIA PharMetrics Plus Claims Data 1/1/2013 – 3/31/2018; ClearView Analysis.

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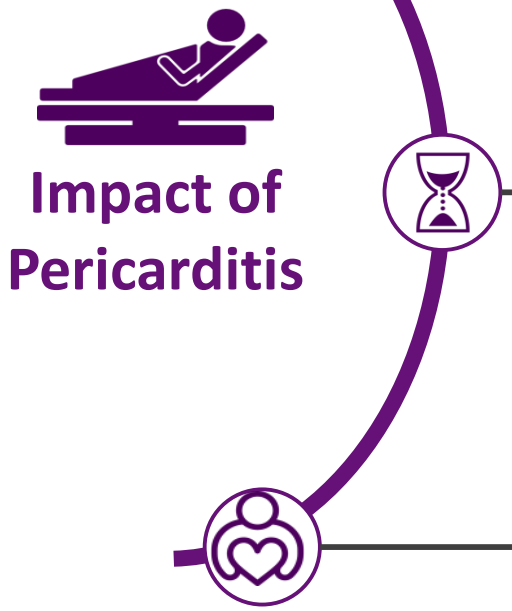
Recurrence burden significantly impacts morbidity and impairs quality of life



Impact of Pericarditis

Refractory and steroid dependent patients have the highest recurrence burden, with ~30 – 40% of patients experiencing ≥2 annual episodes, significantly higher than the broad recurrent population

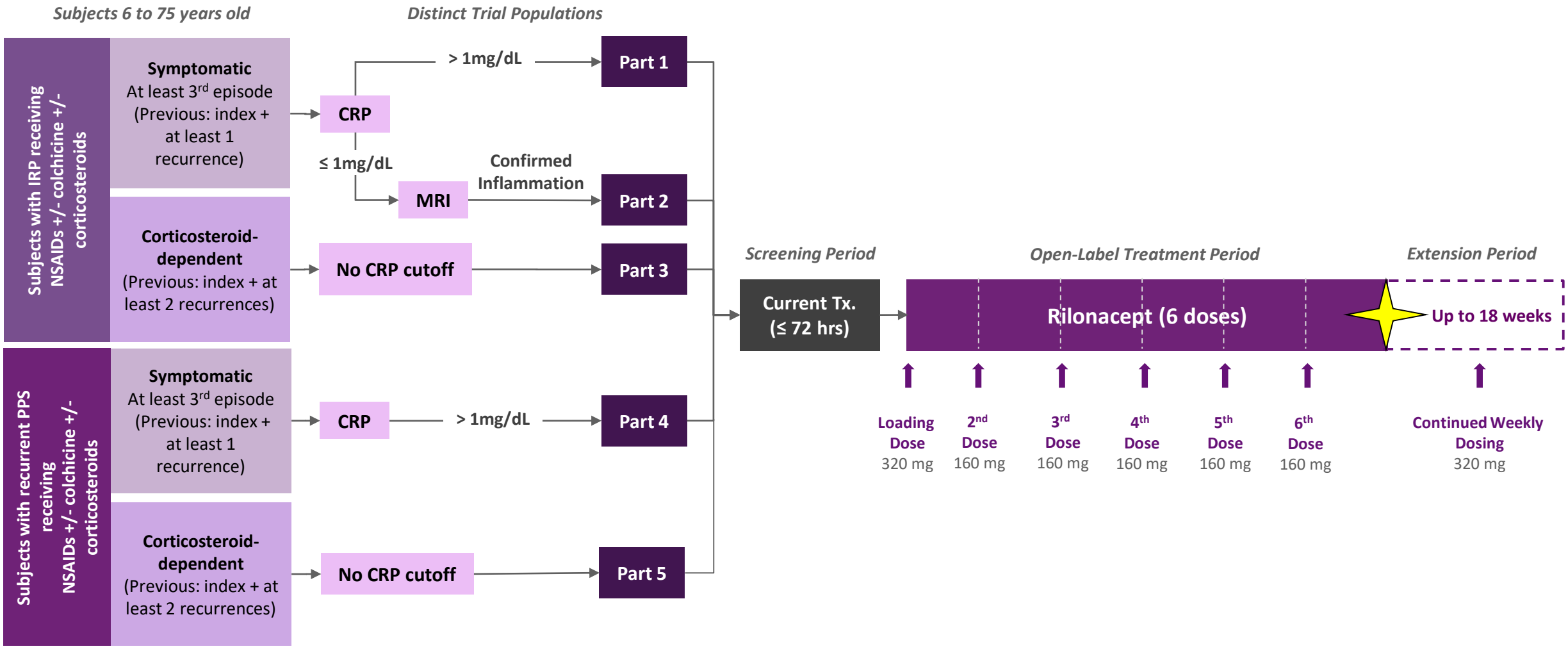
Over the last two years, **~6% of refractory and steroid dependent patients also had constrictive pericarditis** and ~8% of refractory patients had cardiac tamponade

Patients report **fear and anxiety due to the unpredictability of flares and the severity of recurrences**, impeding their ability to have a normal family or work life

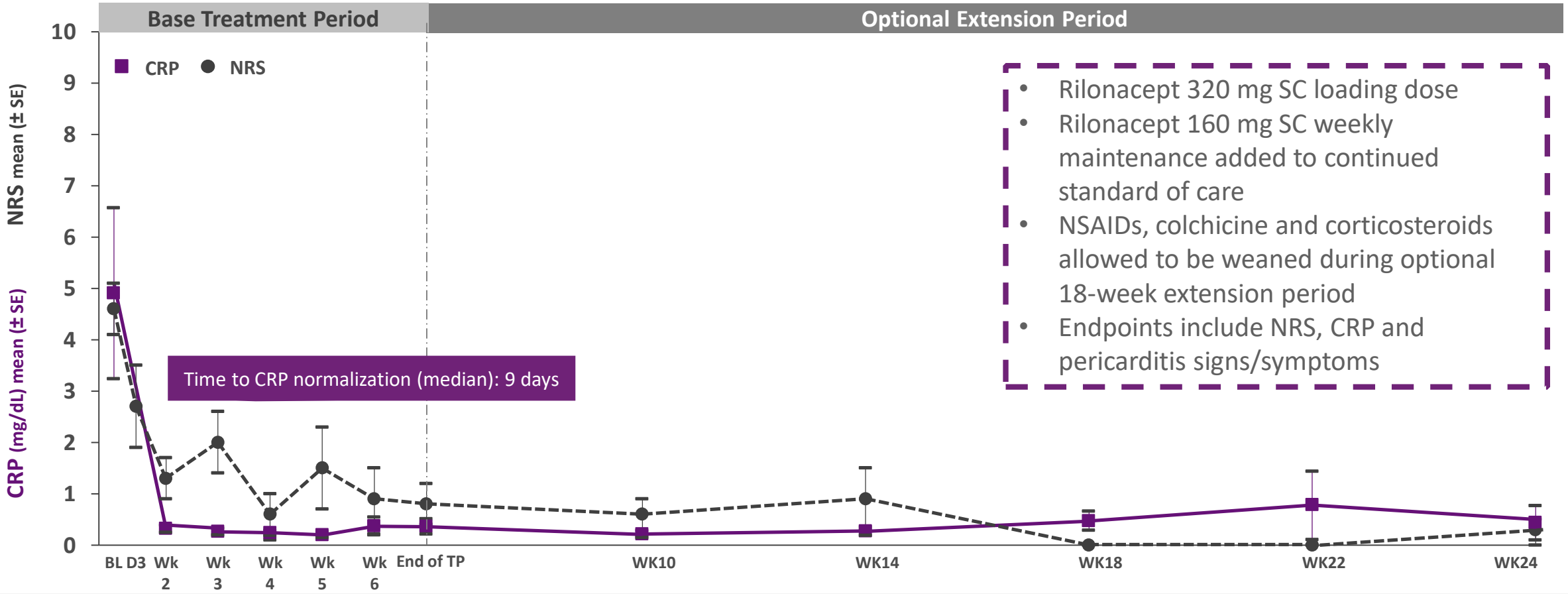
Based on multiple claims data

Source: IQVIA PharMetrics Plus Claims Data 1/1/2013 – 3/31/2018; ClearView Analysis.

Open-label Phase 2 clinical trial of rilonacept in pericarditis populations



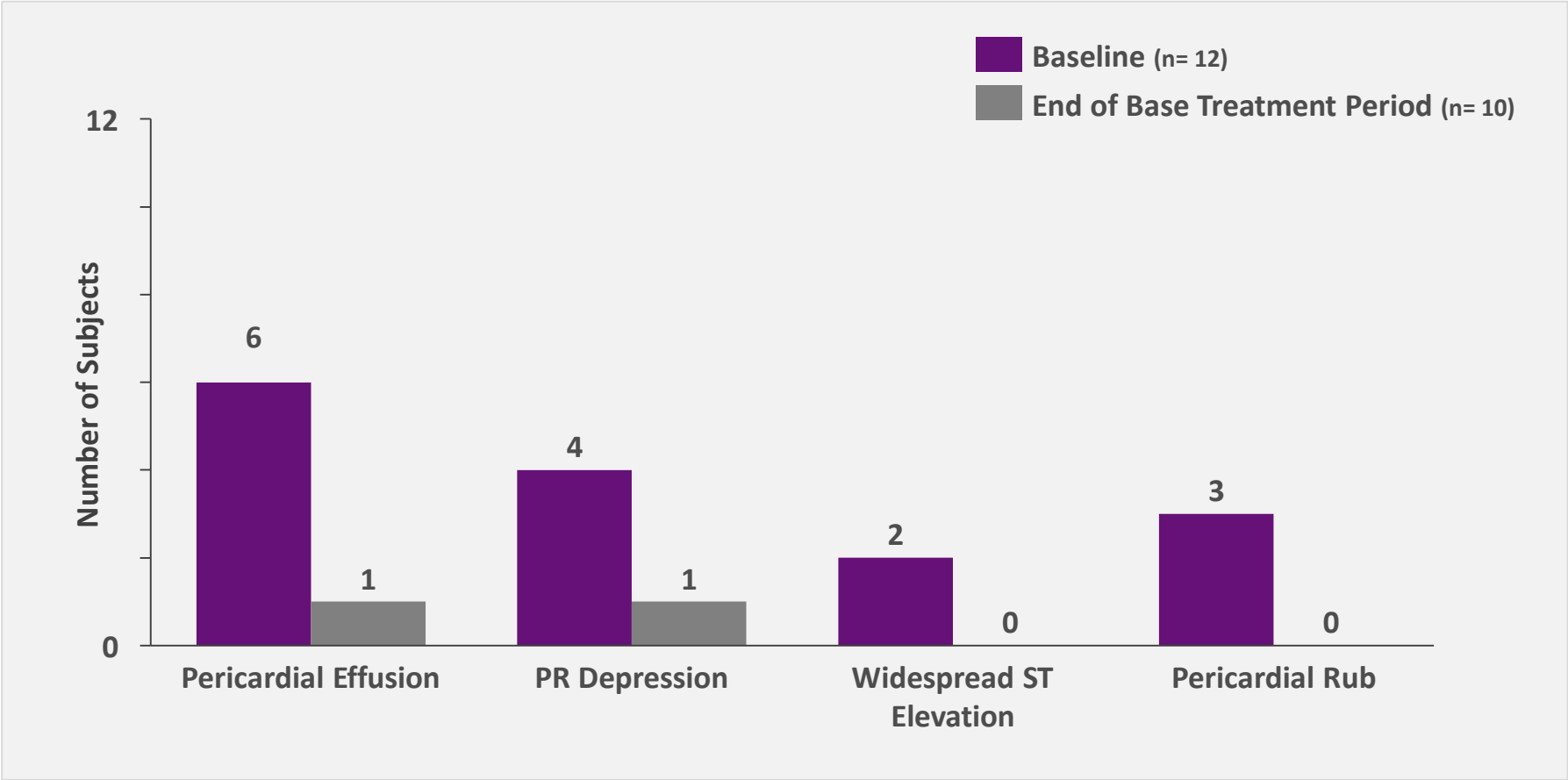
Open-label interim Phase 2 data showed reduction in both the inflammation biomarker and reported pain



		BL	D3	Wk 2	Wk 3	Wk 4	Wk 5	Wk 6	EoTP	Wk10	Wk14	Wk18	Wk22	Wk24
CRP	# of Subjects	12		9	11	10	9	4	10	7	7	3	2	4
CRP	CRP mean	4.91		0.32	0.26	0.24	0.20	0.37	0.36	0.21	0.27	0.47	0.78	0.44
Pain	# of Subjects	12	10	12	12	7	12	8	10	7	7	5	6	4
Pain	Pain mean	4.6	2.7	1.3	2.0	0.6	1.5	0.9	0.8	0.6	0.9	0.0	0.0	0.3

Notes: Interim data from on-going study (Part1) as of Nov 1st, 2018; Baseline = rilonacept 320mg loading dose; Week 1 through Week 6= rilonacept 160mg; EoTP= End of Treatment Period

Pericardial signs resolved during rilonacept 6-week base treatment period



Note: Interim data from on-going study (Part1) as of Nov 1st, 2018

Summary of adverse events

- Rilonacept was generally well-tolerated
- 7/12 subjects experienced at least one treatment-related adverse event during the treatment period
- The most common adverse events were mild transient injection site reaction and gastrointestinal disorders
- One patient discontinued from the study due to a Treatment-Emergent Serious Adverse Event, skin abscess

Treatment-Related and Non-Treatment-Related TEAEs

Category	Subjects (n=12)
Subjects with at least one TEAE	12
Subjects with at least one treatment-related TEAE	7
Subjects with at least one serious TEAE	2
Subjects with a serious Treatment-Related TEAE*	1
Subjects with at least one TEAE leading to treatment discontinuation*	1
Subjects with at least one TEAE leading to death	0

AEs Occurring at Least Once (by Affected Organ System)

Organ System	Preferred Term	Part 1 (n=12)
Number (%) of subjects who had at least one AE		12 (100%)
Gastrointestinal disorders		6 (50%)
General disorders and administration site conditions		5 (41.7%)
Infections and infestations		5 (41.7%)
Investigations		5 (41.7%)
	Liver function test increased	2 (16.7%)
	Blood cholesterol increased	1 (8.3%)
	Blood creatine phosphokinase increased	1 (8.3%)
	HDL increased	1 (8.3%)
Musculoskeletal and connective tissue disorders		2 (16.7%)

* 1 patient discontinued due to SAE of skin abscess (occurred after the Nov 1st data cutoff)

Notes: Interim data from on-going study (Part1) as of November 1st, 2018; AE = Adverse Event; TEAE = Treatment Emergent Adverse Event

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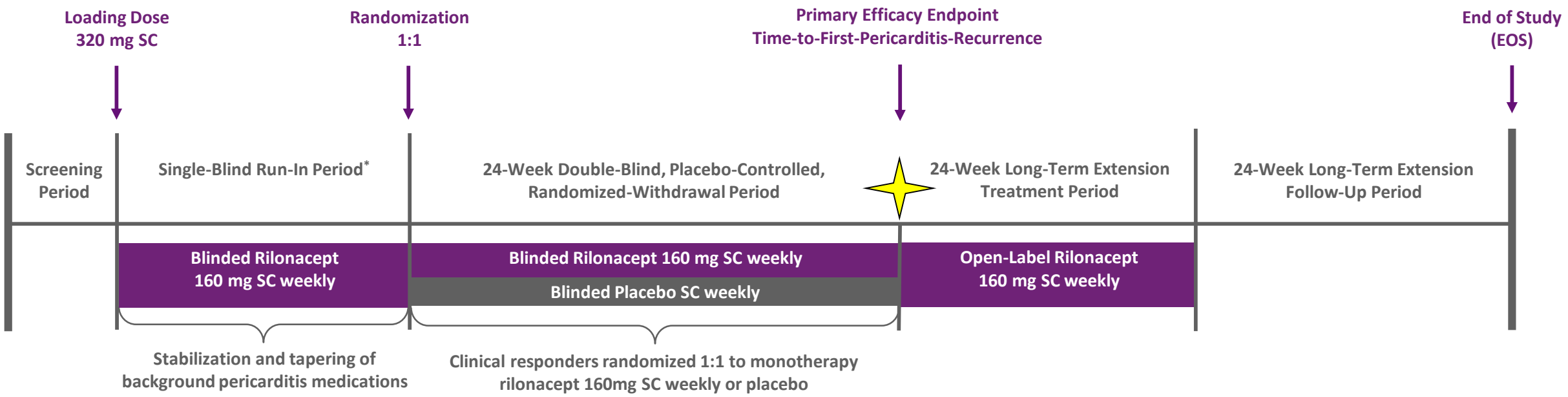
Pivotal Phase 3 clinical trial of rilonacept for recurrent pericarditis



Inclusion Criteria:
- Present at screening with at least a third pericarditis episode, defined as at least 1 day with NRS pain of ≥ 4
- 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 pericarditis recurrence

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.

2 Mavrilimumab – Phase 2

(monoclonal antibody inhibitor targeting GM-CSFRα)

Rilonacept | **Mavrilimumab** | KPL-716 | KPL-045 | KPL-404

Mechanistic rationale for focusing on high unmet need vasculitides & inflammatory cardiomyopathies

Mechanism of Action[1]	Monoclonal antibody inhibitor targeting GM-CSFRα; a key mediator of inflammation and autoimmunity
Lead Indication	Giant Cell Arteritis (GCA)
Addressable Population[2]	~75k - 150k prevalent in the U.S.; similar prevalence in other major markets
Competition[3]	Only one FDA-approved therapy for GCA, but unmet needs remain
Clinical Development	Enrolling a global Phase 2 proof-of-concept clinical trial
Rights	Worldwide

1) Sources: Wicks, Roberts, Nature Review Immunology, 2015; Hamilton, Expert Review of Clinical Immunology, 11:4, 457-465; 2) Chandran et al., Scand J Rheumatol, 2015; Trinity Consulting – HCUP/Medicare Data, Quantitative Survey (n=102 rheumatologists); 3) Cortellis,;UpToDate; Correspondence, Trial of Tocilizumab in Giant-Cell Arteritis, NEJM, 2017

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GCA is a serious condition characterized by inflammation of medium-large blood vessels; it can lead to bilateral blindness if left untreated

1 **Chronic Inflammation of Medium-Large Blood Vessels**

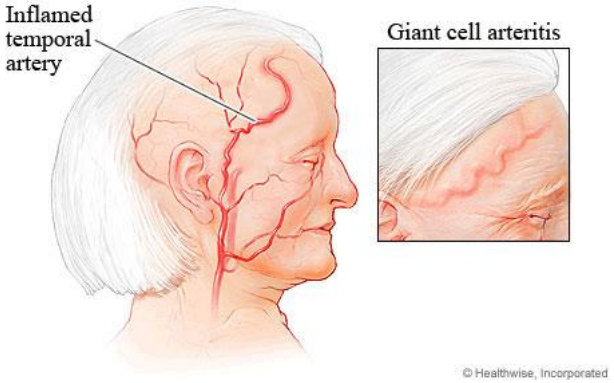
- GCA is characterized by inflammation of medium-large blood vessels with **predisposition for the cranial branches of the carotid artery** and is typically **found in patients over 50 years old.**
- Due to the impact on the carotid arteries, GCA is **often characterized by temporal specific symptoms 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**; treatment with high-dose steroids effectively prevents complications

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



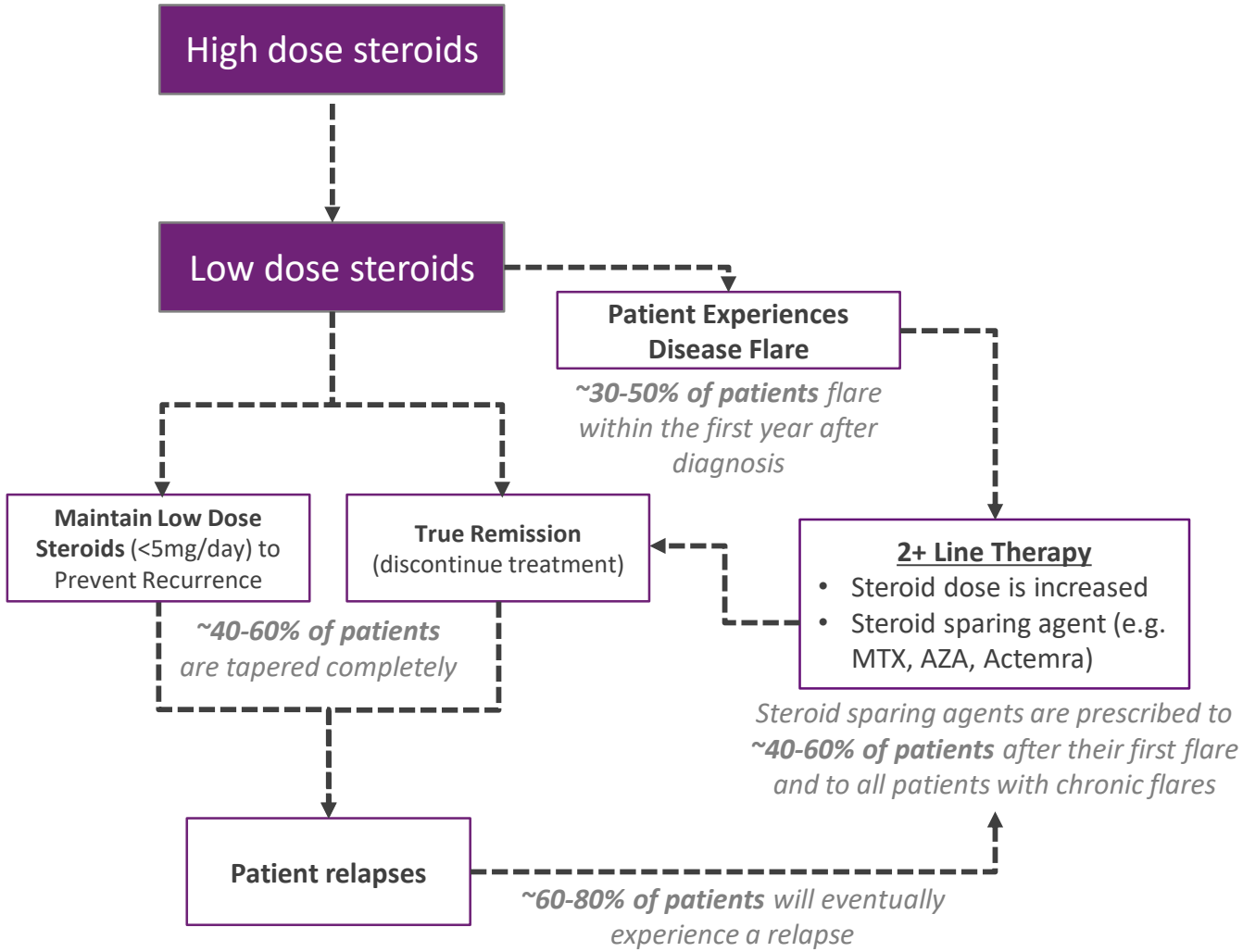
> *"There is an urgency of treatment with these patients, compared to other conditions it's serious."* – Rheumatologist

> *"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 to go blind."*
> – GCA Patient

Sources: Medcape; Trinity Partners primary market research

Current treatment paradigm for GCA involves high-dose steroids for all patients upon clinical suspicion



All Patient Receive High-Dose Steroids:

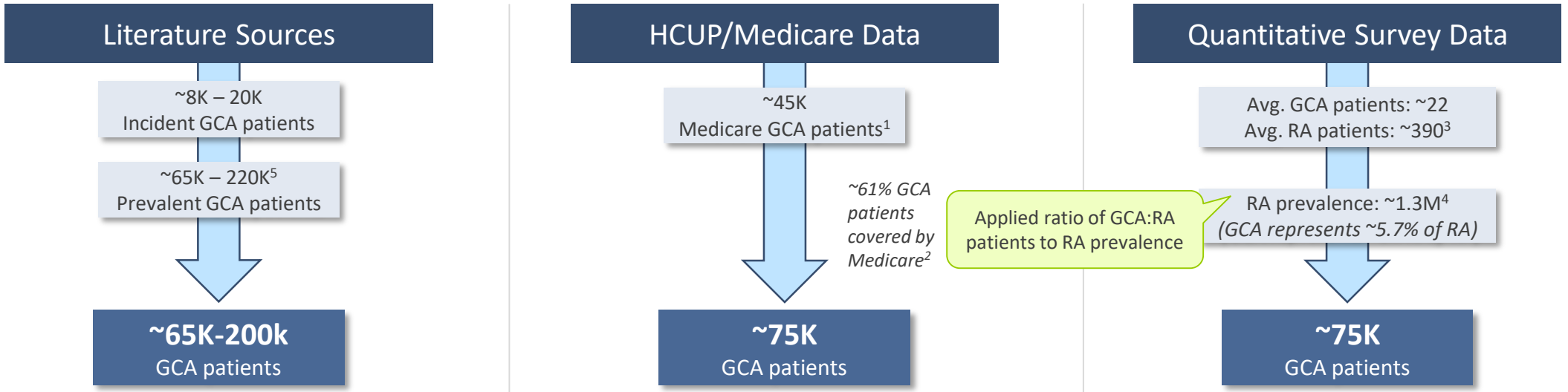
- High-dose steroids are **effective at preventing disease related complications;** however, **they may lead to life altering side-effects** like osteoporosis and diabetes

No Algorithmic Treatment Approach:

- A few treaters initiate **steroid sparing agents** early on in the treatment paradigm, relying on them more for the chronic treatment of GCA
- Others treat GCA in more of a stepwise fashion, adding new agents on top of steroids only following disease flares/relapse

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

GCA prevalence in the U.S. estimated to be between 75k-150k



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 ~75k-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

Estimated U.S. prevalence of ~75k-150k[1]; ~50-70% of patients are refractory or steroid-dependent[2]

1	**GM-CSF and GM-CSFRα are overexpressed in GCA lesions**	• Both the receptor[3] and the GM-CSF[4] 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[5] and non-classical macrophages (CD16+)[6] • GM-CSF has been shown to induce endothelial cell migration and proliferation[7] • 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[8] • 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) Chandran et al., Scand J Rheumatol, 2015; Trinity Consulting – HCUP/Medicare Data, Quantitative Survey (n=102 rheumatologists); 2) Alba et. al., Medicine 2014
3.) Unpublished Kiniksa Data; 4.) Weyand et al., Ann. Int. Med. 1994; 5.) Yoshihara et al., Immunology 2003; 6.) van Sleen et al., Sci Reports, 2017; 7.) Bussolino et al., Letters to Nature 1989; 8.) Samson et al Autoimm. Rev. 2017

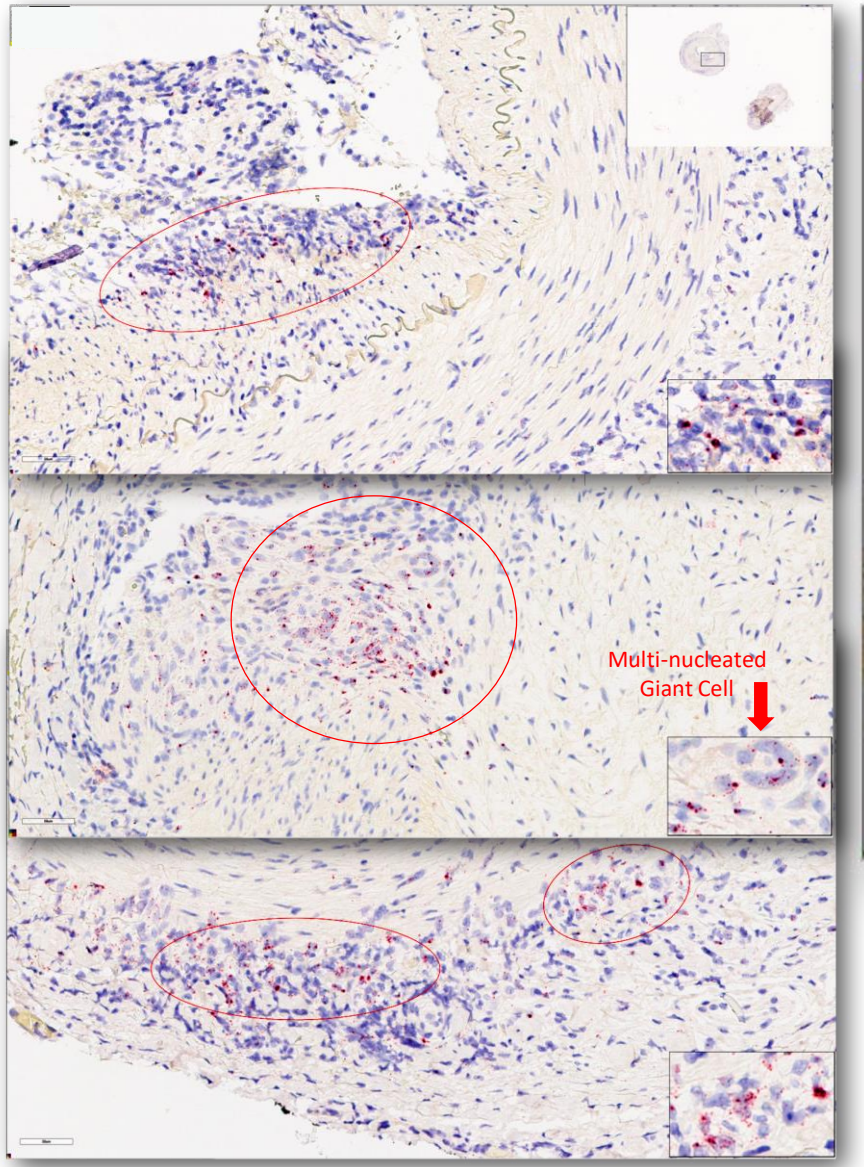
High GM-CSF-Rα mRNA expression via RNAscope in GCA positive biopsies vs control

GCA Positive Biopsies

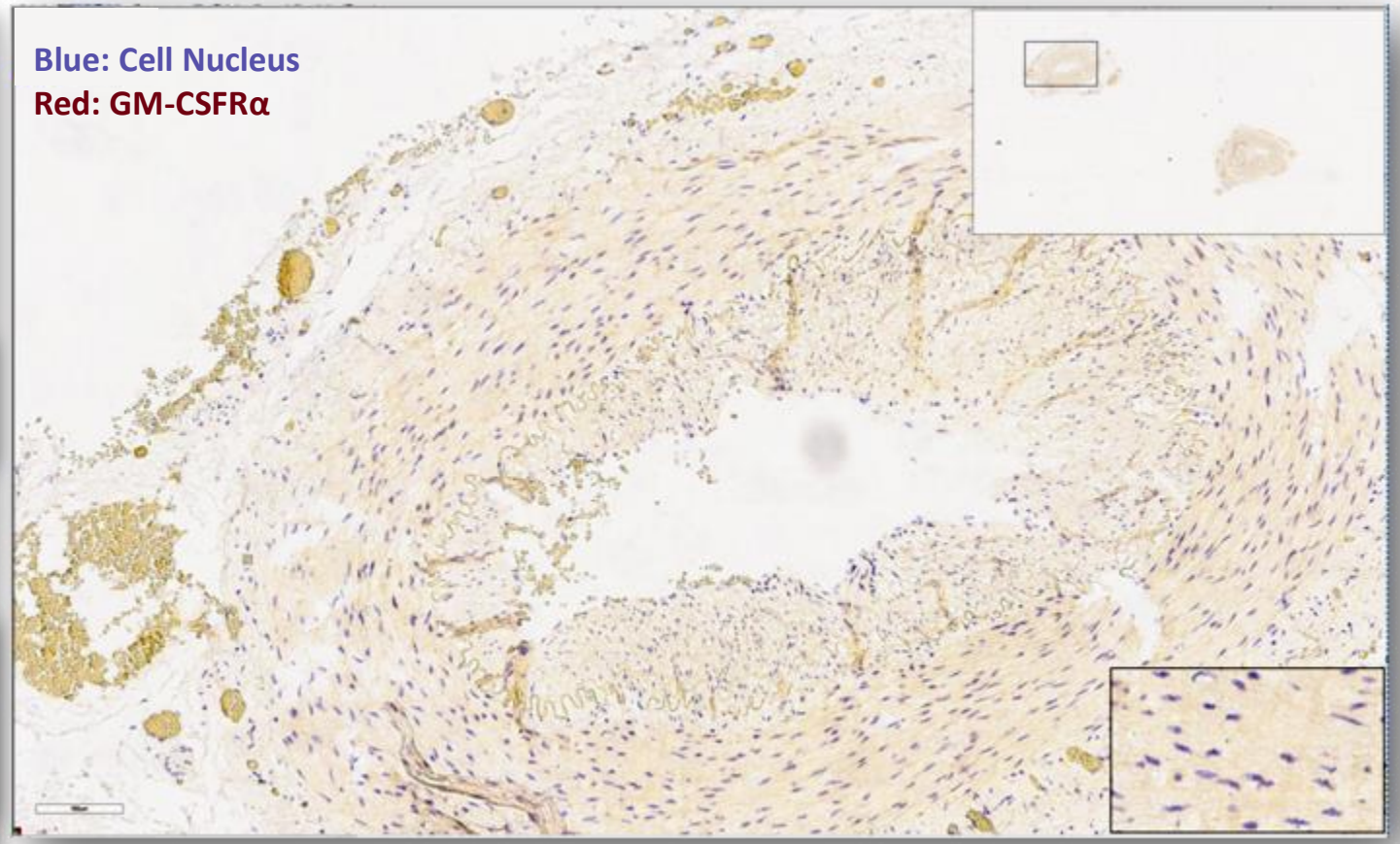
Intima

Media

Adventitia



GCA Negative Control Biopsy



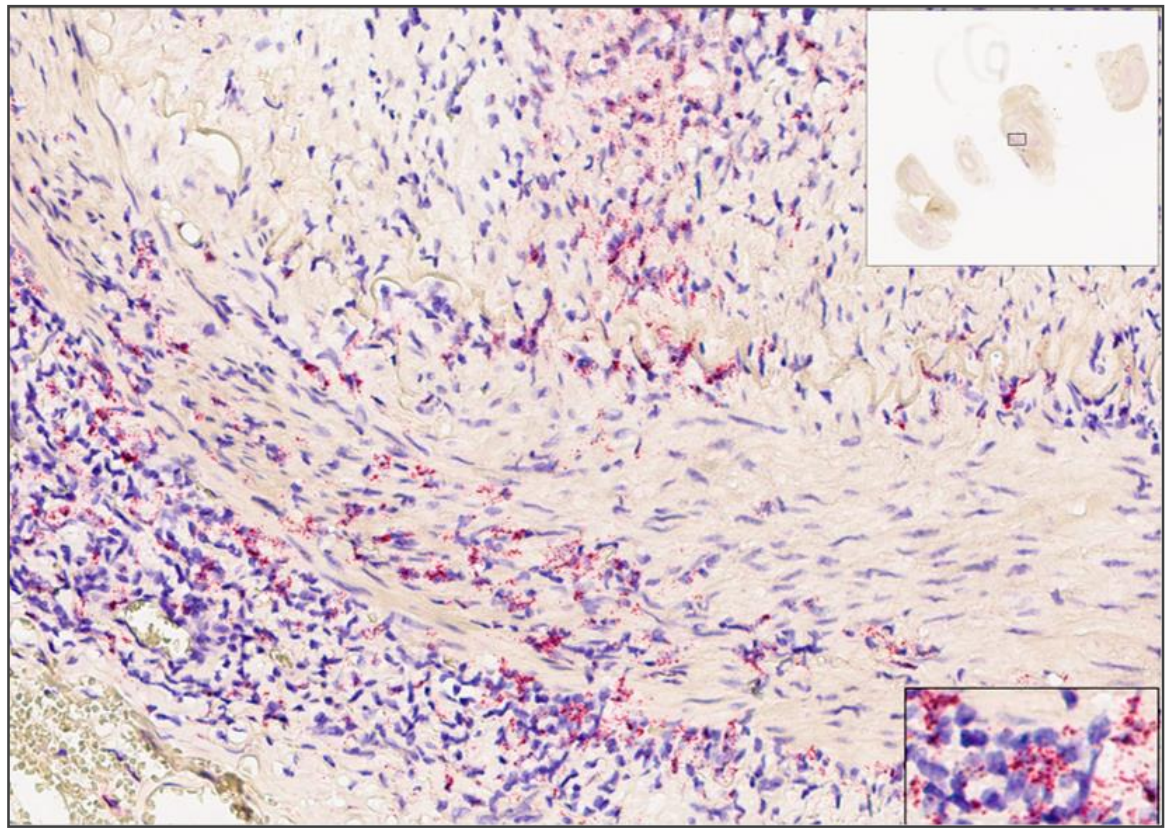
Elevated GM-CSFRα expression in all 3 layers of the artery (adventitia, media and intima) in GCA positive biopsies compared to controls.

Notes: Preliminary Internal Kiniksa data generated at Advanced Cell Diagnostics in November 2018; * in-situ hybridization

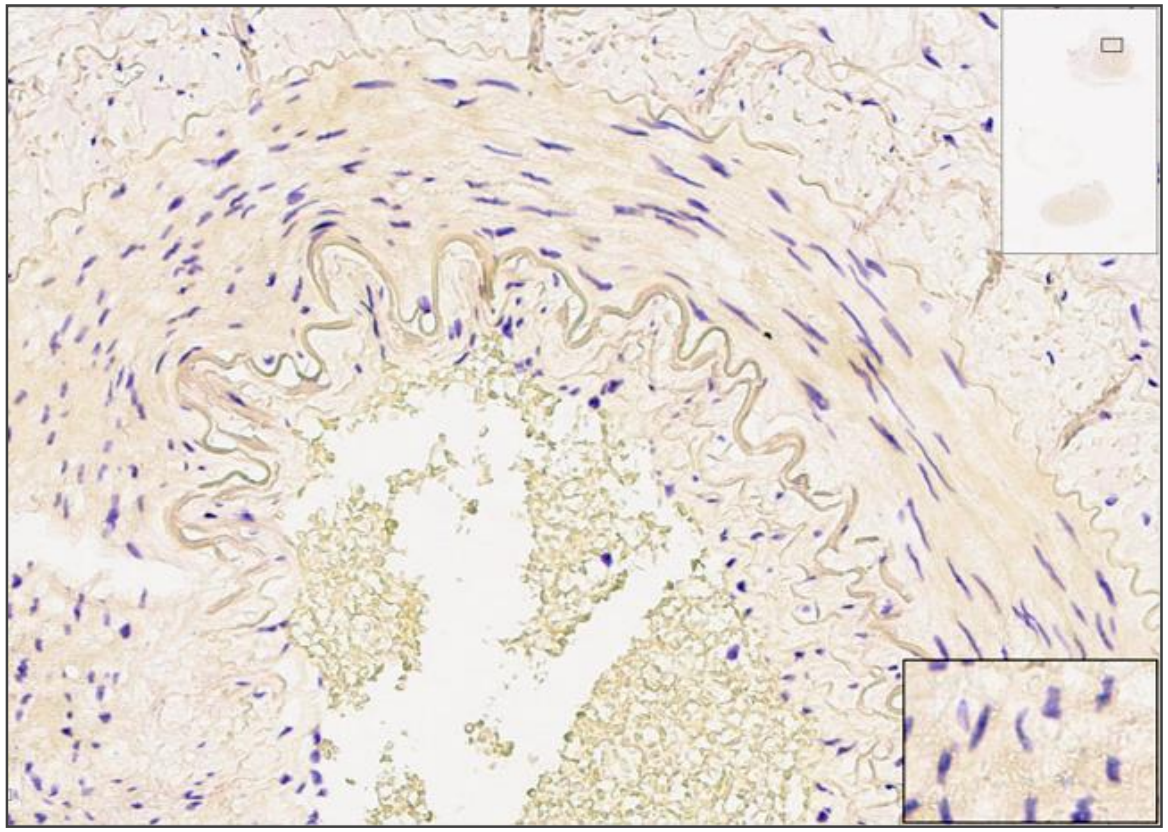
High PU.1 mRNA expression via RNAscope in GCA positive biopsies

Blue: Cell Nucleus
Red: PU.1 transcription factor

GCA Positive Biopsies



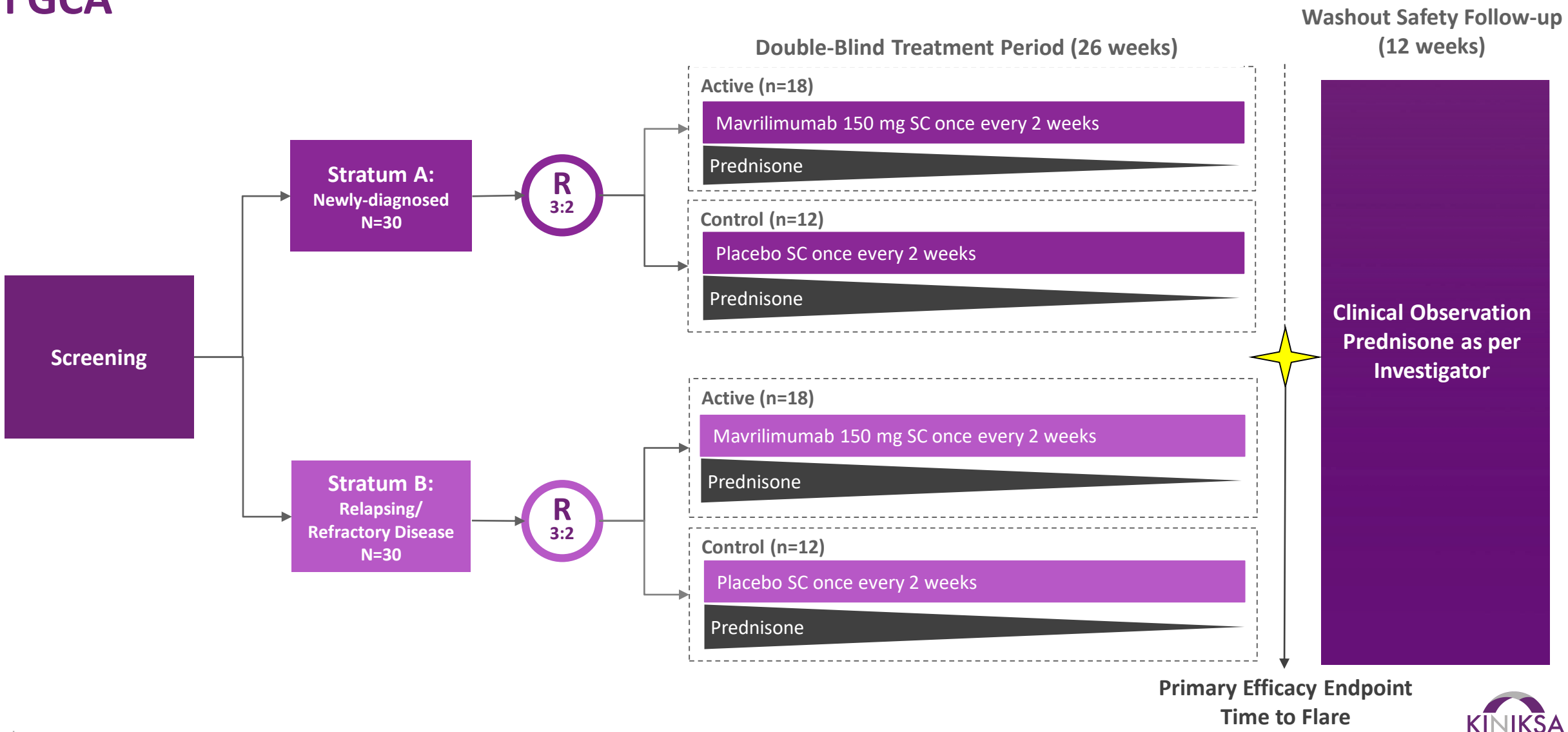
GCA Negative Control Biopsy



Elevated expression of downstream transcription factor for colony stimulating factors in all 3 layers of the artery (adventitia, media and intima) in GCA positive biopsies compared to controls

Notes: Preliminary internal Kiniksa data generated at Advanced Cell Diagnostics in November 2018; * in-situ hybridization

Randomized, double-blind, placebo-controlled Phase 2 study of mavrilimumab in GCA



3 KPL-716 – Phase 2

(monoclonal antibody inhibitor targeting OSMRβ)

Rilonacept | Mavrilimumab | **KPL-716** | KPL-045 | KPL-404

Differentiated molecule with potential to treat variety of pruritic, inflammatory and fibrotic indications

Mechanism of Action[1]	Monoclonal antibody inhibitor targeting OSMRβ; a key receptor subunit shared by IL-31 and Oncostatin M
Lead Indication	Chronic pruritic diseases, including prurigo nodularis (inflammatory skin disease) and atopic dermatitis
Addressable Population[2]	~300k PN and ~300k moderate-to-severe AD patients eligible for systemic biologics in the U.S.
Competition[3]	Potential for differentiated efficacy and safety; competitors block either IL-31 or OSM activity alone
Clinical Development	Plan to initiate adaptive design Phase 2a/2b in PN and Phase 2 in multiple diseases characterized by chronic pruritus in 1H 2019
Rights	Worldwide

1) Trinity Qualitative Interviews; 2) 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., Britis Journal of Dermatology, 2001; 3) Simpson et al., N Engl J Med, 2016; Ruzicka et al., N Engl J Med, 2017; Reid et al., 2016 ACR Abstract # 1881; Cortellis

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Prurigo nodularis is characterized by pruritic lesions on patients' extremities, which lead to significant distress and decreased quality of life

1 Numerous itchy lesions on extremities and lower back

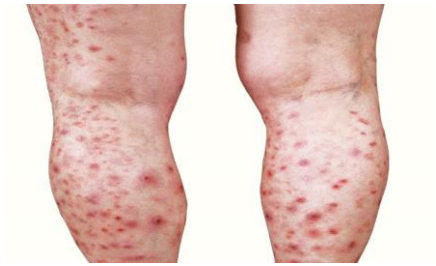
- PN is characterized by the presence of **one or many raised lesions** in areas that can be scratched or picked at and an **intense itching sensation** in the surrounding area
- PN typically **occurs in middle aged patients, ranging from 35-80 years old**
- PN typically occurs when there is a trigger, such as a rash or bug bite, prompting patients to start a **feedback loop of itching and picking**

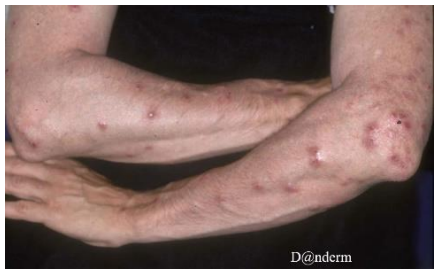
2 Presence of lesions and intense desire to itch typically leads to significant distress

- PN typically results in a **decrease in quality of life** due to psychological issues caused by/associated with cosmetic appearance of the lesions and constant itch sensation
- Physicians report that many patients desire to itch may be driven or exacerbated by **psychological or behavioral issues** in some cases

3 Many patients have an underlying skin or allergic condition in addition to PN

- **~30-50%** of PN patients **suffer from atopic conditions,** including, but not limited to **atopic dermatitis**, a common dermatologic disease characterized by dry, itchy, and inflamed skin, and other associated skin conditions; symptoms are relieved with creams and topical steroids

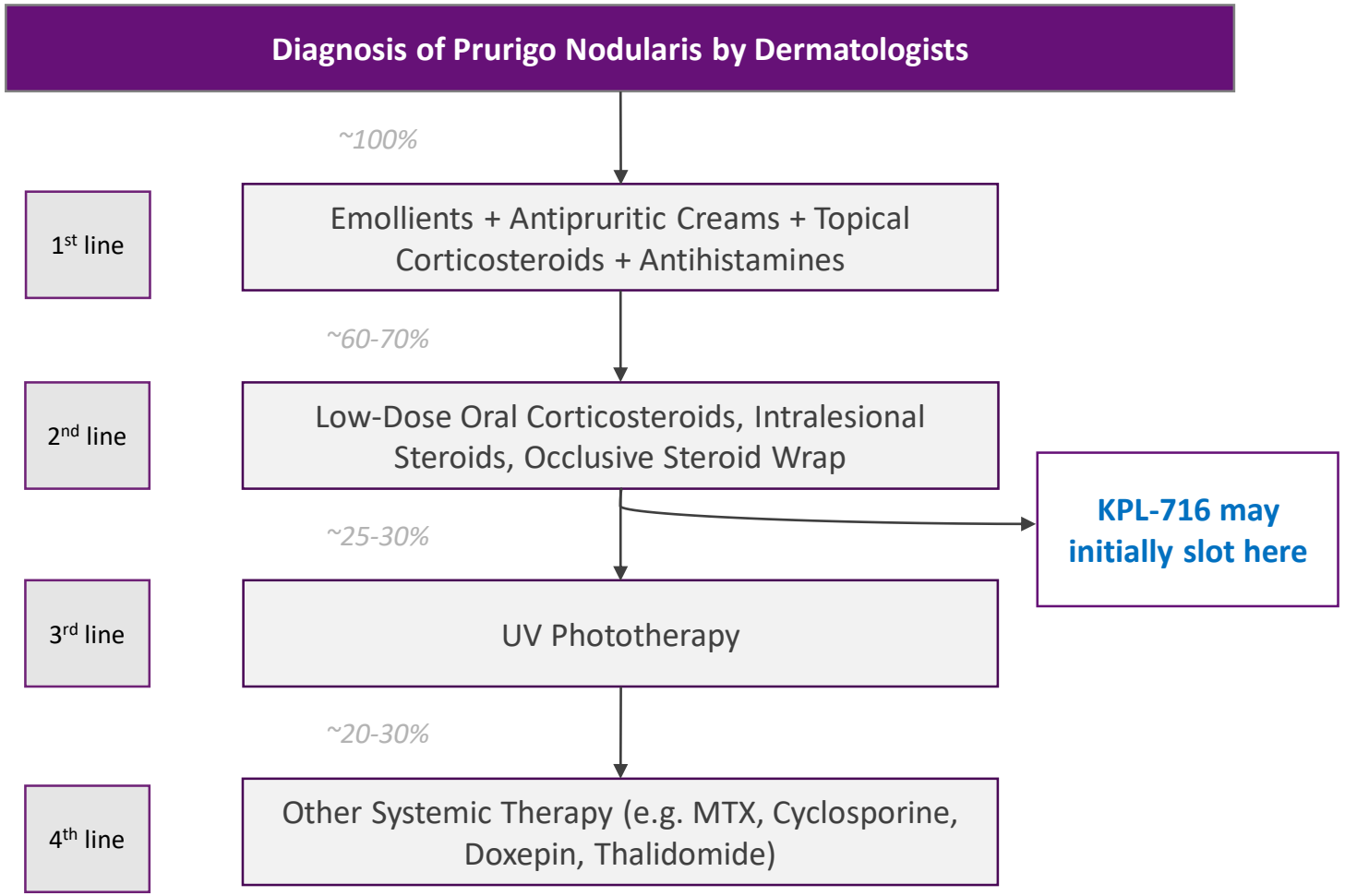




> *"The lesions of mild PN may look similar to skin cancer. However, these discrete lesions are not as well defined."*
> – Dermatologist

> *"Lesions may have a 'thickened' appearance due to the patient scratching, the lesions bursting and then re-healing. Some patients present with lesions that are bleeding."* – Dermatologist

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

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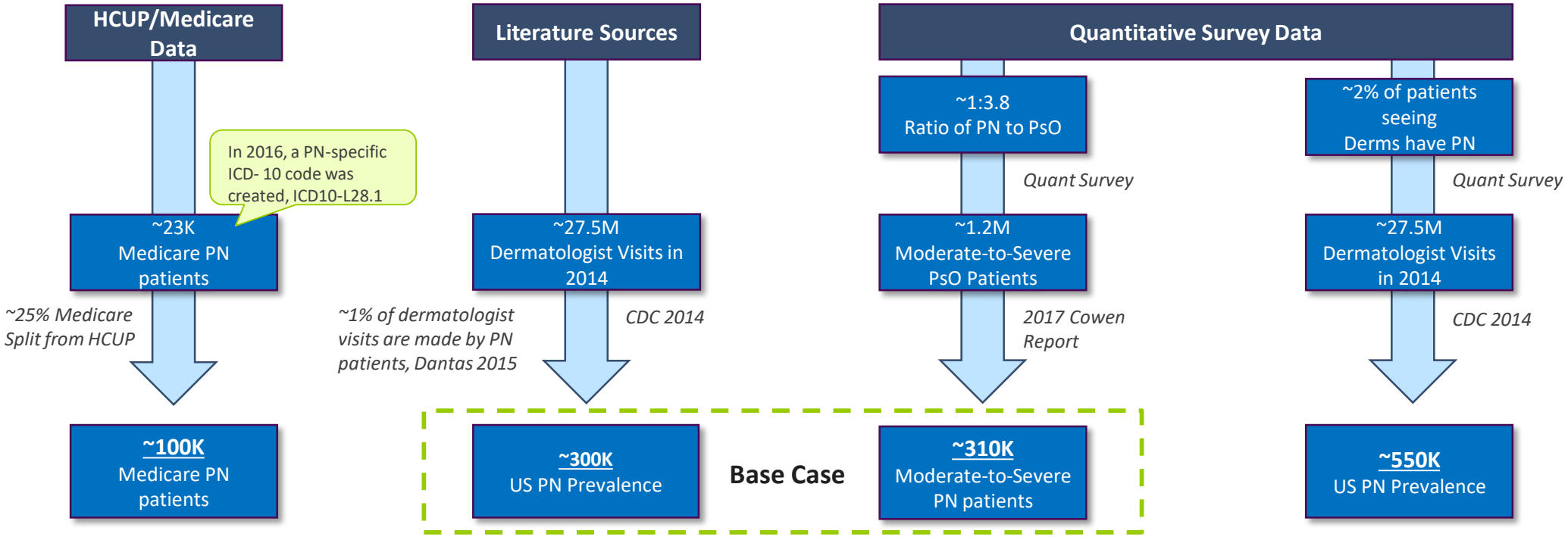
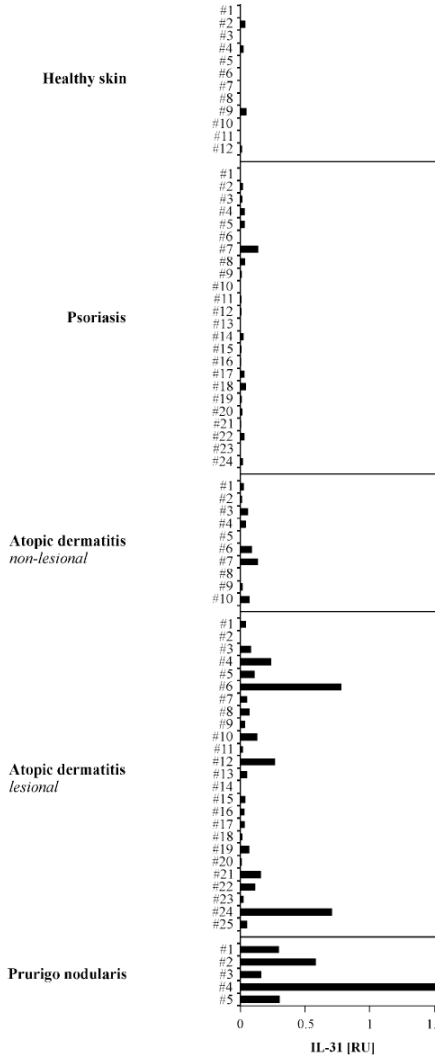
The prevalence of prurigo nodularis is estimated at ~300K in the U.S.

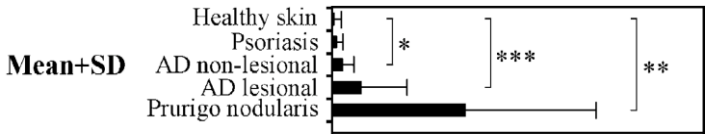


Sources: CDC 2014: National Ambulatory Medical Care Survey: 2014 State and National Summary Tables <https://www.cdc.gov/nchs/data/ahcd/namcs_summary/2014_namcs_web_tables.pdf>; Cowen and Company, Therapeutic Categories Outlook: Comprehensive Study September 2017; Primary Market Research; 3. Dantas, 2015,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

IL-31 and OSM are implicated in the pathology of prurigo nodularis

Quantitative Real-time PCR Analysis of IL-31 mRNA in Human Skin

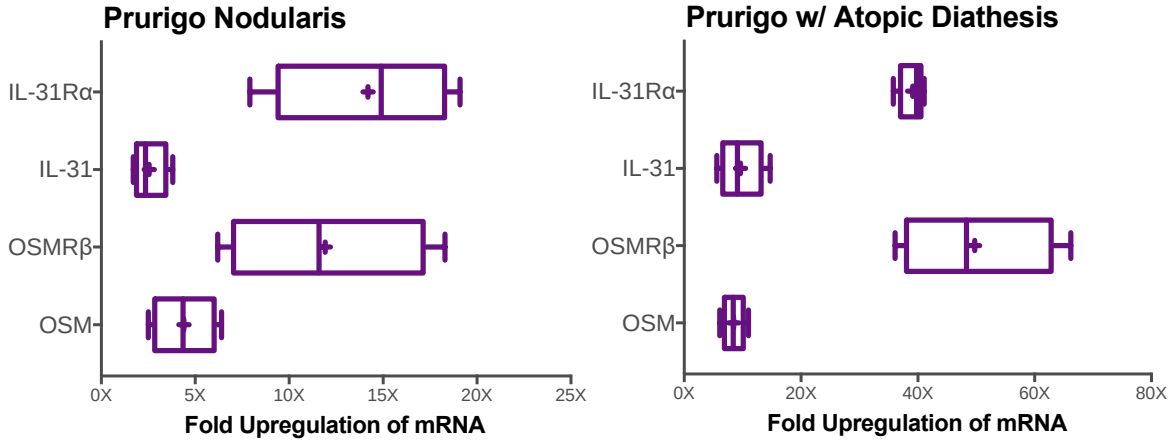




- **IL-31 significantly overexpressed in pruritic skin vs. non-pruritic skin**
  - Highest levels of IL-31 were detected in PN, one of the most pruritic forms of chronic skin inflammation
- **In PN lesions there is a 50-fold upregulation of IL-31 mRNA vs. normal skin and a 4.5-fold upregulation vs. lesional atopic dermatitis**
  - While there was some variability in IL-31 mRNA levels seen among PN patients, levels in all patients were significantly elevated compared with healthy controls

Source: Sonkoly et al., J Allergy Clin Immunol, 2006; Internal Kiniksa Data (Generated by the Loser Lab)

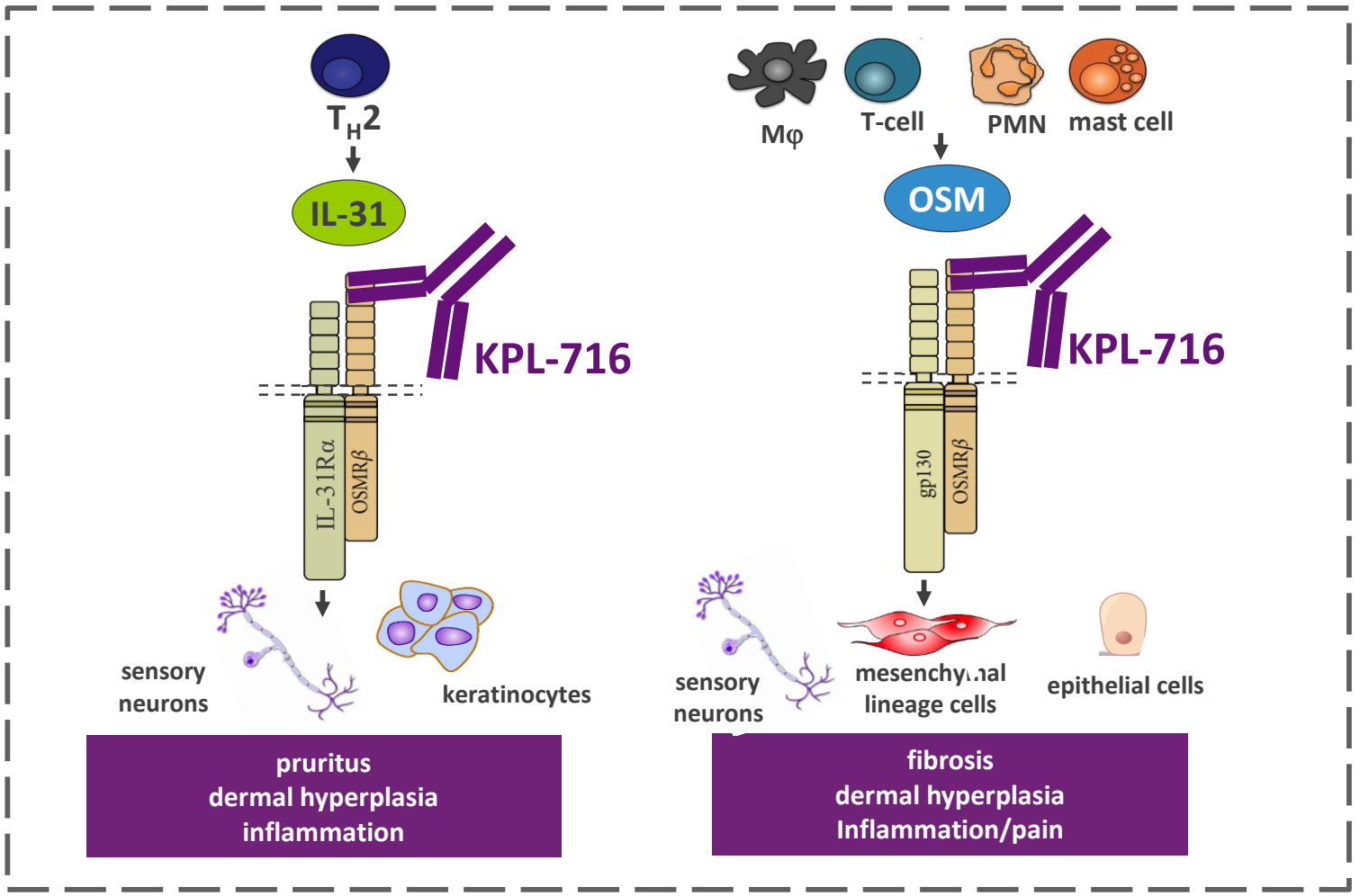
Dual-targeting of OSM and IL-31 though OSMRβ blockade has the potential to be disease modifying

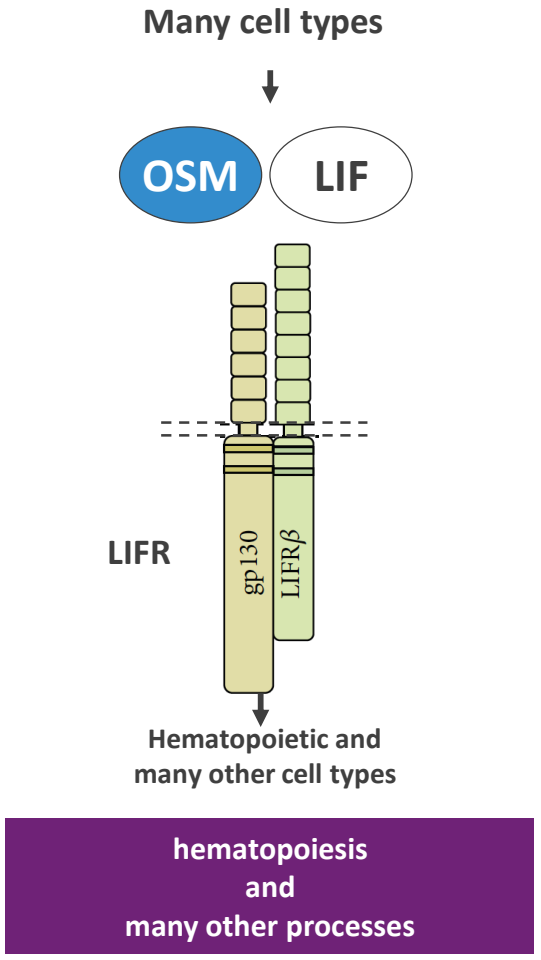


- Messenger RNA levels of IL-31, OSM and their receptor subunits (IL-31Rα and OSMRβ) are significantly elevated in lesions of prurigo nodularis, implicating them as major drivers of pruritus and fibrosis leading to disease pathophysiology
- This phenotype is even more evident in the case of patients with prurigo nodularis that have an atopic diathesis since their receptor subunits are even more highly up-regulated than in prurigo nodularis alone
- These data provide strong mechanistic rationale to target both IL-31 and OSM by blocking OSMRβ

Source: Internal Kiniksa Data (Generated by the Loser Lab)

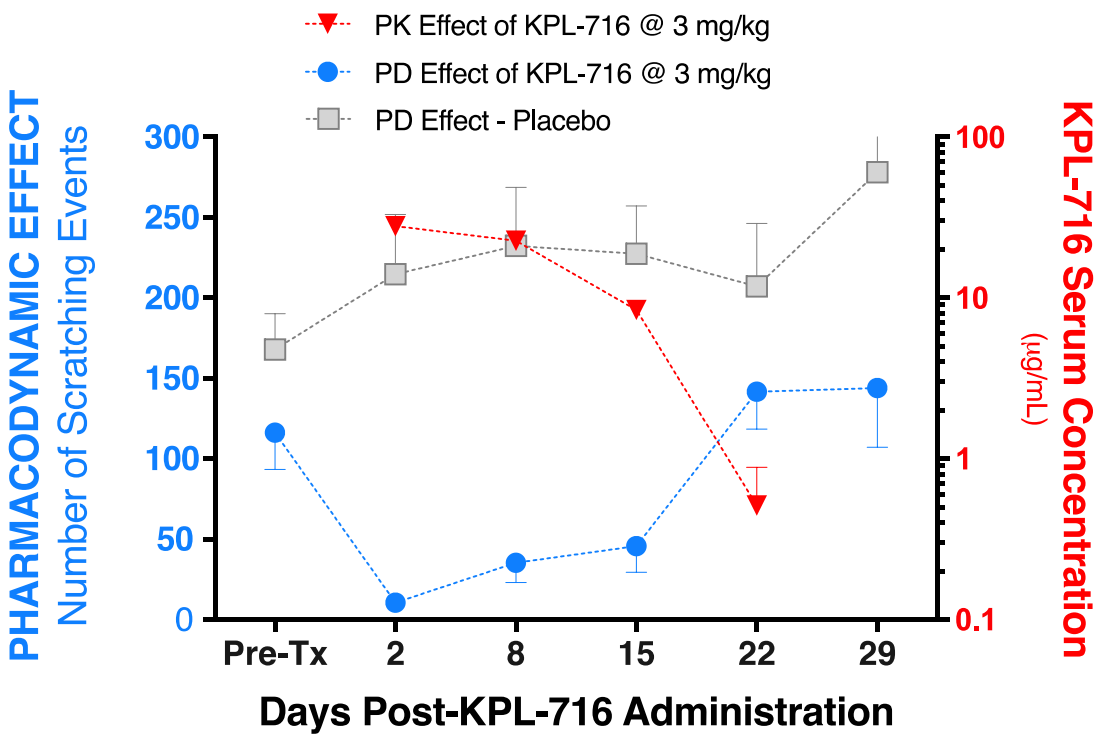
KPL-716 inhibited IL-31 & OSM signaling through OSMRβ but avoided inhibiting signaling critical to hematopoiesis through OSM/LIFR in *in vitro* studies





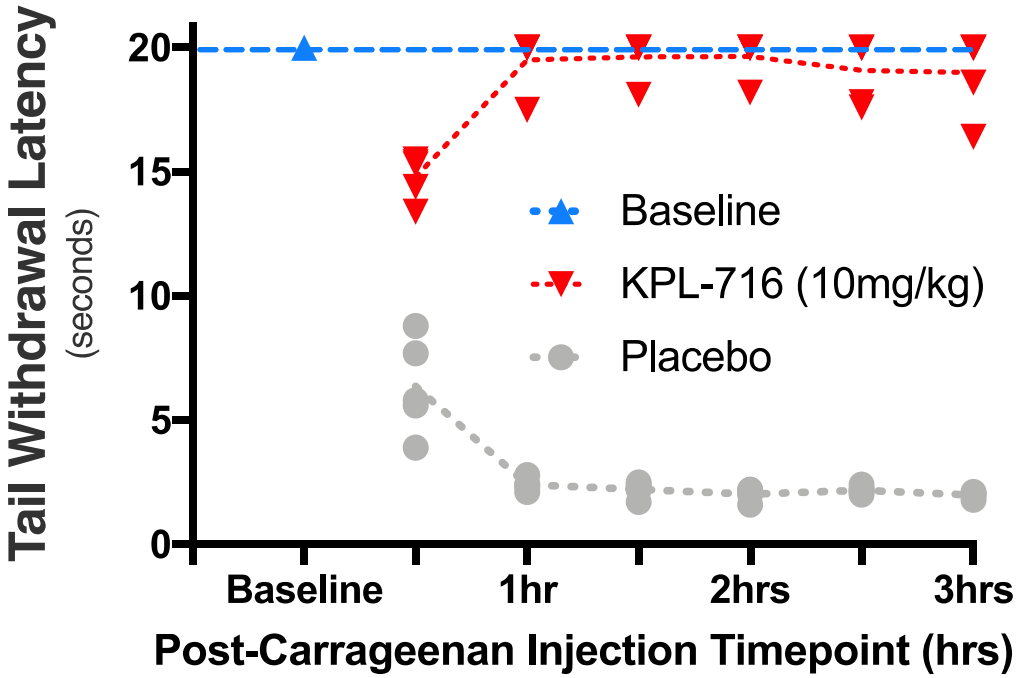
KPL-716 showed signs of potential efficacy in two validated non-human primate models of pruritus and inflammation after a single dose

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

KPL-716 placebo-controlled, single-ascending-dose Phase 1a/1b study design

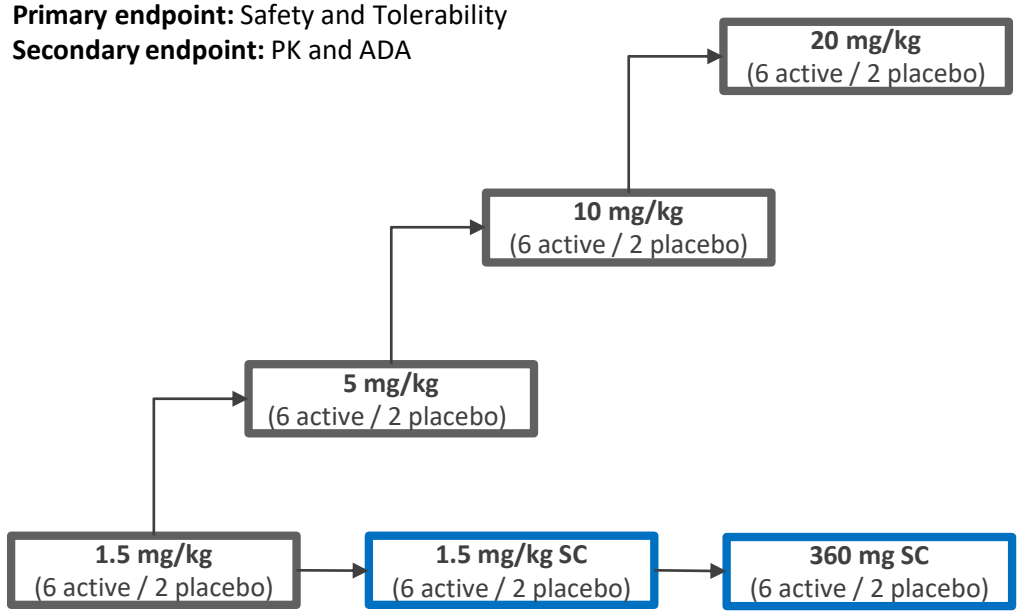
Phase 1a: Normal Healthy Volunteer (n=50)

Dose Groups

Single IV Dose

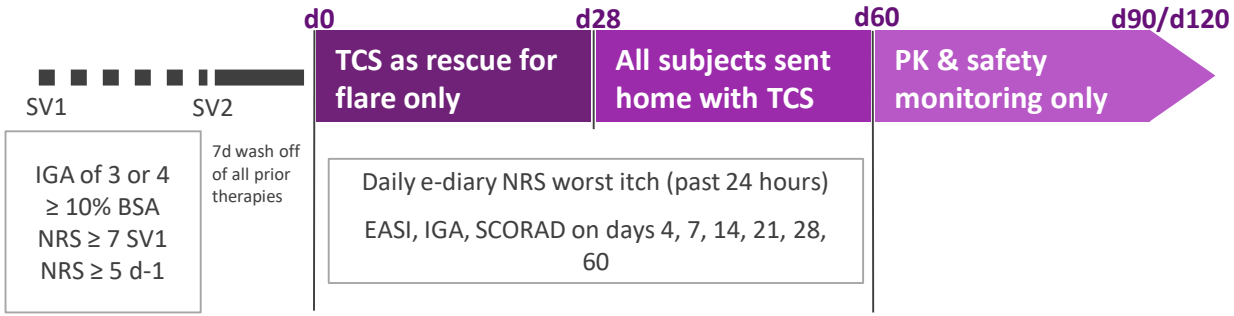
Single SC Dose

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



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

Patient Experience

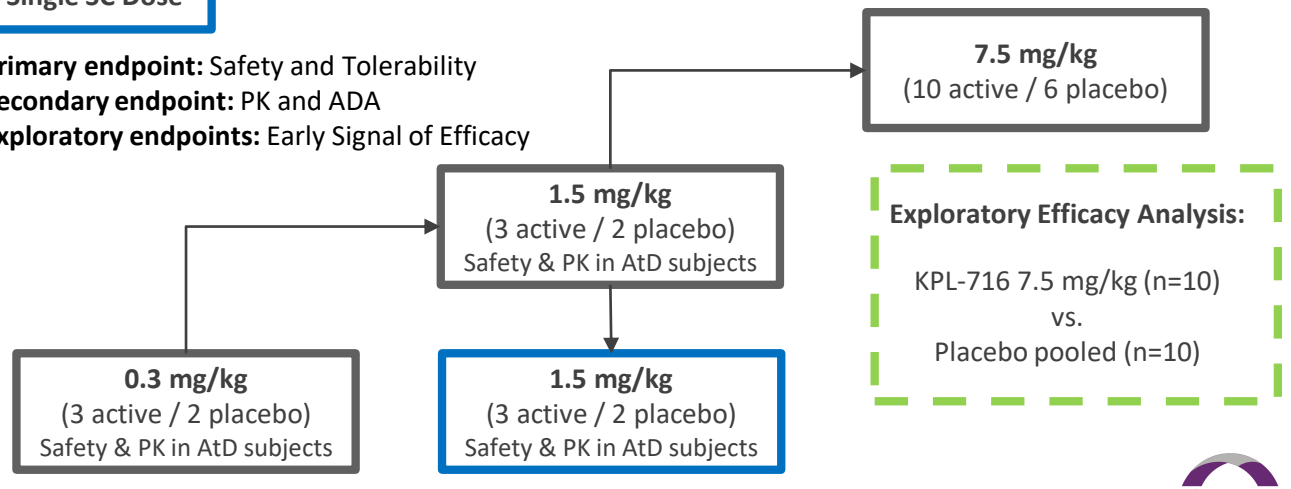


Dose Groups

Single IV Dose

Single SC Dose

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



Baseline parameters were balanced overall

KPL-716 recipients had more atopic dermatitis flares in the year prior to enrollment, suggesting more unstable disease at baseline compared with placebo

Baseline Demographics/Disease Characteristics: AD	KPL-716 7.5 mg/kg IV	Placebo Pooled IV
Age, mean (SD), years	29.7 (11.2)	41.7 (10.9)
Male, %	50	70
White, %	70	70
Elevated IgE, %	60	60
History of any allergic disease, %	40	60
#AD flares in past year, mean (SD)	28.1 (41.6)	3.7 (3.5)
Body surface area affected by AD, mean (SD)	24.2 (8.0)	34.1 (28.0)
Weekly average WI-NRS, mean (SD)	8.0 (1.3)	8.2 (0.7)
Total EASI, mean (SD)	19.9 (7.6)	25.3 (14.1)
Total SCORAD, mean (SD)	66.7 (10.7)	60.7 (13.7)
IGA=3, %	80	80
IGA=4, %	20	20

Baseline is defined as the last measurement prior to dosing, AD = atopic dermatitis, IV = intravenous, IGA = Investigator's Global Assessment (severity scale), WI-NRS = Worst Itch Numerical Rating Scale, EASI = Eczema Area and Severity Index, SCORAD = Scoring atopic dermatitis (severity scale)

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KPL-716 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	KPL-716 (IV)				Placebo (IV)	KPL-716 (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	KPL-716 (IV)			Placebo (IV)	KPL-716 (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.

Exploratory efficacy endpoints and analysis plan

Efficacy Endpoints

- **Pruritus:**
  - Weekly average of daily WI-NRS (worst itch in past 24 hours) collected by daily eDiary
  - Pruritus Visual Analog Scale, a component of SCORAD (average itch in past 3 days) collected at study visits
- **Sleep loss VAS:**
  - A component of SCORAD (average sleep loss in past 3 nights)
- **Eczema Area Severity Index (EASI)**

Post Hoc Efficacy Analysis

- **10 KPL-716 subjects (7.5 mg/kg IV) versus 10 placebo subjects (pooled IV) from baseline to Day 28**
- **"Last Observation Carried Forward" approach used for data values after rescue medication administered. Subject was considered non-responder after rescue (responder analysis).**
  - Two KPL-716: 2 AD flares (d15 and d21)
  - Three placebo: 2 AD flares (d3, d14), 1 anti-histamine use for upper respiratory infection (d26)
- **Similar results obtained if data values after rescue medication administration were included or excluded**

AD = atopic dermatitis, IV = intravenous, WI-NRS = Worst Itch Numerical Rating Scale, EASI = Eczema Area and Severity Index, SCORAD = Scoring atopic dermatitis (severity scale)

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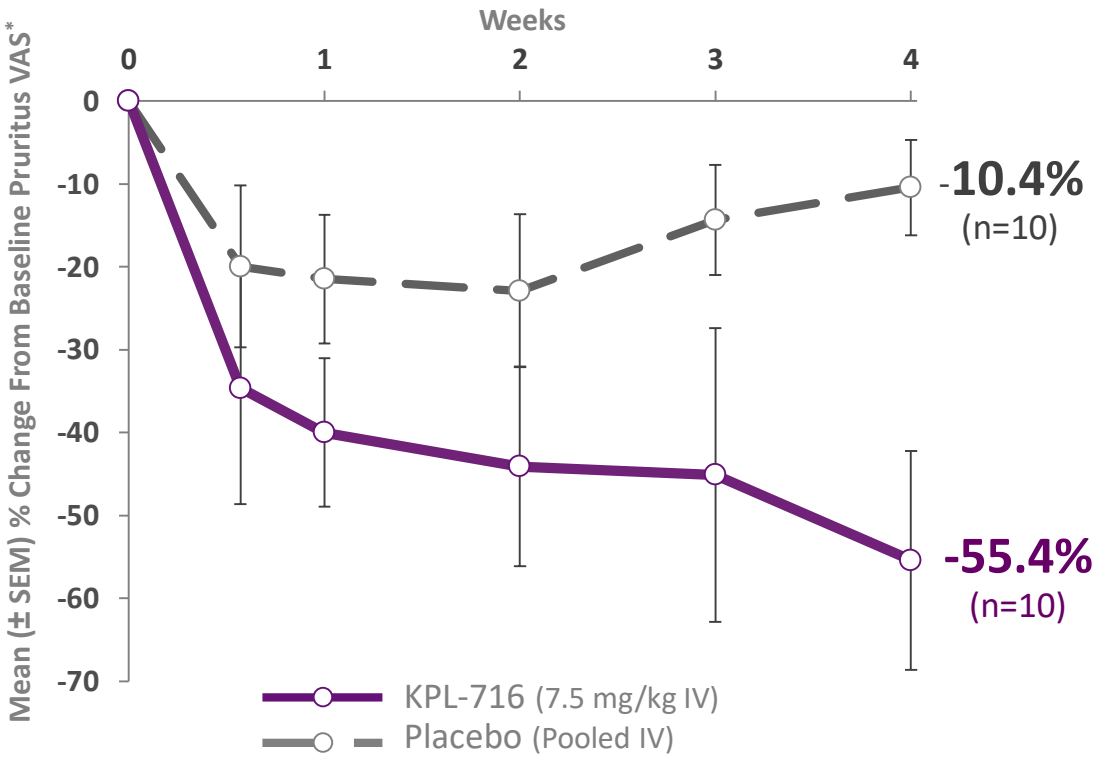
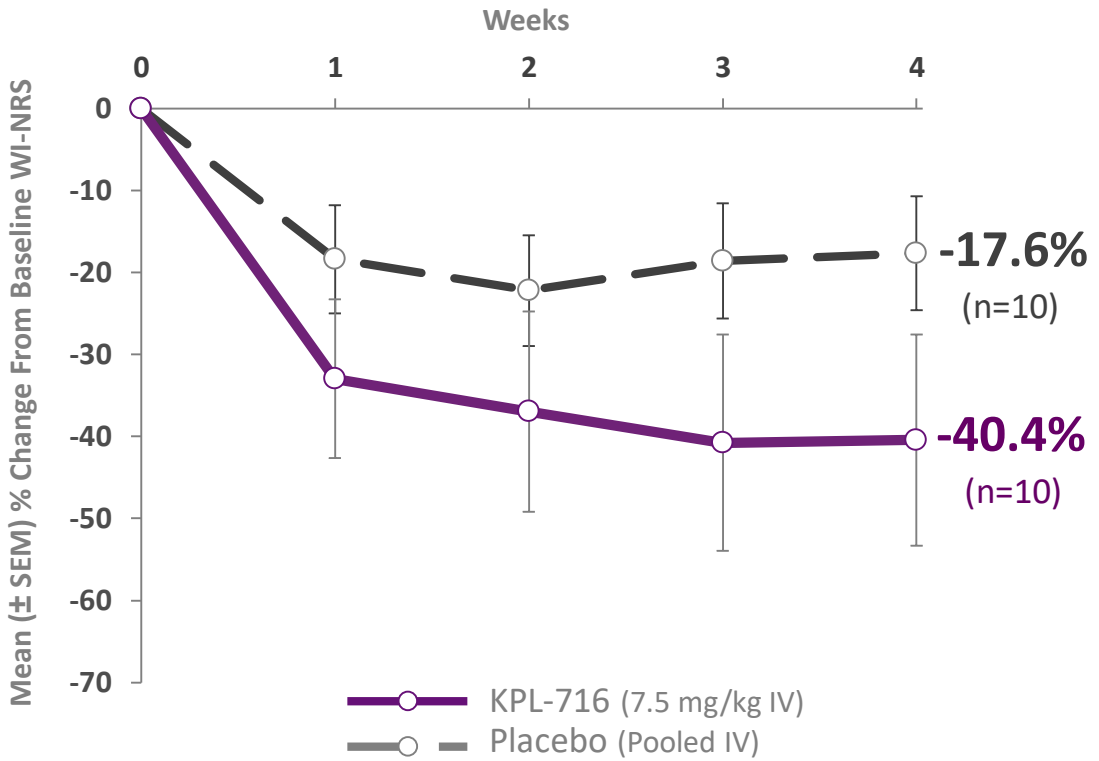
Single doses in Phase 1a/1b provided early evidence indicative of target engagement and showed reduction in pruritus over the 28-day monotherapy period

Pruritus Visual Analog Scale (VAS)*



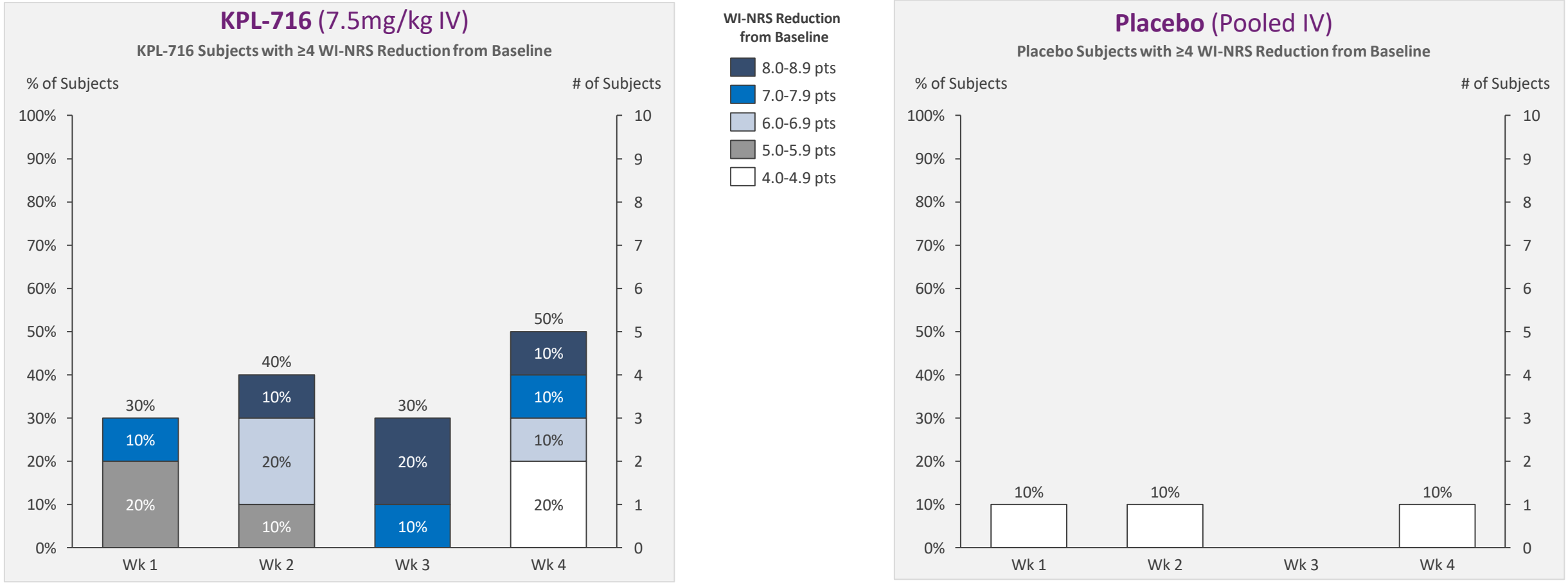
Weekly Average Worst Itch Numerical Rating Scale (WI-NRS)



In subjects who received rescue medication, last observation was carried forward. Two KPL-716 recipients (d15, d21) and three placebo recipients (d3, d14, d26)

* VAS = Visual Analog Scale and a component of SCORAD (Scoring atopic dermatitis) severity scale

The maximum decrease in WI-NRS at day 28 in the absence of concomitant TCS was ≥ 8-points in KPL-716 recipients compared to ≥ 4-points in placebo

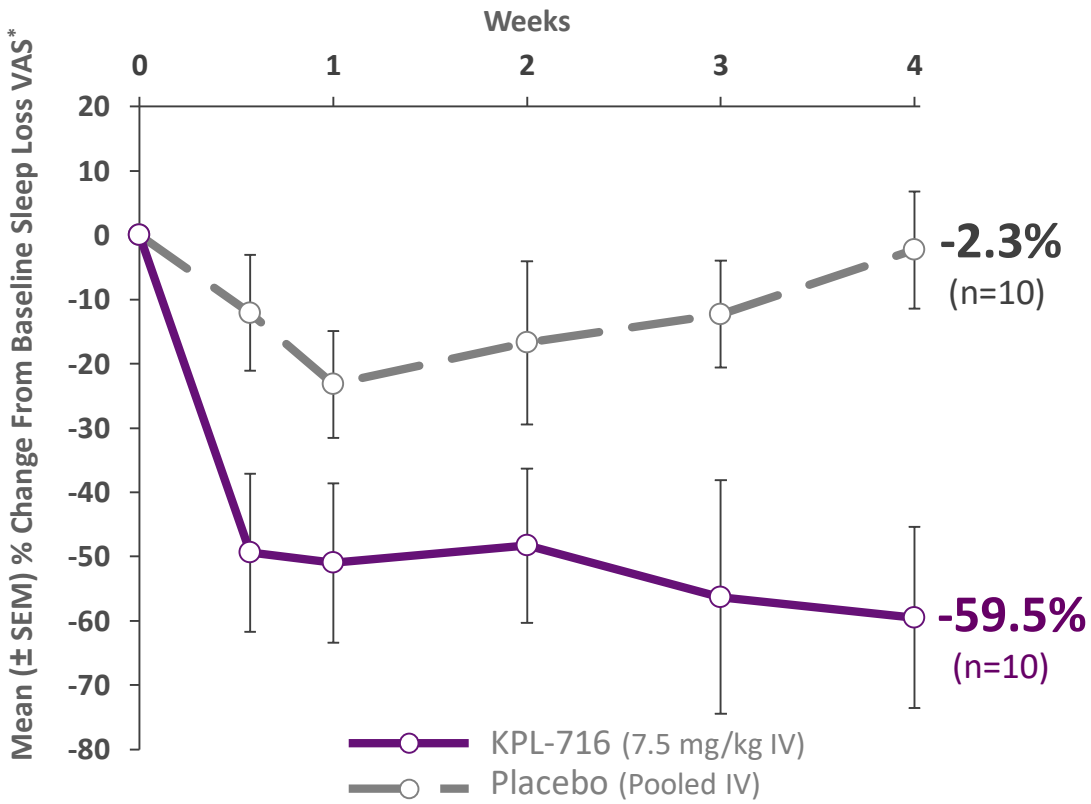


Subjects were treated as non-responders after rescue. Two KPL-716 recipients (d15, d 21) and three placebo recipients (d3, d14, d26).

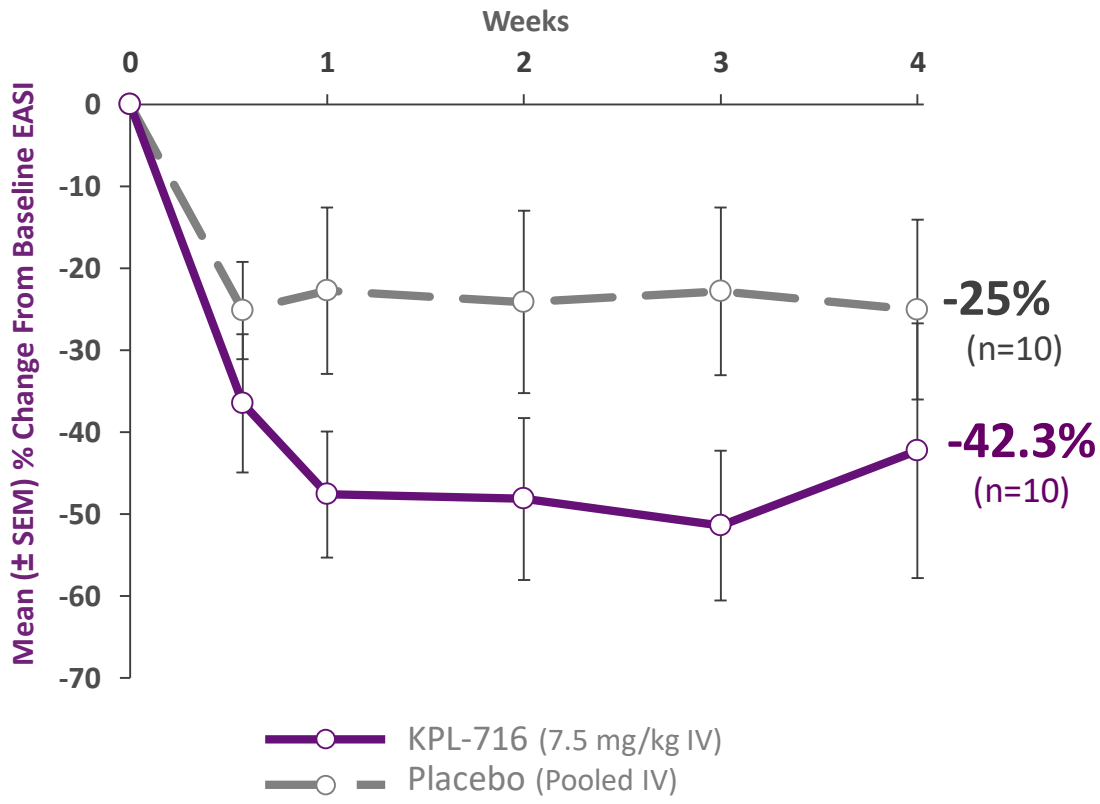
WI-NRS = Worst Itch Numerical Rating Scale, TCS = topical corticosteroids

Single doses in Phase 1a/1b showed reduction in sleep loss and disease severity over the 28-day monotherapy period

Sleep Loss VAS*



Eczema Area and Severity Index (EASI)

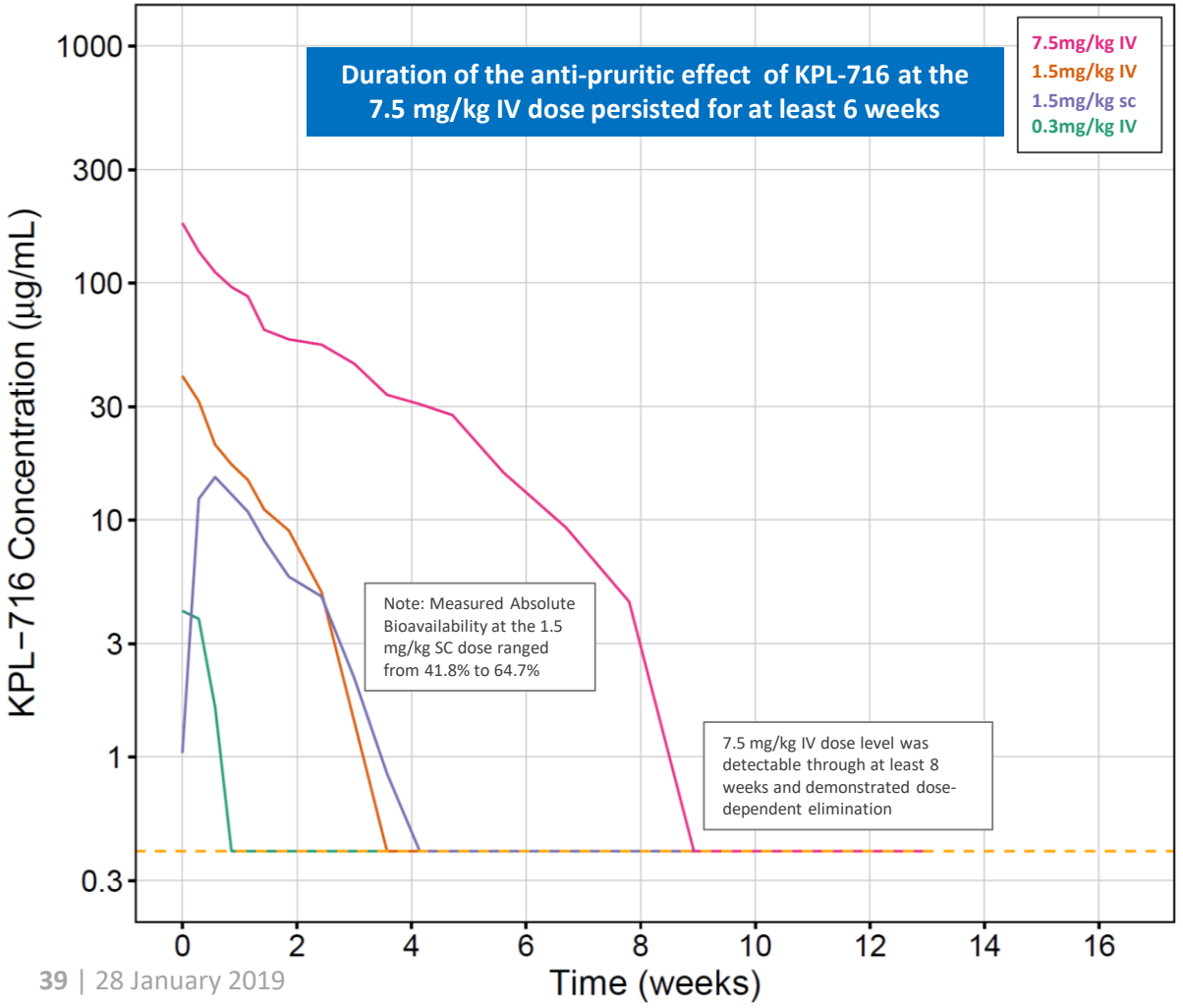


In subjects who received rescue medication, last observation was carried forward. Two KPL-716 recipients (d15, d21) and three placebo recipients (d3, d14, d26)

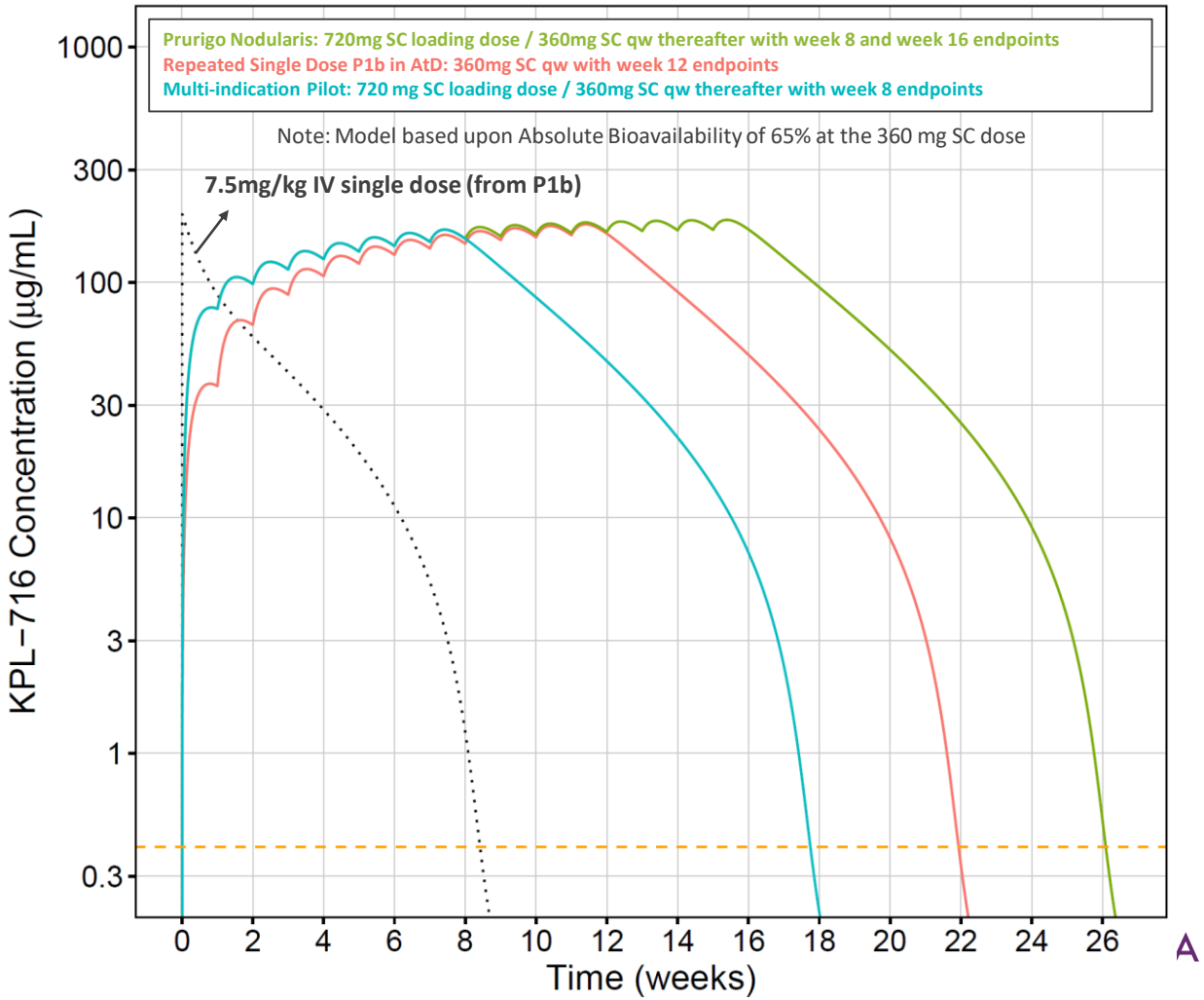
* VAS = Visual Analog Scale and a component of SCORAD (Scoring atopic dermatitis) severity scale

PK/PD model predicts that weekly SC dosing provides sufficient/high exposures for current POC studies as well as studying alternate dosing regimens in future dose-finding studies (e.g., q2w and/or qm)

Measured KPL-716 PK From P1b Single Dose



Phase 1b data used to build predictive PK/dosing model for currently ongoing multiple-dose studies (RSD, PN, Chronic pruritus pilot)

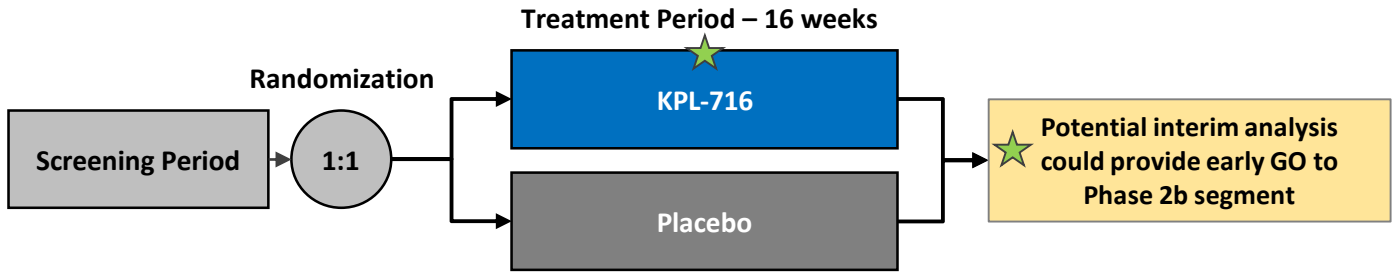


A

Planned KPL-716 adaptive design Phase 2a/2b trial in prurigo nodularis

Ph2a Proof-of-Concept (POC) Segment

- **Objective:** Assess pruritus reduction
- **Sample size:** n=100
- **Dose:** 720 mg SC loading dose --> 360 mg single SC QW thereafter



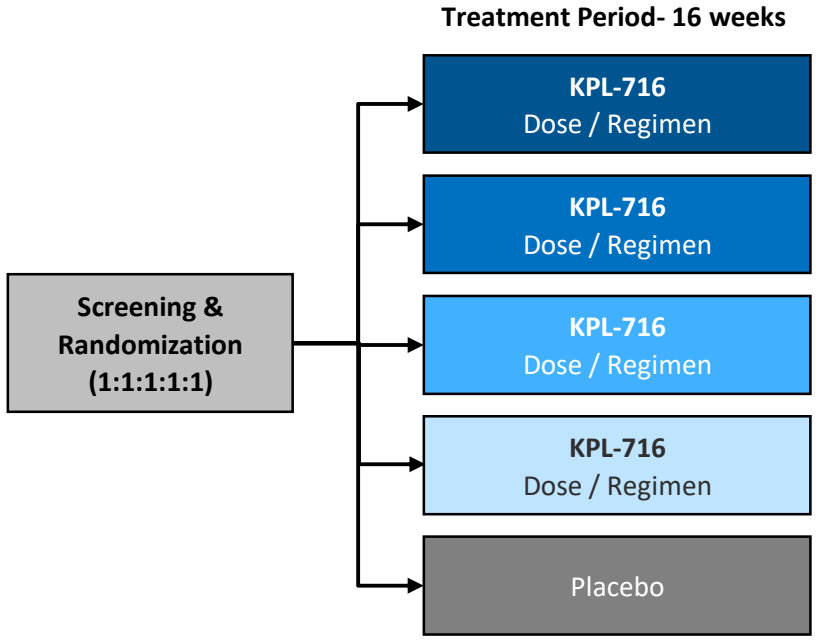
Primary Endpoint:
- % change from baseline in weekly average Worst Itch-Numeric Rating Scale (WI-NRS)

Key Secondary Endpoints:
- Proportion of subjects achieving at least a 4-point reduction from baseline in weekly average WI-NRS
- % change from baseline in pruritus Visual Analog Scale (VAS)

Other Secondary Endpoints:
- Exploratory tools will be used to measure disease modification

Ph2b Dose Range-Finding Segment:

- **Objective:** Define optimal KPL-716 dose/regimen on pruritus endpoint
- **Sample size:** n=300 (anticipated)
- **Doses/Interval:** TBD



Primary Endpoint:
- Likely identical to Ph2a, but will be adjusted if needed based on Ph2a data

Secondary Endpoints:
- Will be determined based on observations from Ph2a

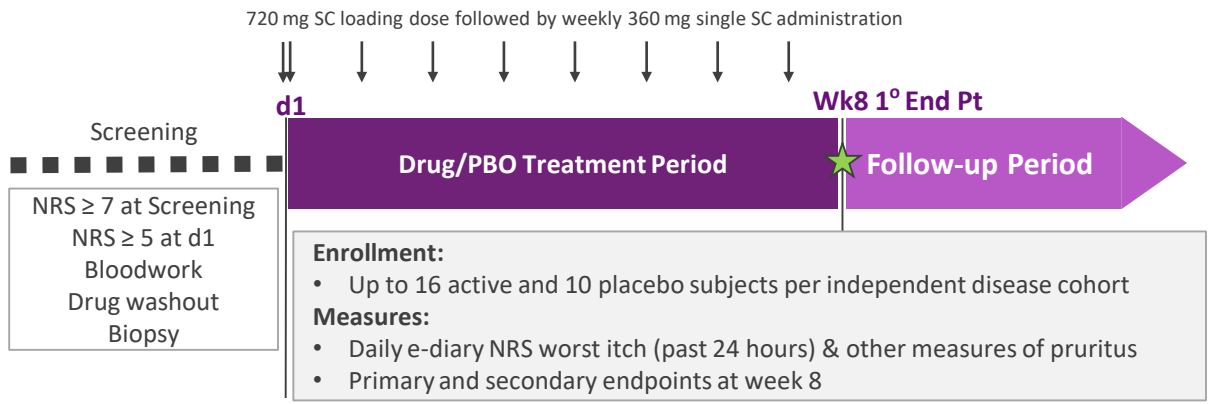
Planned KPL-716 exploratory pilot study in multiple diseases characterized by chronic pruritus

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 KPL-716 to clinical response
(3) Diseases where IL-31 is NOT present (based on post-hoc biopsy analysis) → Investigate whether blocking OSMRβ has any effect

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

Subject Experience in Each Disease Cohort

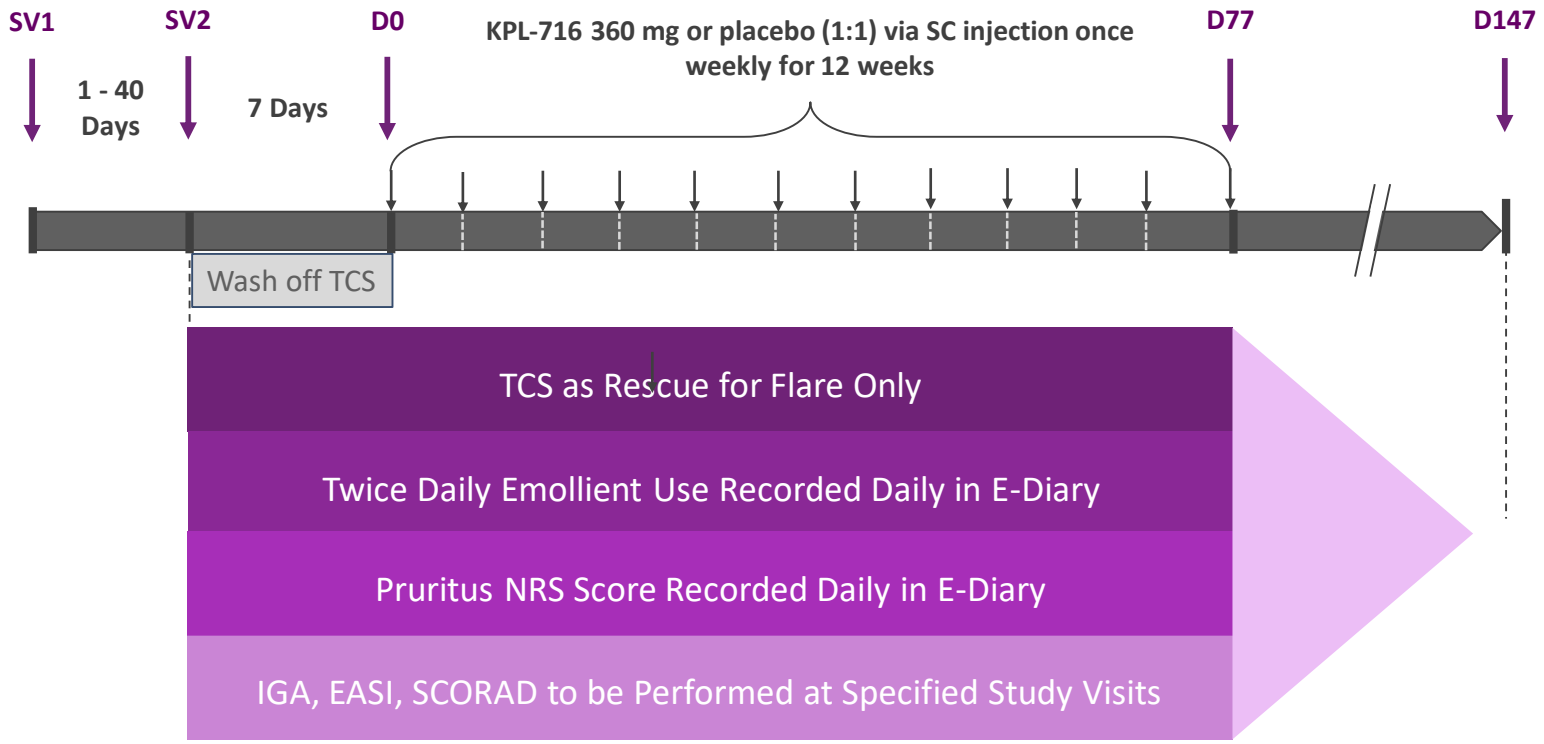


Note: US prevalence figures are estimates based on references which may include only a single EU country and/or based on primary market research where physicians were asked to relate the estimated number of patients they treat with the target disease in relation to another disease they treat where the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

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

KPL-716 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



4 KPL-045 – Preclinical

(monoclonal antibody targeting CD30L)

Rilonacept | Mavrilimumab | KPL-716 | **KPL-045** | KPL-404

Fully-human monoclonal antibody inhibitor of signaling between CD30 and CD30L

- Involved in T-effector memory function, humoral response & T_H2 immunity
- CD30L is expressed at high levels on activated T cells
- Proof-of-mechanism established in mice and non-human primates
- Continuing preclinical activities

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5 KPL-404 – Preclinical
(monoclonal antibody targeting CD40)

Rilonacept | Mavrilimumab | KPL-716 | KPL-045 | **KPL-404**

Humanized monoclonal antibody inhibitor of signaling between CD40L and CD40

- CD40/CD40L interaction between B & T-cells are required for humoral responses
- Antigen presenting cells express and require signaling through CD40 for activation
- Proof-of-mechanism established in non-human primates
- Continuing preclinical activities

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Kiniksa at a glance

Corporate Highlights

Bermuda-Based Corporate Entity

5
Pipeline Programs

>180
Issued Patents

Financial Highlights

$490M
Gross Proceeds Raised to Date

$338M
Cash and Short-Term Investments*

49.5M
Shares Outstanding

Capital Allocation to Highest Value Opportunities Across Existing Portfolio, Internal R&D and Business Development

* As of September 30, 2018

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Anticipated Achievements by Year-End 2019

- **5** clinical-stage programs
- **10** investigational indications
- **1** pivotal Phase 3 trial
- **3** Phase 2 trials
- **1** Phase 2 trial complete
- **1** Phase 1 trial complete
- **2** clinical data readouts
- **multiple** internal, discovery-stage projects

Summary of anticipated corporate milestones for 2019-2020

Program	Milestone	Anticipated Timing
Rilonacept	Present Phase 2 trial data in recurrent pericarditis at ACC	**1H 2019**
	Top-line data from Phase 3 RHAPSODY trial in recurrent pericarditis	**2H 2020**
Mavrilimumab	Top-line data from global Phase 2 trial in GCA	**2H 2020**
	Provide data from non-clinical and biomarker studies on the role of GM-CSF in GCA	**2H 2019**
	Announce additional investigational indication for mavrilimumab	**2H 2019**
KPL-716	Initiate adaptive design Phase 2a/Phase 2b in prurigo nodularis	**1H 2019**
	Initiate Phase 2 exploratory pilot study in multiple diseases characterized by chronic pruritus	**1H 2019**
	1. chronic idiopathic pruritus	
	2. chronic spontaneous urticaria	
	3. plaque psoriasis	
	4. lichen simplex chronicus	
	5. lichen planus	
	Provide data from non-clinical and biomarker studies of IL-31 and OSM in prurigo nodularis and atopic dermatitis	**2H 2019**
	Present top-line data from repeated-single-dose Phase 1b in atopic dermatitis	**2H 2019**
	Present top-line data from Phase 2a trial in PN	**1H 2020**
	Present top line data from Phase 2a exploratory pilot study in multiple diseases characterized by chronic pruritus	**2H 2020**
KPL-045	File IND	**2H 2019**
	Initiate Phase 1 trial	**1H 2020**
KPL-404	File IND	**2H 2019**
	Initiate Phase 1 trial	**1H 2020**

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Relentless. Passionate. Focused. ™