

PASTORALE: A Pivotal Phase 3 Trial of the Investigational IL-1 Receptor Antagonist KPL-387 in Recurrent Pericarditis

Study design and Phase 2 dose-focusing data supporting selection of the once-monthly subcutaneous dose level

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Phase 2 dose-focusing data supported selection of the once-monthly subcutaneous KPL-387 dose level and initiation of pivotal Phase 3 PASTORALE

BACKGROUND

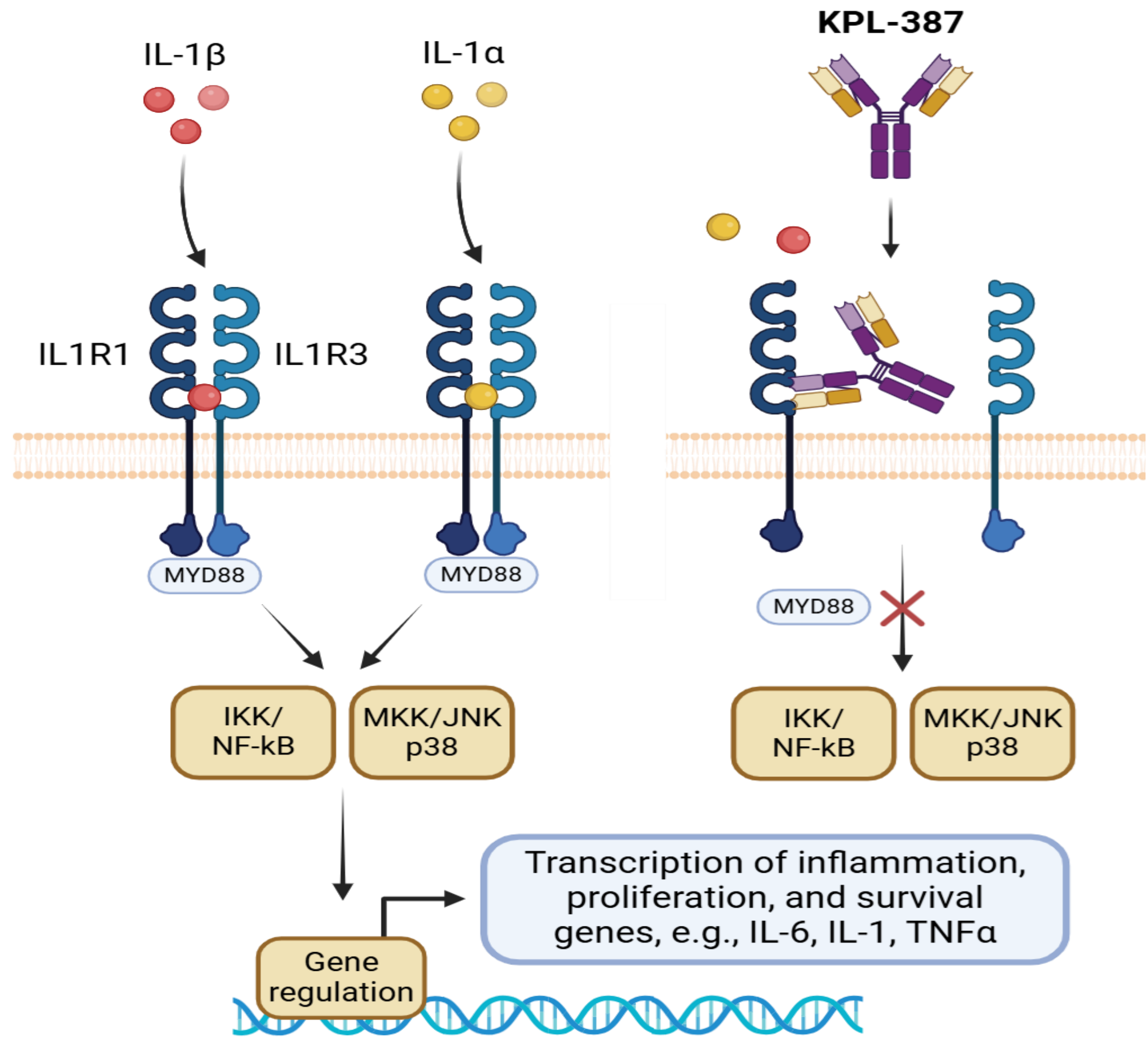
Recurrent Pericarditis

- Recurrent pericarditis (RP) is an interleukin (IL)-1-mediated chronic autoinflammatory disease that may require treatment for the duration of disease¹⁻⁴.
- Data implicating IL-1 α and IL-1 β in RP pathophysiology informed a novel approach to disease control^{2,3}.

KPL-387

- KPL-387, an investigational, fully human immunoglobulin G2 monoclonal antibody, binds human IL-1 receptor 1 and inhibits IL-1 α and IL-1 β signaling and was designed for monthly dosing with a single subcutaneous self-injection in liquid formulation (**Figure 1**).
- The KPL-387 Phase 2/3 trial consists of 3 overlapping parts in one streamlined protocol: Phase 2 Dose-Focusing portion, pivotal Phase 3 portion (PASTORALE), and Long-Term Extensions.
- PASTORALE is a Phase 3 outcomes study assessing treatment of RP and reduction in recurrence risk.

Figure 1. KPL-387 Mechanism of Action



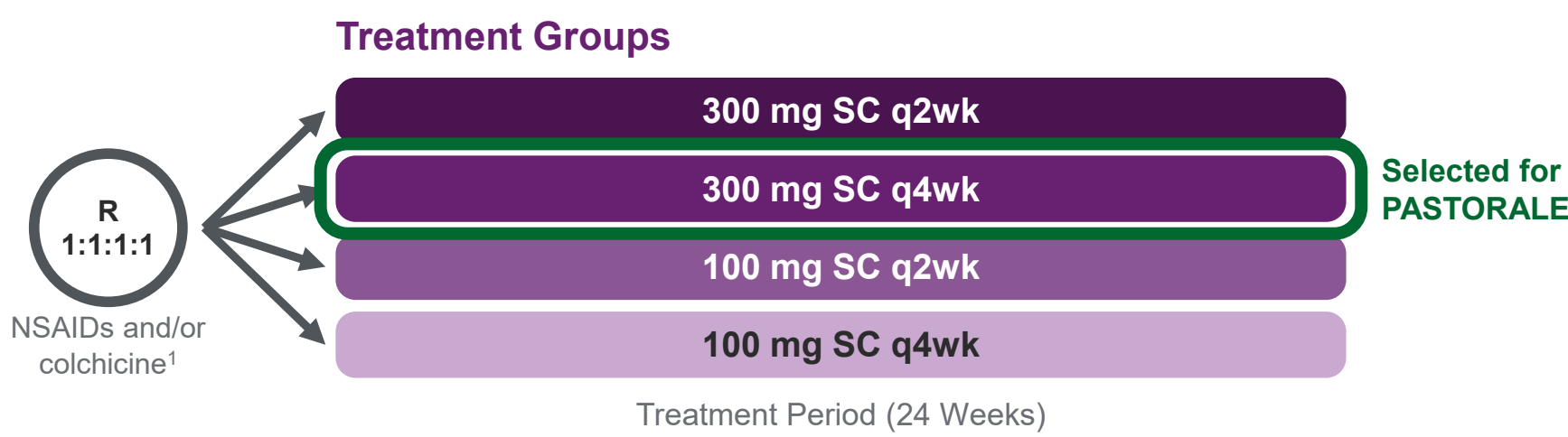
IgG2, immunoglobulin G2; IKK, I κ B kinase; IL-1R1, interleukin-1 receptor 1; IL-1R3, interleukin-1 receptor 3; IL-6, interleukin 6; IL-1 α , interleukin-1 alpha; IL-1 β , interleukin-1 beta; JNK, jun N-terminal kinase; MYD88, myeloid differentiation primary response 88; MAPK, mitogen-activated protein kinase; NF- κ B, nuclear factor-kappa B; p38, p38 mitogen-activated protein kinase; PASTORALE, A Phase 3 Study of Participants with Recurrent Pericarditis Evaluating the Efficacy and Safety of KPL-387; TNF α , tumor necrosis factor-alpha.

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PHASE 2 DOSE-FOCUSING: SUPPORTING DATA

- Phase 2 evaluates dose response and safety across four double-blinded KPL-387 dose levels: 100 or 300 mg administered subcutaneously (SC) every 2 (q2wk) or 4 weeks (q4wk). Primary efficacy endpoint is Time to Treatment Response.
- In an interval analysis of the Phase 2 portion, patients receiving KPL-387 300 mg SC q4wk had a median Time to Treatment Response[†] of 4.0 days (95% CI, 3.0-6.0; **Figure 2**), with durable efficacy throughout the dosing interval. Median times to Pain Response and CRP Normalization were 4.0 and 8.0 days, respectively.
- KPL-387 was well tolerated. These data supported selection of 300 mg SC q4wk for PASTORALE.

Figure 2. Phase 2 Interval Analysis

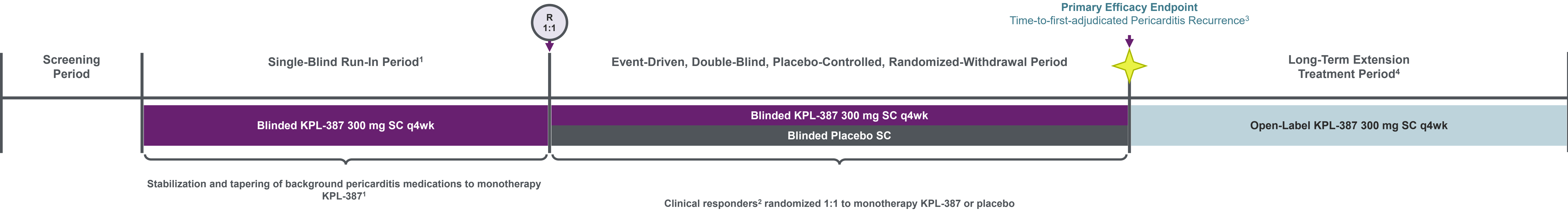


Primary and Secondary Endpoints* 300 mg SC q4wk Group	
Time to Treatment Response [†]	4.0 (3.0, 6.0) days
Time to Pain Response	4.0 (3.0, 6.0) days
Time to CRP Normalization [§]	8.0 (7.0, 9.0) days

*Results from interval analysis; reported as median (95% CI). [†]Treatment Response is defined as Pain Response (NRS score ≤ 2 on the 11-point daily pericarditis NRS pain scale) and at least one CRP level ≤ 0.5 mg/dL within 7 days before or after the day of Pain Response. [§]CRP normalization defined as CRP ≤ 0.5 mg/dL. [†]KPL-387 is added to conventional oral pericarditis medications (NSAIDs and/or colchicine) at baseline; oral medications are then weaned to achieve KPL-387 monotherapy. CI, confidence interval; CRP, C-reactive protein; NRS, numerical rating scale; NSAID, non-steroidal anti-inflammatory drug; R, randomization. Phase 2 data presented here are based on an interval analysis of the ongoing Phase 2 study and are subject to change following study completion, final data cleaning, and completion of analyses. Final results may differ from those presented herein.

PASTORALE: PIVOTAL PHASE 3 DESIGN

Figure 3. Study Flow Diagram



Population

- Up to ~85 patients diagnosed with RP presenting at screening with a qualifying pericarditis episode despite treatment with conventional oral therapies

Treatment

- During a single-blind Run-In, patients will receive KPL-387 300 mg SC q4wk while conventional oral therapies are weaned and discontinued¹.
- Participants achieving Clinical Response² during Run-In will be randomized 1:1 to receive continued KPL-387 or placebo in the Randomized-Withdrawal Period.
- Long-Term Extension: open-label KPL-387 300 mg SC q4wk⁴.

Primary Efficacy Endpoint

- Primary efficacy endpoint is time to first adjudicated pericarditis recurrence³.
- Only CEC-confirmed Pericarditis Recurrences are counted as events for the primary efficacy endpoint analysis.
- PASTORALE (**Figure 3**) is an ongoing event-driven, double-blind, placebo-controlled randomized-withdrawal study.

¹Duration of the Run-In Period undisclosed in order to maintain study subjects blinded to the start of the Randomized-Withdrawal Period. ²Clinical Response defined as the weekly average of daily pericarditis pain ≤ 2.0 on the 11-point NRS and a CRP level ≤ 0.5 mg/dL, while receiving monotherapy KPL-387 without a recurrence. ³Time to Pericarditis Recurrence is defined as the time from randomization in the Randomized-Withdrawal Period to the date of the first Pericarditis Recurrence for each participant. Only CEC-confirmed Pericarditis Recurrences will be considered as events for the primary efficacy endpoint analysis in the Phase 3 pivotal study. ⁴Up to 24 months or the time KPL-387 is approved for commercial use in that region to treat recurrent pericarditis. CEC, Clinical Endpoint Committee; CRP, C-reactive protein; NRS, numerical rating scale; PASTORALE, A Phase 3 Study of Participants with Recurrent Pericarditis Evaluating the Efficacy and Safety of KPL-387; q4wk, once every 4 weeks; R, randomization; RP, recurrent pericarditis; SC, subcutaneous.

CONCLUSIONS

- Phase 2 interval data demonstrated rapid and sustained reductions in pain and inflammation (CRP) at the 300 mg SC q4wk dose level, supporting initiation of PASTORALE.
- KPL-387 could expand treatment options, potentially enabling once-monthly dosing with a single self-injection in liquid formulation.

KPL-387 is an investigational product; the efficacy and safety have not been evaluated by any regulatory authority

ACKNOWLEDGEMENTS

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DISCLOSURES

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REFERENCES

1. Ceriani E, Agozzino F, Berra S, et al. ACR Open Rheumatol. 2025;7(1):e11776. 2. Imazio M, Lazaros G, Gattorno M, et al. Eur Heart J. 2022;43(31):2946-2957. 3. Chiabrando JG, Bonaventura A, Vecchié A, et al. J Am Coll Cardiol. 2020;75(1):76-92. 4. Brucato A, Lazaros G, Klein A, et al. Presented at: European Society of Cardiology Myocardial & Pericardial Diseases Annual Meeting 2025; November 28-29, 2025; Trieste, Italy.