IL-6 Landscape Analysis

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Modern decision intelligence for the bioeconomy

Executive Summary

IL-6 Landscape Analysis

1. **LANDSCAPE SCOPE:** The IL-6 pipeline contains 101 named programs, but only 4 target cardiovascular indications. Of 55 preclinical programs, just 1 pursues CV — the rest focus on rheumatoid arthritis, oncology, and autoimmune diseases.

2. **LATE-STAGE CONCENTRATION**: Three programs control the 2027-2029 CV approval window: Novo Nordisk's ziltivekimab (6,200-patient MACE trial in ASCVD+CKD), CSL's clazakizumab (dialysis/ESKD), and Tourmaline/Pfizer's pacibekitug (ASCVD+AAA). Preclinical entrants cannot catch this timeline.

3. **EFFICACY CEILING:** All IL-6 programs achieve 85-94% hs-CRP reductions regardless of indication, eliminating biomarker superiority as a differentiation lever. Competition must occur on population selection or endpoint innovation.

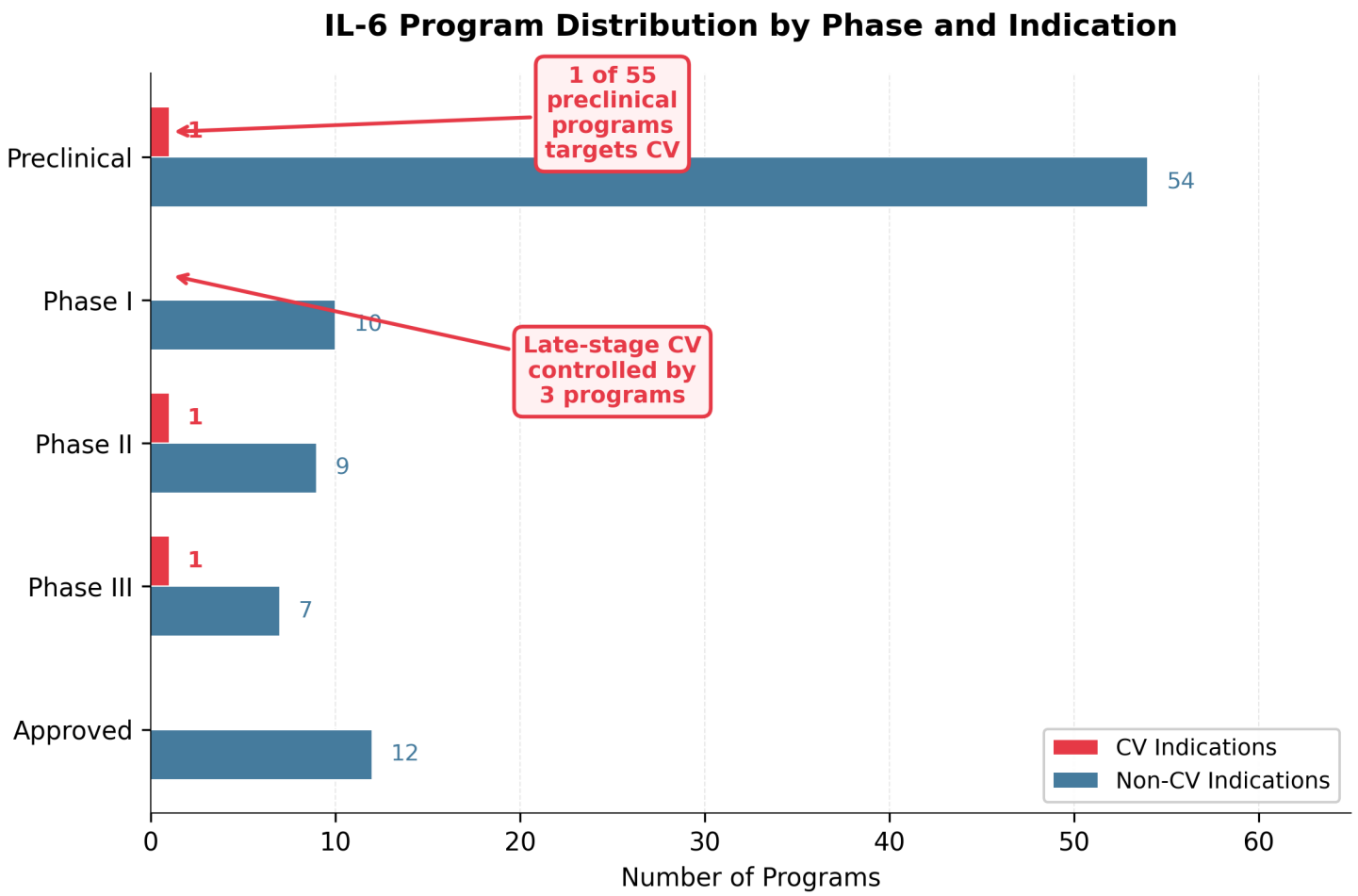
4. **WHITE SPACE OPPORTUNITY:** HFpEF and abdominal aortic aneurysm have zero IL-6 clinical programs despite biological rationale. These emerging indications offer genuine differentiation but require sponsors to pioneer regulatory endpoints without precedent.

5. **STRATEGIC IMPLICATION:** Preclinical programs should avoid broad ASCVD pursuit and instead target high-inflammation subgroups (CKD/dialysis enrichment) or emerging indications (HFpEF, AAA) where late-stage competitors have not yet established dominance.

IL-6 = interleukin-6. CV = cardiovascular. ASCVD = atherosclerotic cardiovascular disease. CKD = chronic kidney disease. ESKD = end-stage kidney disease. AAA = abdominal aortic aneurysm. HFpEF = heart failure with preserved ejection fraction. hs-CRP = high-sensitivity C-reactive protein. MACE = major adverse cardiovascular events.

Preclinical IL-6 programs have abandoned cardiovascular indications

Only 1 of 55 preclinical programs targets CV while late-stage players control the 2027–2029 window.



- 54 of 55 preclinical programs focus on non-CV indications — the CV opportunity has been structurally ceded.
- Only 3 late-stage programs compete for CV labels, all with 2027-2029 approval timelines preclinical entrants cannot match.
- The single preclinical CV program lacks capital to compete with Novo's 6,200-patient ZEUS trial.
- Preclinical sponsors must differentiate on population enrichment or emerging indications, or accept that cardiovascular IL-6 is effectively closed.

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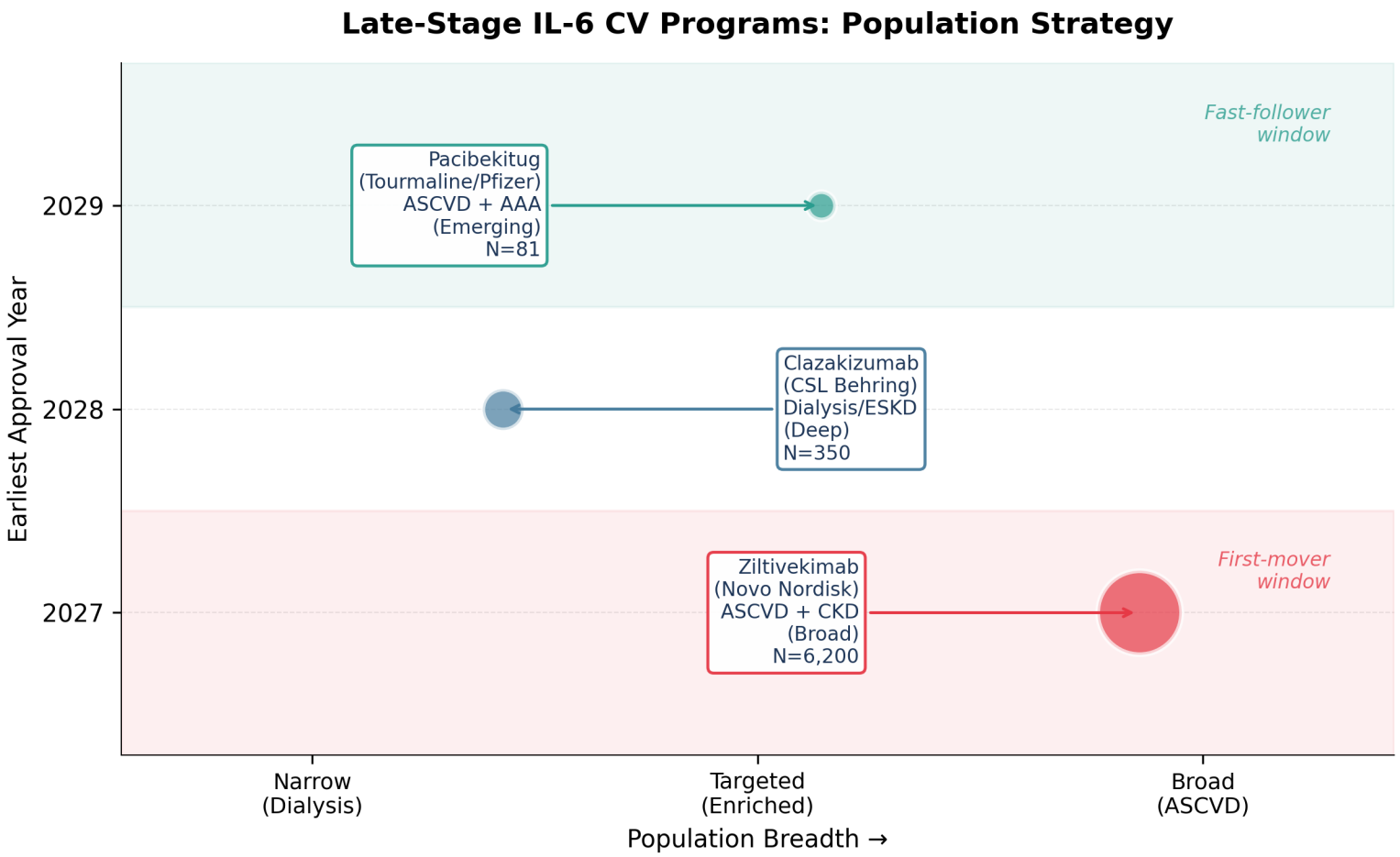
Analysis of 101 named programs; January 2025. IL-6 = interleukin-6. CV = cardiovascular.

Three players have carved up the cardiovascular IL-6 landscape

Novo pursues broad ASCVD+CKD, CSL targets dialysis depth, and Tourmaline bridges with AAA optionality.



- Ziltivekimab (Novo): 6,200-patient MACE trial in ASCVD+CKD; 2027 approval establishes first-mover advantage.
- Clazakizumab (CSL): targets dialysis/ESKD pts with highest baseline inflammation and accepted CV mortality endpoints.
- Pacibekitug (Tourmaline/Pfizer): pursues AAA and emerging indications with 2029 approval window.
- Limited white space remains as broad ASCVD is contested, CKD and dialysis niches are claimed, and emerging indications require regulatory pioneering.

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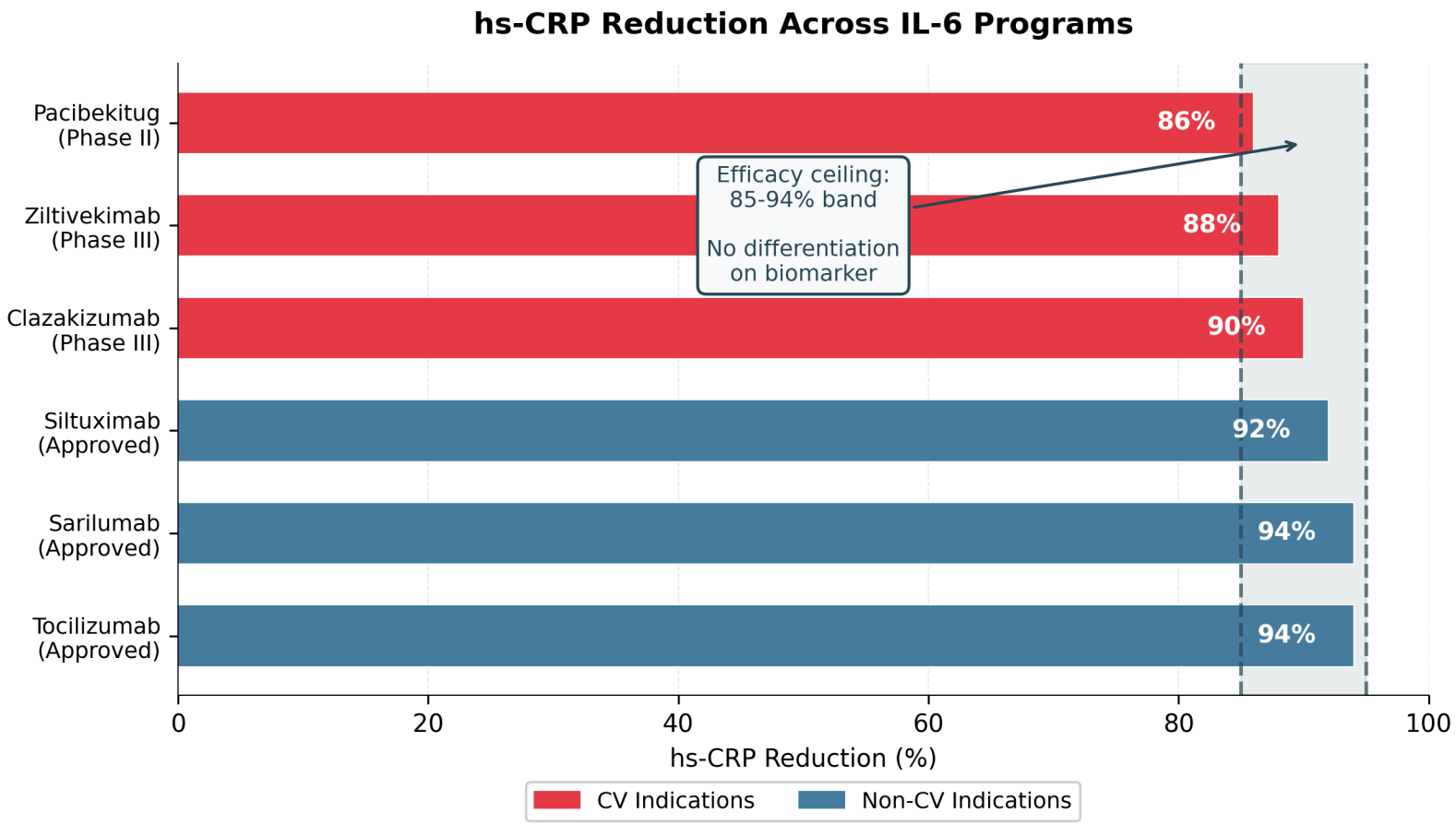
Trial sizes and timelines from company disclosures. ASCVD = atherosclerotic cardiovascular disease. CKD = chronic kidney disease. ESKD = end-stage kidney disease. AAA = abdominal aortic aneurysm. MACE = major adverse cardiovascular events.

All IL-6 programs hit the same efficacy ceiling

hs-CRP reductions cluster in a narrow 85-94% band regardless of indication or development phase.



- Approved IL-6R antagonists achieve 92-94% hs-CRP reductions — the mechanistic ceiling CV programs cannot exceed.
- CV-focused programs (ziltivekimab 88%, pacibekitug 86%, clazakizumab 90%) fall within the same band.
- "Better inflammation reduction" is not a viable differentiation strategy because all programs converge on similar biomarker effect sizes.
- Preclinical programs must compete on patient selection or endpoint innovation rather than biomarker potency.

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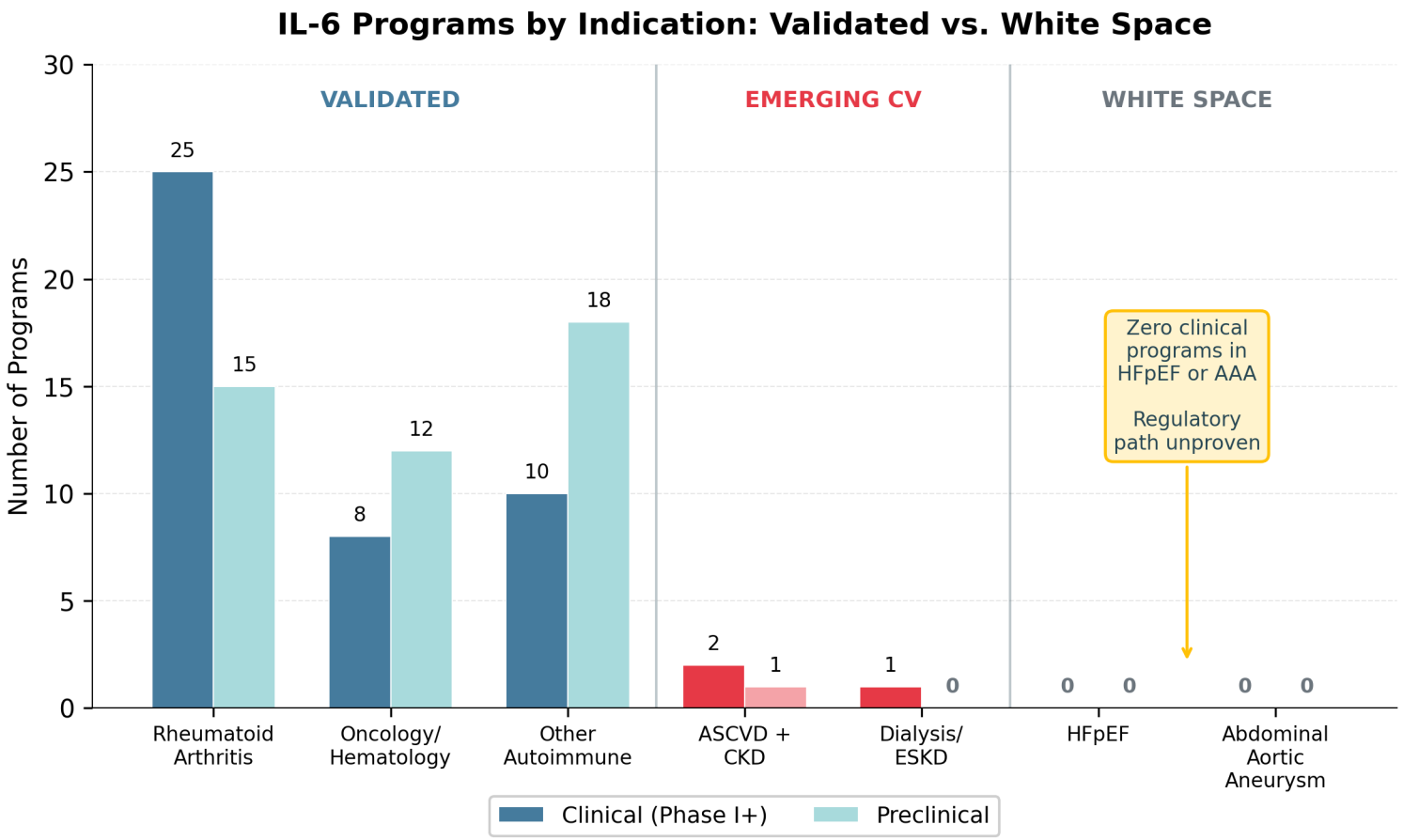
Data from published Phase II-III trials. hs-CRP = high-sensitivity C-reactive protein. IL-6 = interleukin-6.

HFpEF and AAA are genuine white space but require pioneering

No IL-6 programs have entered the clinic for these emerging CV indications despite strong biological rationale



- Validated indications (RA, oncology, autoimmune) have 40+ clinical programs but face crowded dynamics.
- Emerging CV (ASCVD+CKD, dialysis) has 2-3 late-stage programs defining regulatory standards.
- HFpEF and AAA have zero IL-6 clinical programs despite biological rationale.
- The strategic tradeoff is clear: validated paths offer lower regulatory risk but higher competition, while white space offers differentiation but demands first-mover investment.

Program counts from 101 named IL-6 assets. HFpEF = heart failure with preserved ejection fraction. AAA = abdominal aortic aneurysm. ASCVD = atherosclerotic cardiovascular disease. CKD = chronic kidney disease. CV = cardiovascular.