STAT6 Dermatology Analysis

Sleuth

Modern decision intelligence for the bioeconomy

Executive Summary

STAT6 Dermatology Analysis

1. **PATHWAY SHIFT IS COMPLETE:** All 39 programs target STAT6 directly via intracellular modulation rather than upstream IL-4/IL-13 cytokine blockade. The landscape divides into 18 inhibitors, 12 degraders, and 9 gene/RNA programs, with gene therapy concentrated entirely in oncology.

2. **CLINICAL BOTTLENECK DEFINES TIMING:** Only 2 of 39 programs have reached clinical stage, with Kymera's KT-621 as the sole dermatology asset in clinic. Phase 1b data showed ~63% EASI reduction and ~40% pruritus improvement in open-label results. Partnership timing should index to controlled trial readouts.

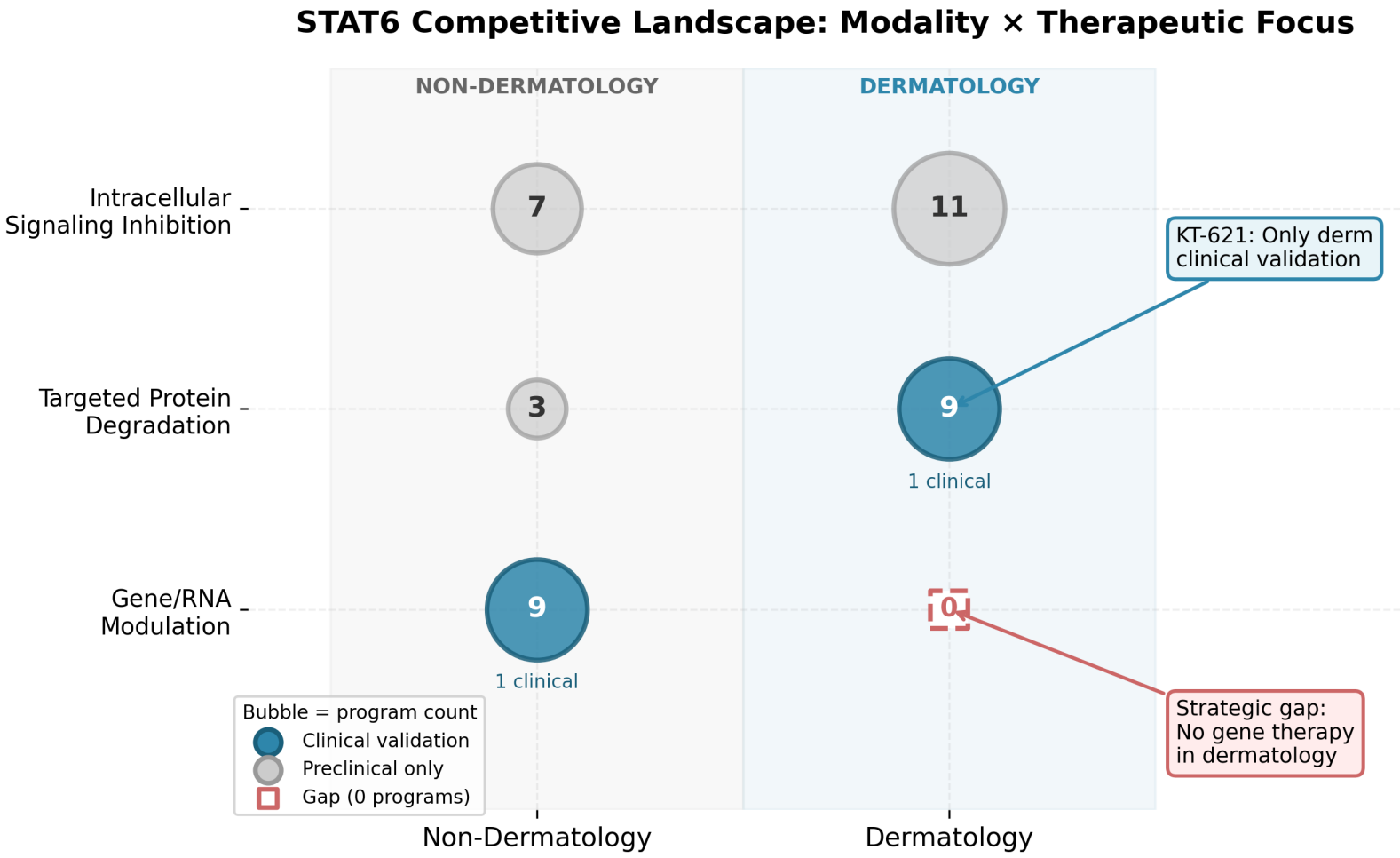
3. **DEGRADERS LEAD ON VALIDATION DESPITE SMALLER PIPELINE:** Targeted protein degradation has fewer programs than inhibitors (12 vs 18) but holds the only clinical proof in dermatology. Biotech dominates degrader development while Pharma is acquiring rather than building internally.

4. **ORAL CONSENSUS CREATES TOPICAL WHITE SPACE:** 65% of dermatology programs target oral delivery, converging on the "dupilumab-in-a-pill" thesis. Pure topical approaches are entirely absent, representing potential differentiation for sponsors targeting mild-to-moderate segments or safety-focused positioning.

5. **KT-621 COMPETITIVE MOAT:** 23 competitor programs sit in the "PD-validated but preclinical" quadrant, years behind KT-621's clinical data. The BROADEN2 Phase 2b trial positions Kymera to establish the efficacy benchmark before any competitor reaches the clinic.

GTx exits derm as STAT6 race narrows to inhibitors vs degraders

39 programs mapped across three intervention modalities and two therapeutic focus areas



- All 39 programs target STAT6 directly rather than upstream cytokines — a decisive shift from the IL-4/IL-13 blockade paradigm.
- Inhibitors lead on volume (18 programs), but degraders hold the only clinical validation in dermatology through Kymera's KT-621.
- Gene/RNA modulation (9 programs) has bypassed dermatology entirely, concentrating in oncology.
- 37 of 39 programs remain preclinical, making KT-621's readouts the mechanism validation event for the class.

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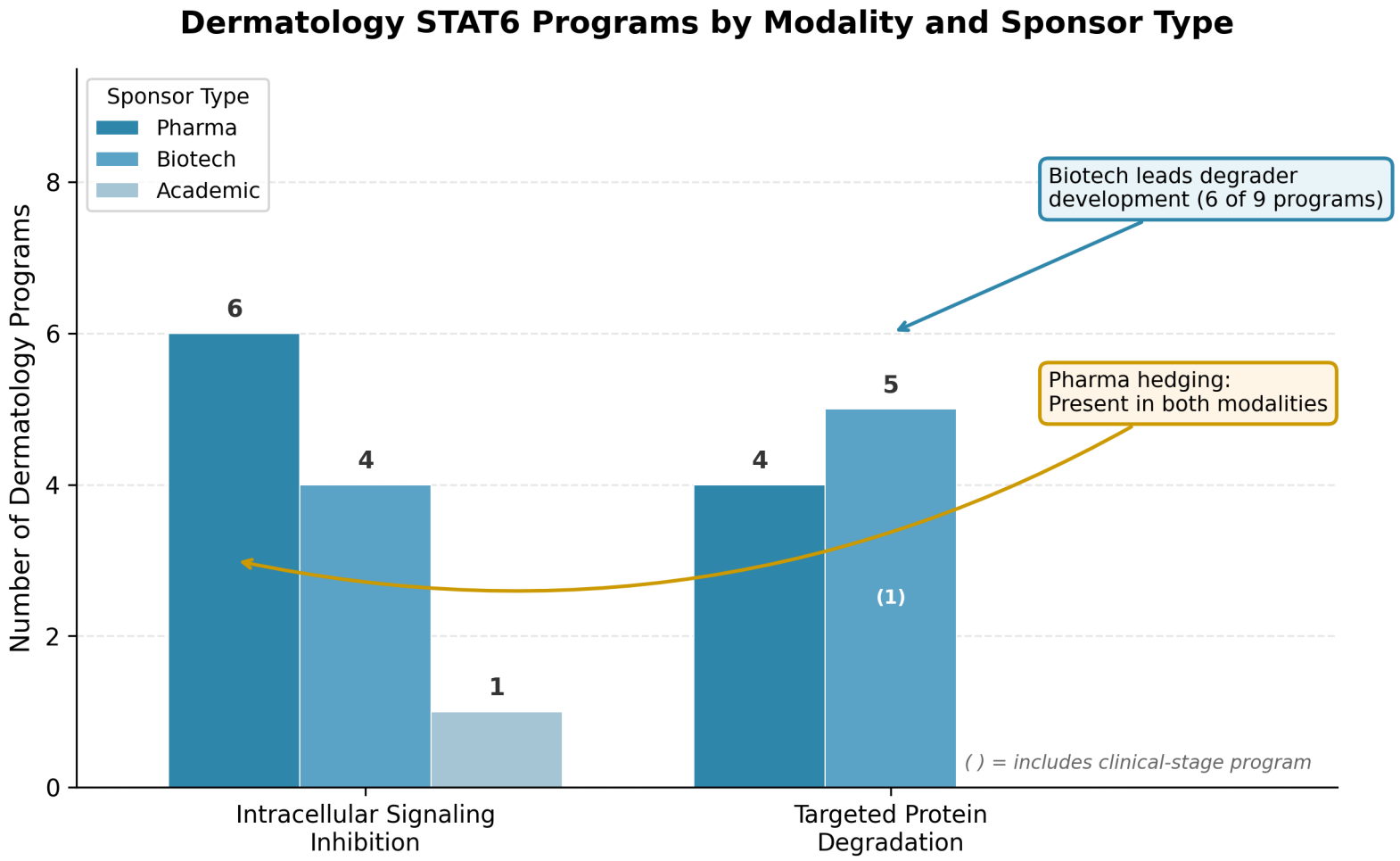
Sleuth analysis of 39 STAT6-targeting programs. Modalities: Intracellular signaling inhibition, Targeted protein degradation, Gene/RNA modulation.

Biotech leads degraders as Pharma hedges across both modalities

20 dermatology-focused programs segmented by intervention type and sponsor category



- Biotech dominates degraders with 6 of 9 dermatology programs, led by Kymera's clinical-stage KT-621.
- Pharma is hedging rather than committing — J&J licensed an inhibitor (KP-723), Sanofi partnered on both modalities.
- Academic programs cluster in inhibitors (2 vs 0 in degraders), reflecting the capital intensity of TPD platforms.
- No Pharma-originated degrader programs suggests Big Pharma views TPD as a platform to acquire, not build.

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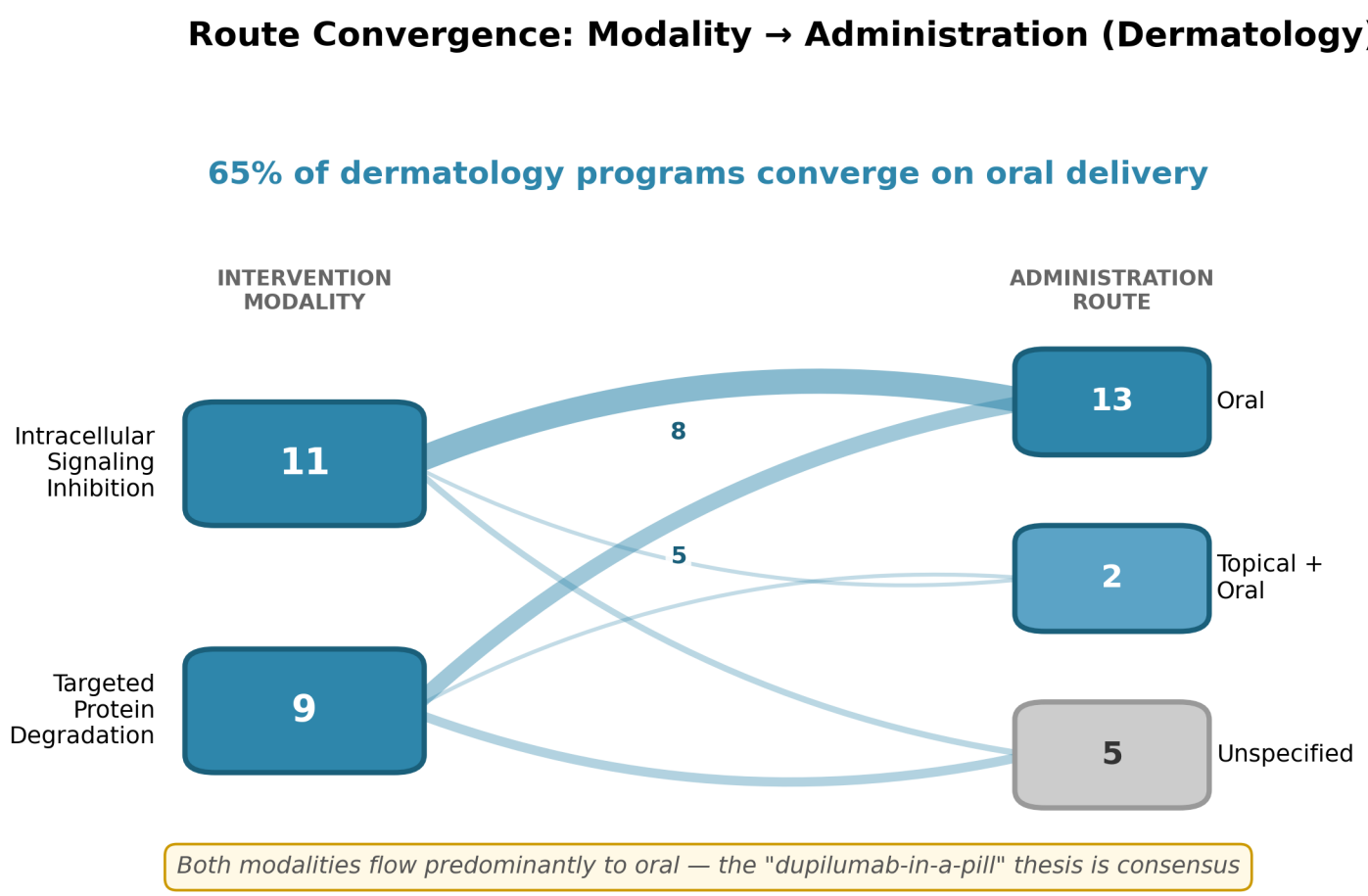
Dermatology programs only (n=20). Sponsor classification based on company type at program origination.

65% target oral as "dupilumab-in-a-pill" becomes consensus

Administration route distribution across 20 dermatology STAT6 programs



- 65% of dermatology programs (13 of 20) target oral delivery, positioning against injectable biologics on convenience.
- Both inhibitors and degraders flow to oral routes — the convergence is commercial, not modality-driven.
- Pure topical approaches are absent, representing white space for mild-to-moderate or safety-differentiated positioning.
- The 5 unspecified programs are early preclinical; oral convergence will likely strengthen as they mature.

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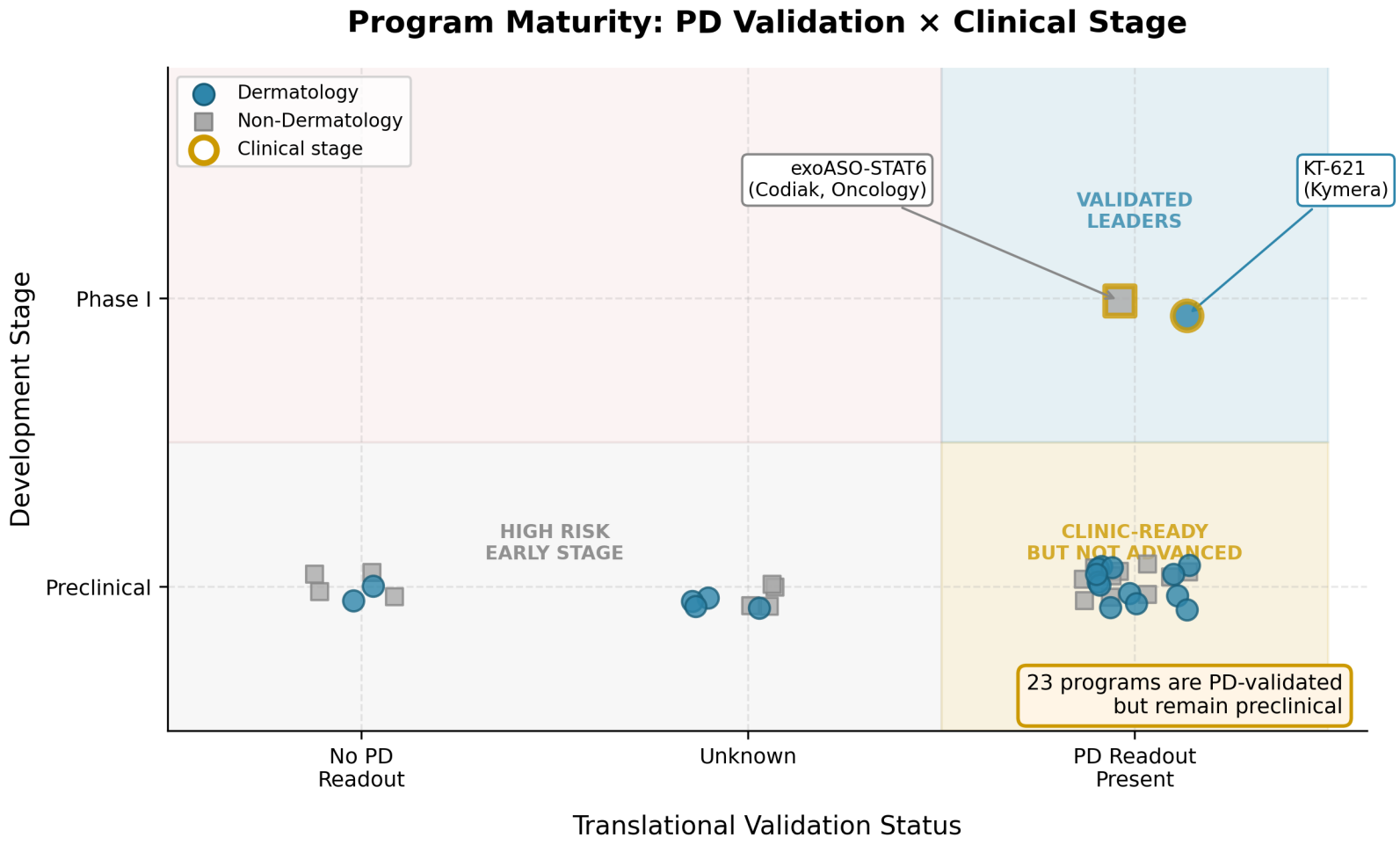
Dermatology programs only (n=20). Routes: Oral, Topical + Oral, or Unspecified based on sponsor disclosures.

23 competitors remain stalled at preclinical despite PD validation

Program maturity assessed by PD readout presence and development stage



- 62% of programs report on-pathway PD signals (STAT6 degradation, pSTAT6, TARC, IgE) but 95% remain preclinical.
- 23 competitor programs sit in "clinic-ready but not advanced," years behind KT-621's human data.
- Only KT-621 has clinical validation in dermatology; the only other Phase I asset (exoASO-STAT6) is oncology-focused.
- 14 programs lack PD readouts entirely, facing both mechanism and execution risk before reaching the clinic.

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All 39 STAT6 programs assessed. PD readout based on disclosed STAT6 engagement biomarkers.