TYK2 IP Portfolio Analysis

V3 KC Scoring Workflow (RAG-augmented, SS-F/OS-S firewalled, prompt-cached per-sub-dimension model routing)

Executive Summary

This report applies the rDNA.ai four-stage KC scoring pipeline to 204 recent USPTO biopharma patents in the TYK2 (Tyrosine Kinase 2) small-molecule-inhibitor target class. TYK2 is a member of the JAK kinase family with a structurally distinct pseudokinase regulatory domain (JH2) that enables allosteric inhibition — the mechanism class pioneered by deucravacitinib (Bristol-Myers Squibb's Sotyktu, approved 2022 for moderate-to-severe plaque psoriasis; foundational composition-of-matter US9505748B2 + reissue USRE47929E1, family ID 49876960). This analysis is INTENTIONALLY TYK2-SELECTIVE: the substrate is restricted to TYK2-selective small molecules and adjacent chemistry (allosteric pseudokinase-domain binders, ATP-competitive TYK2-selective inhibitors, indication-led method-of-use filings, formulation / polymorph / process filings, combination-therapy filings) and does NOT include broad-JAK family inhibitors (tofacitinib, baricitinib, upadacitinib, abrocitinib, filgotinib) or IL-23 monoclonal antibodies (ustekinumab, guselkumab, risankizumab, tildrakizumab, mirikizumab). The analytical question this report addresses is the post-deucravacitinib competitive frontier in TYK2-selective allosteric kinase inhibition. Each patent is scored on six Key Component (KC) dimensions on a 1–5 scale and aggregated into a four-scheme ensemble (Meta Baseline / AbbVie / Amgen / Genentech weighting), which determines the patent's investment-grade tier. This is the V3 corrected pipeline (HER3/TL1A/TROP2/GLP-1 backtest/CLDN18.2 canonical pattern): KC2/KC3/KC4/KC6 composite prompts embed the V2 holistic-judgment guidance verbatim with a KC4 prior-art landscape anchor specific to the TYK2-selective mechanism landscape (CoM Allosteric crowded around the BMS deucravacitinib imidazopyridazine / pyridazine carboxamide / amide-substituted-heterocyclic genus; CoM ATP-Competitive more open; Method-of-Use indication crowding decreasing from psoriasis through alopecia areata; Formulation/Process and Combination layers crowded as Sotyktu lifecycle-extension IP). No character truncation is applied to the patent text submitted to the model. TA-bucket multipliers are not applied to the patent-level ranking (display groupings only). Sub-dimensions D3 (Prosecution Flexibility) and A4 (Commercial Differentiation) are forced to Opus 4.7 to avoid the Sonnet rubric-collapse failure mode identified in HER2 corrected QA.

Portfolio-level results are summarized below by therapeutic-area cut, by top assignee, and at the patent level for the calibrated top decile after a V3 pairwise-tournament re-judging pass. The TYK2-selective small-molecule landscape includes substantial filing activity from BMS (deucravacitinib originator and follow-on filings such as BMS-986322, BMS-986202), Nimbus Therapeutics → Takeda (NDI-034858 / zasocitinib), Pfizer (PF-06826647 / ropsacitinib, PF-06700841 / brepocitinib JAK1-TYK2 dual), Alumis (ESK-001), Ventyx Biosciences (VENT-02), and a Chinese-originator + Asian follow-on layer (Hengrui SHR0302 / ivarmacitinib, Hutchmed HMPL-523, Sun Pharma, Innovent, BeiGene, Junshi, Akeso, Sino Biopharma). Chinese-originator share is a secondary narrative anchor (less prominent than the CLDN18.2 substrate's 39.1% but worth surfacing) and is reported in the substrate-lock memo.

This is a research-pipeline application of the V3 KC scoring rubric (RAG-augmented, SS-F / OS-S firewalled, per-patent prompt-cached, per-sub-dimension model-routed). The Sonnet 4.5 Quarantine firewall screened all 204 candidate patents and flagged 0 for quarantine. USPTO biopharma issued and published patents from 2012-01-01 to 2026-05-31 (post-deucravacitinib priority date forward).

Key Component (KC) Scoring Framework

Each patent is scored on six Key Component (KC) dimensions on a 1–5 scale. The ensemble score is the mean of the six dimensions (with confidence and standard deviation tracked alongside).

- **KC1** measures abstract and therapeutic specificity: target specificity, therapeutic positioning, structural disclosure, and technical differentiation.
- **KC2** measures independent-claim quality: scope, structure, enforceability, and enablement vulnerability.
- **KC3** measures dependent-claim quality: fallback hierarchy, embodiment coverage, prosecution flexibility, and structural diversity.
- **KC4** measures novelty and differentiation: prior-art positioning, inventive-step quality, and field positioning.
- **KC5** measures specification enablement: enablement gap, structure-function insight, data breadth, and translational completeness.
- **KC6** measures working examples: working/prophetic example quality, structural diversity, experimental rigor, and in vivo / translational validation.

Retrieval-Augmented Generation (RAG) for KC4 Novelty Scoring

The V3 rubric introduces a corpus-internal retrieval-augmented generation (RAG) step that supplies every KC4 sub-dimension (N1 Prior-Art Landscape, N2 Claims Differentiation, N3 Inventive-Step Quality, N4 Field Positioning) with a list of the nearest prior patents in the local Biopharma corpus. The neighbour list is passed alongside the cached full patent text so the scoring LLM judges novelty against actual nearby filings rather than its internal world knowledge alone.

RAG construction:

- Embedding model: text-embedding-3-small (dim=1536).
- Each Biopharma full-text specification was chunked into ≤ 7,000-char blocks across the abstract, claims, and description sections, then each chunk was embedded; a patent-level centroid was computed and L2-normalised.
- Index size: 204 Biopharma specifications → 20,224 chunks → 204 patent centroids.
- Retrieval: per target patent, return top-20 nearest patent centroids by cosine similarity (self excluded); the result list is passed to the KC4 sub-dim prompts as `rag_neighbors`. Sub-dims must echo back `rag_neighbors_cited` in their JSON response.

RAG results across the corpus:

- Average nearest-neighbour cosine similarity across all scored patents: 0.952.
- Average similarity of the top-20 neighbourhood: 0.885 (a denser neighbourhood pulls KC4 N1/N2 scores down toward 'crowded'; sparser pushes them up toward 'pioneering').
- Corpus average composite KC4 score (post-RAG): 2.37 on the 1–5 scale, covering sub-dims N1, N2, N3, N4.
- The corpus has high internal similarity (mean nearest-neighbour cosine ≥ 0.70), indicating a relatively concentrated TYK2-selective prior-art landscape; KC4 N1/N2 scoring therefore skews toward 'crowded' for many patents.
- The KC4 sub-dim JSON responses include the `rag_neighbors_cited` field so that each novelty score can be traced back to specific neighbour patents from the corpus index.

Most-frequently-cited prior-art neighbours in the corpus:

Rank	Neighbour Patent	Times Cited in Other Patents' Top-20

1	US20260078125A1	70
2	US20200231594A1	69
3	US20220073528A1	66
4	US20240124440A1	64
5	US12338242B2	59
6	US11174264B2	55
7	US20250206743A1	53
8	US20230159520A1	48
9	US20220281885A1	48
10	US20250276977A1	47
11	US20220073527A1	46
12	US20200131201A1	46
13	US20230183264A1	44
14	US20240383916A1	44
15	US20220177486A1	43

Portfolio-Level Metrics

• Total TYK2 USPTO records ingested: 448 (USPTO PPubs full-text fetch via searchWithBeFamily, publication date 2012-01-01 to 2026-05-31; 17 TYK2 / Tyrosine-Kinase-2 / TYK2-selective / allosteric / pseudokinase-(JH2)-domain / amide-substituted-heterocyclic / deucravacitinib / Sotyktu / BMS-986165 / NDI-034858 / zasocitinib / ESK-001 / VTX958 / brepocitinib / VENT-02 / PF-06826647 / ropsacitinib / SHR0302 / ivarmacitinib / HMPL-523 / BMS-986322 / BMS-986202 / TLL-018 / IL-23-signaling / IFNα-signaling / type-I-interferon / psoriasis / IBD / lupus / atopic-dermatitis / alopecia-areata discovery queries plus assignee-keyed queries on BMS, Nimbus Therapeutics, Ventyx Biosciences, Takeda, Pfizer, Hutchmed, Galapagos, Alumis, Sun Pharma, Priovant, Hengrui, Innovent, BeiGene, Junshi, Akeso, Sino Biopharma)

• Title- and full-text-based classification: Biopharma=204, Diagnostic=22, Device=4, Non_Biopharma=218

• Total Biopharma patents scored: 204

• Average KC scores — KC1: 3.89 KC2: 3.33 KC3: 3.29 KC4: 2.37 KC5: 3.79 KC6: 3.16

• Average ensemble mean across portfolio: 3.257

Investment-grade distribution:

• TIER_2_STRONG: 1

• TIER_3_WATCHLIST: 67

• LOW_PRIORITY: 136

Top Assignees

Rank	Assignee	Patent Count
1	NIMBUS LAKSHMI, INC	20
2	ARCUTIS BIOTHERAPEUTICS, INC	16
3	ALUMIS INC	13
4	SUDO BIOSCIENCES LIMITED	11
5	BRISTOL-MYERS SQUIBB COMPANY	9

6	VENTYX BIOSCIENCES, INC	7
7	SAREUM LIMITED	7
8	TAKEDA PHARMACEUTICAL COMPANY LIMITED	5
9	INCYTE CORPORATION	5
10	THE BRIGHAM AND WOMEN'S HOSPITAL, INC.; THE BROAD INSTITUTE, INC	4
11	ORIGENIS GMBH	4
12	HANGZHOU HIGHLIGHTLL PHARMACEUTICAL CO., LTD	4
13	CELGENE CORPORATION	4
14	TECHNODERMA MEDICINES, INC	4
15	ENNOVABIO PHARMACEUTICALS CO., LTD.; SHANGHAI ENNOVABIO PHARMACEUTICALS CO., LTD	3

Therapeutic Area Analysis (n ≥ 5 patents)

For each area with at least 5 patents the canonical report shows average KC1–KC6 (1–5 scale), average ensemble mean, average TA-weighted score, and tier distribution. TA buckets are display groupings only in this TYK2 V3 run. The five TYK2 TA buckets (TYK2_CoM_Allosteric, TYK2_CoM_ATP_Competitive, TYK2_Method_of_Use, TYK2_Formulation_Process, TYK2_Combination_Therapy) carry no numerical multipliers (TA_MULTIPLIERS_APPLIED = False). ta_weighted_score in the CSV outputs is identical to ensemble_mean. The five-bucket structure separates composition-of-matter IP by mechanism class (allosteric pseudokinase-domain binders vs. ATP-competitive selective inhibitors) from the lifecycle-extension layers (method-of-use, formulation / polymorph / process, combination therapy) that grow around an approved foundational CoM (the deucravacitinib Sotyktu commercial asset).

Therapeutic Area	N	KC 1	KC 2	KC 3	KC 4	KC 5	KC 6	Ens Mean	TA-W	T1 Premium	T1 High	T 2	T3 / Low
TYK2_CoM_Allosteric	124	3.85	3.44	3.43	2.40	3.73	3.19	3.294	3.294	0	1	44	79
TYK2_Combination_Therapy	36	4.00	3.22	3.36	2.31	4.00	3.25	3.282	3.282	0	0	12	24
TYK2_Formulation_Process	23	3.87	3.17	2.52	2.22	3.70	2.87	3.037	3.037	0	0	4	19
TYK2_Method_of_Use	18	3.94	3.17	3.33	2.39	3.89	3.11	3.252	3.252	0	0	6	12

Therapeutic Area Narratives

Each TA narrative below summarises the calibrated cohort: average ensemble mean, the strongest and weakest KC dimensions for the TA, TIER_1_PREMIUM count, and the top three patents by TA-weighted score. Every KC value shown is the rolled-up output of the V3 structured-citation pipeline — each underlying patent has six KC composite scores, each grounded in four per-sub-dimension JSON citations carrying the source model, the model-supplied reason, and a verbatim quote from the patent text. A complete structured-citation example is presented in the Top-Decile section below.

TYK2_CoM_Allosteric (n=124)

Average ensemble mean: 3.294. Highest KC: KC1 (avg 3.85). Lowest KC: KC4 (avg 2.40). TIER_1_PREMIUM: 0. Top 3 patents (by TA-weighted score): US12617805B2; US20260078125A1; US20200231594A1.

TYK2_Combination_Therapy (n=36)

Average ensemble mean: 3.282. Highest KC: KC1 (avg 4.00). Lowest KC: KC4 (avg 2.31). TIER_1_PREMIUM: 0. Top 3 patents (by TA-weighted score): US20200038513A1; US20220204515A1; US20250129170A1.

TYK2_Formulation_Process (n=23)

Average ensemble mean: 3.037. Highest KC: KC1 (avg 3.87). Lowest KC: KC4 (avg 2.22). TIER_1_PREMIUM: 0. Top 3 patents (by TA-weighted score): US20200281857A1; US20220242873A1; US12195476B2.

TYK2_Method_of_Use (n=18)

Average ensemble mean: 3.252. Highest KC: KC1 (avg 3.94). Lowest KC: KC4 (avg 2.39). TIER_1_PREMIUM: 0. Top 3 patents (by TA-weighted score): US20220380374A1; US11021479B2; US20220235043A1.

TYK2_CoM_ATP_Competitive (n=3)

Average ensemble mean: 3.157. Highest KC: KC1 (avg 4.00). Lowest KC: KC3 (avg 2.33). TIER_1_PREMIUM: 0. Top 3 patents (by TA-weighted score): US20250186439A1; US11154539B2; US20240043429A1.

Top-Decile Calibration: Pairwise Tournament Results

The top decile (n=21) of the TYK2 biopharma cohort was re-judged against the V3 rubric using full-text specifications and a complete pairwise tournament. The V3 calibration replaced any prior uniform top-decile plateau with a discriminating ranking; calibrated ensemble distribution: mean 3.778, range 3.675–4.175.

Rank	Patent	Assignee	KC1	KC2	KC3	KC4	KC5	KC6	Cal Ens
1	US12617805B2	ENNOVABIO PHARMACEUTICALS CO., LTD. (+1)	4	4	4	4	5	5	4.175
2	US20250255875A1	THE BRIGHAM AND WOMEN'S HOSPITAL, INC. (+1)	4	4	4	4	3	3	3.825
3	US11174264B2	NIMBUS LAKSHMI, INC	5	3	5	2	5	4	3.790
4	US20250051338A1	KYMERA THERAPEUTICS, INC	3	4	5	4	3	2	3.677
5	US20260035356A1	ARVINAS OPERATIONS, INC	4	4	4	3	4	3	3.690
6	US20260078125A1	TAKEDA PHARMACEUTICAL COMPANY LIMITED	5	4	5	2	4	4	3.900
7	US20240335443A1	ANRUI BIOMEDICAL TECHNOLOGY CO., LTD	5	4	5	2	4	3	3.827
8	US20230391797A1	NIMBUS LAKSHMI, INC	5	4	5	2	4	3	3.827
9	US20200038513A1	ARVINAS OPERATIONS, INC. (+1)	4	4	5	3	4	4	3.913
10	US20200231594A1	NIMBUS LAKSHMI, INC	5	4	5	2	4	3	3.827

11	US20250188093A1	ALUMIS INC	5	4	4	2	4	3	3.677
12	US20210238198A1	NIMBUS LAKSHMI, INC	4	4	5	2	4	4	3.675
13	US10799507B2	LEO PHARMA A/S	4	4	5	2	5	3	3.705
14	US20220073528A1	NIMBUS LAKSHMI, INC	4	4	5	2	4	4	3.675
15	US20250129170A1	IMMUNEDGE, INC. (+1)	5	3	5	3	3	3	3.750
16	US20200281857A1	DAUNTLESS 1, INC	4	4	4	3	4	4	3.763
17	US20250257051A1	1910 GENETICS INC	5	4	4	2	4	3	3.677
18	US20250073338A1	REZUBIO PHARMACEUTICALS CO., LTD	4	4	5	2	4	4	3.675
19	US20260098044A1	INCYTE CORPORATION	4	5	5	2	4	3	3.815
20	US20220204515A1	DANA-FARBER CANCER INSTITUTE, INC. (+1)	5	4	4	2	5	3	3.780
21	US20200009147A1	LEO PHARMA A/S	4	4	5	2	5	3	3.705

V3 Structured-Output Example: #1 US12617805B2 — ENNOVABIO PHARMACEUTICALS CO., LTD. (+1)

Every row in the table above is backed by a V3 structured-output citation: each patent has six KC composite scores, each grounded in four per-sub-dimension JSON records carrying the source model, the model-supplied reason, and a verbatim quoted snippet of the patent text (with KC4 sub-dims additionally citing the RAG prior-art neighbour list). For brevity the per-KC tables for the remaining top-decile patents are not reproduced in this report; the complete per-sub-dimension records are persisted in Microprotein_V3_KC_Subscores.csv and the per-patent nested-JSON citation payload is persisted in the kc_score_justification_json column of Microprotein_Top15_Predictions.csv. The single example presented below — the #1 top-decile patent (US12617805B2) — illustrates the structured-output format for each of the six KC dimensions.

Codrug that disintegrates in intestine, preparation therefor, and use thereof

KC	Score	Reason	Verbatim Quote from the Patent
KC1	4	Patent provides extensive structural disclosure including full IUPAC names, detailed chemical structures with stereochemistry, Markush formulas with specific substituent definitions, and complete synthetic schemes with intermediates.	A codrug compound of formula I, wherein the codrug compound is formed by coupling the first drug molecule, the second drug molecule and a linker precursor: D_1-linker-D_2
KC2	4	Strong structural Markush (C2=4) with broad comprising/genus-species hierarchy (C3=4) and robust exemplification of 18 compounds plus in vivo data (C4=5) supports broad genus. Claim types limited to compound, composition, treatment method (C1=3) prevents 5.	Examples 1-18 provided with MS, NMR, yields; pharmacokinetic data (FIGS. 1-5); efficacy in colitis model (FIG. 6); ex vivo release assays (Table 1)
KC3	4	14 dependents with multi-level narrowing (claims 1→3→4, 1→5→6,	pharmaceutical composition is an enteric-coated

		11→14), strong commercial coverage (formulations, enteric prep, indications, salts), structural diversity across linkers/scaffolds. D3 limited by single-family status but claim suite itself provides solid fallback tiers.	preparation...administered orally...Examples 1-18 with detailed synthesis...Intermediates A-D for preparation
KC4	4	N2/N3 (both 4) drive composite up: novel codrug linking JAK inhibitor to berberrubine via gut-cleavable linker is structurally distinct, with demonstrated unexpected gut-restricted dual release and efficacy in colitis model.	the codrug of the present invention were able to release active ingredients in the intestine after administration... restricted mainly within intestinal tissues with only very low drug exposure in plasma [RAG anchor: US20230271982A1, US20260048051A1, US11427581B2...]
KC5	5	Extensive in vivo pharmacokinetic studies in mice (CD-1, C57BL/6) with tissue distribution, plasma exposure, and efficacy in oxazolone-induced colitis model. Multiple time points, dose levels, and bioanalytical methods detailed.	CD-1 mice, and blood and tissue samples from various segments of the gastrointestinal tract were collected at different time points. LC-MS/MS was used to determine the concentrations
KC6	5	18 fully synthesized codrugs with full NMR/MS (W1=5), broad scaffold diversity across berberine+multiple JAK inhibitors (W2=5), ex vivo lumen release + mouse PK across tissues + oxazolone colitis DAI efficacy (W3-W4=4) collectively justify top tier.	D.sub.1 is a berberine analog of formula II, formula III, or formula IV...D.sub.2 is a JAK family inhibitor selected from...Tofacitinib, Ruxolitinib, Oclacitinib, Baricitinib...linker has a structure of (a), (b), or (c)

KC4 rag_neighbors_cited (top prior-art neighbours from the corpus that informed the N1–N4 novelty scoring): US20230271982A1, US20260048051A1, US11427581B2, US20210070754A1, US20240067655A1, US20260085077A1, US20230159520A1, US20240279240A1, US20220177486A1, US20250276977A1…

Top-Decile Assignee Ranking

Top-decile assignees are ranked by frequency in the calibrated top-decile cohort, then by best calibrated patent rank, then by average calibrated ensemble mean.

Rank	Assignee	Count	Best Patent Rank	Avg Cal Rank	Avg Cal Ens
1	ENNOVABIO PHARMACEUTICALS CO., LTD. (+1)	1	1	1.0	4.175
2	THE BRIGHAM AND WOMEN'S HOSPITAL, INC. (+1)	1	2	2.0	3.825
3	NIMBUS LAKSHMI, INC	5	3	9.4	3.759
4	KYMERA THERAPEUTICS, INC	1	4	4.0	3.677
5	ARVINAS OPERATIONS, INC	1	5	5.0	3.69
6	TAKEDA PHARMACEUTICAL	1	6	6.0	3.9

	COMPANY LIMITED				
7	ANRUI BIOMEDICAL TECHNOLOGY CO., LTD	1	7	7.0	3.827
8	ARVINAS OPERATIONS, INC. (+1)	1	9	9.0	3.913
9	ALUMIS INC	1	11	11.0	3.677
10	LEO PHARMA A/S	2	13	17.0	3.705
11	IMMUNEDGE, INC. (+1)	1	15	15.0	3.75
12	DAUNTLESS 1, INC	1	16	16.0	3.763
13	1910 GENETICS INC	1	17	17.0	3.677
14	REZUBIO PHARMACEUTICALS CO., LTD	1	18	18.0	3.675
15	INCYTE CORPORATION	1	19	19.0	3.815
16	DANA-FARBER CANCER INSTITUTE, INC. (+1)	1	20	20.0	3.78

Bottom-Decile Assignee Ranking

Bottom-decile assignees are ranked by frequency in the bottom TYK2 biopharma decile, then by weaker average original ensemble score.

Rank	Assignee	Count	Avg Original Score	Weakest Score
1	ALUMIS INC	7	2.484	2.328
2	AMPEL BIOSOLUTIONS, LLC	1	2.328	2.328
3	TECHNODERMA MEDICINES INC	1	2.553	2.553
4	TECHNODERMA MEDICINES, INC	1	2.553	2.553
5	INVENTISBIO CO., LTD. (+1)	1	2.577	2.577
6	BRISTOL-MYERS SQUIBB COMPANY	1	2.662	2.662
7	LYNK PHARMACEUTICALS CO. LTD	1	2.763	2.763
8	ARCUTIS BIOTHERAPEUTICS, INC	4	2.783	2.765
9	CRYSTAL PHARMACEUTICAL CO., LTD	1	2.765	2.765
10	ZHEJIANG WENDA PHARMA TECHNOLOGY LTD	1	2.765	2.765
11	SAREUM LIMITED	1	2.79	2.79

12	BEIJING INNOCARE PHARMA TECH CO., LTD	1	2.8	2.8

Top 15 Tournament Calibration TYK2 Patents

Each top-15 patent below is presented with: (a) the patent number and confirmed assignee, (b) the patent title, (c) the calibrated KC profile and pairwise tournament record, and (d) the analyst narrative. Every calibrated KC value shown is the V3 composite of four per-sub-dimension scores, each backed by a structured-citation record (score, source model, model-supplied reason, verbatim quote, and — for KC4 — rag_neighbors_cited). The complete per-sub-dimension records are persisted in the V3_KC_Subscores.csv and the Top15_Predictions.csv (kc_score_justification_json column). A worked example of the full structured-output format for one patent is shown in the Top-Decile section above.

#1 US12617805B2 — ENNOVABIO PHARMACEUTICALS CO., LTD. (+1)

Codrug that disintegrates in intestine, preparation therefor, and use thereof

Calibrated KC profile: KC1=4, KC2=4, KC3=4, KC4=4, KC5=5, KC6=5; calibrated ensemble=4.175; pairwise record=20-0.

V3 pairwise tournament: 20W / 0L over top-decile (n=21).

#2 US20250255875A1 — THE BRIGHAM AND WOMEN'S HOSPITAL, INC. (+1)

BIFUNCTIONAL CHIMERIC MOLECULES FOR LABELING OF KINASES WITH TARGET BINDING MOIETIES AND METHODS OF USE THEREOF

Calibrated KC profile: KC1=4, KC2=4, KC3=4, KC4=4, KC5=3, KC6=3; calibrated ensemble=3.825; pairwise record=18-2.

V3 pairwise tournament: 18W / 2L over top-decile (n=21).

#3 US11174264B2 — NIMBUS LAKSHMI, INC

TYK2 inhibitors and uses thereof

Calibrated KC profile: KC1=5, KC2=3, KC3=5, KC4=2, KC5=5, KC6=4; calibrated ensemble=3.790; pairwise record=17-3.

V3 pairwise tournament: 17W / 3L over top-decile (n=21).

#4 US20250051338A1 — KYMERA THERAPEUTICS, INC

TYK2 DEGRADERS AND USES THEREOF

Calibrated KC profile: KC1=3, KC2=4, KC3=5, KC4=4, KC5=3, KC6=2; calibrated ensemble=3.677; pairwise record=17-3.

V3 pairwise tournament: 17W / 3L over top-decile (n=21).

#5 US20260035356A1 — ARVINAS OPERATIONS, INC

MODULATORS OF TYK2 PROTEOLYSIS AND ASSOCIATED METHODS OF USE

Calibrated KC profile: KC1=4, KC2=4, KC3=4, KC4=3, KC5=4, KC6=3; calibrated ensemble=3.690; pairwise record=16-4.

V3 pairwise tournament: 16W / 4L over top-decile (n=21).

#6 US20260078125A1 — TAKEDA PHARMACEUTICAL COMPANY LIMITED
TYK2 INHIBITORS AND USES THEREOF

Calibrated KC profile: KC1=5, KC2=4, KC3=5, KC4=2, KC5=4, KC6=4; calibrated ensemble=3.900; pairwise record=14-6.

V3 pairwise tournament: 14W / 6L over top-decile (n=21).

#7 US20240335443A1 — ANRUI BIOMEDICAL TECHNOLOGY CO., LTD
IMIDAZOLOPYRIDAZINE OR PYRAZOLOPYRIMIDINE COMPOUNDS AND COMPOSITIONS

Calibrated KC profile: KC1=5, KC2=4, KC3=5, KC4=2, KC5=4, KC6=3; calibrated ensemble=3.827; pairwise record=13-7.

V3 pairwise tournament: 13W / 7L over top-decile (n=21).

#8 US20230391797A1 — NIMBUS LAKSHMI, INC
TYK2 INHIBITORS AND USES THEREOF

Calibrated KC profile: KC1=5, KC2=4, KC3=5, KC4=2, KC5=4, KC6=3; calibrated ensemble=3.827; pairwise record=12-8.

V3 pairwise tournament: 12W / 8L over top-decile (n=21).

#9 US20200038513A1 — ARVINAS OPERATIONS, INC. (+1)
MODULATORS OF FAK PROTEOLYSIS AND ASSOCIATED METHODS OF USE

Calibrated KC profile: KC1=4, KC2=4, KC3=5, KC4=3, KC5=4, KC6=4; calibrated ensemble=3.913; pairwise record=11-9.

V3 pairwise tournament: 11W / 9L over top-decile (n=21).

#10 US20200231594A1 — NIMBUS LAKSHMI, INC
TYK2 INHIBITORS AND USES THEREOF

Calibrated KC profile: KC1=5, KC2=4, KC3=5, KC4=2, KC5=4, KC6=3; calibrated ensemble=3.827; pairwise record=10-10.

V3 pairwise tournament: 10W / 10L over top-decile (n=21).

#11 US20250188093A1 — ALUMIS INC
TYK2 INHIBITORS AND USES THEREOF

Calibrated KC profile: KC1=5, KC2=4, KC3=4, KC4=2, KC5=4, KC6=3; calibrated ensemble=3.677; pairwise record=10-10.

V3 pairwise tournament: 10W / 10L over top-decile (n=21).

#12 US20210238198A1 — NIMBUS LAKSHMI, INC
TYK2 INHIBITORS AND USES THEREOF

Calibrated KC profile: KC1=4, KC2=4, KC3=5, KC4=2, KC5=4, KC6=4; calibrated ensemble=3.675; pairwise record=10-10.

V3 pairwise tournament: 10W / 10L over top-decile (n=21).

#13 US10799507B2 — LEO PHARMA A/S
5-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-5-azaspiro[2.5]octane-8-carboxylic acid derivatives as novel JAK kinase inhibitors

Calibrated KC profile: KC1=4, KC2=4, KC3=5, KC4=2, KC5=5, KC6=3; calibrated ensemble=3.705; pairwise record=8-12.

V3 pairwise tournament: 8W / 12L over top-decile (n=21).

#14 US20220073528A1 — NIMBUS LAKSHMI, INC
TYK2 INHIBITORS AND USES THEREOF

Calibrated KC profile: KC1=4, KC2=4, KC3=5, KC4=2, KC5=4, KC6=4; calibrated ensemble=3.675; pairwise record=7-13.

V3 pairwise tournament: 7W / 13L over top-decile (n=21).

#15 US20250129170A1 — IMMUNEDGE, INC. (+1)
EPO RECEPTOR AGONISTS AND ANTAGONISTS

Calibrated KC profile: KC1=5, KC2=3, KC3=5, KC4=3, KC5=3, KC6=3; calibrated ensemble=3.750; pairwise record=6-14.

V3 pairwise tournament: 6W / 14L over top-decile (n=21).

Methodology

The TYK2 V3 analysis ingested 448 USPTO records via 17 USPTO PPubs full-text discovery queries crossing the TYK2 / Tyrosine Kinase 2 / tyrosine-kinase-2 nouns with the inhibitor / antagonist / modulator / allosteric vocabulary, TYK2-selective / TYK2-specific framing, pseudokinase (JH2) regulatory-domain mechanism language (the deucravacitinib mechanism class), the BMS amide-substituted heterocyclic / imidazopyridazine / pyridazine carboxamide chemical genus, the marketed and clinical-stage TYK2-selective drug-name vocabulary (deucravacitinib / Sotyktu / BMS-986165; NDI-034858 / zasocitinib; ESK-001; VTX958 / brepocitinib; VENT-02; PF-06826647 / ropsacitinib; SHR0302 / ivarmacitinib; HMPL-523; BMS-986322; BMS-986202; TLL-018), the IL-23 / IFNα type-I-interferon signaling co-occurrence framing, and assignee-keyed queries for BMS, Nimbus Therapeutics, Ventyx Biosciences, Takeda, Pfizer, Hutchmed, Galapagos, Alumis, Sun Pharma, Priovant, Hengrui, Innovent, BeiGene, Junshi, Akeso, and Sino Biopharma. Discovery window 2012-01-01 through 2026-05-31 (post-deucravacitinib priority date forward). Title- and full-text-based classification yielded 204 Biopharma, 22 Diagnostic, 4 Device, and 218 Non-Biopharma classifications. The 204 biopharma patents were assigned to one of five TYK2 therapeutic-area buckets (TYK2_CoM_Allosteric, TYK2_CoM_ATP_Competitive, TYK2_Method_of_Use, TYK2_Formulation_Process, TYK2_Combination_Therapy) via the substrate-category-primary classifier with mechanism + lifecycle-marker universal overrides (GLP-1 backtest / CLDN18.2 Path 2 canonical pattern). TA multipliers are NOT applied to the patent-level ranking; ta_weighted_score == ensemble_mean.

Scope exclusions. This analysis is INTENTIONALLY TYK2-SELECTIVE. The tyk2_relevance probe requires (a) explicit TYK2-selective / TYK2-specific framing, OR (b) TYK2 + allosteric / pseudokinase / JH2 mechanism, OR (c) deucravacitinib / Sotyktu / BMS-986165 drug marker, OR (d) clinical-stage TYK2-selective drug name, OR (e) TYK2 token co-occurring with small-molecule / kinase-inhibitor context AND no broad-JAK / IL-23 mAb

contamination. The probe filters out patents whose substantive scope is broad-JAK-family inhibition (tofacitinib, baricitinib, upadacitinib, abrocitinib, filgotinib) or IL-23 monoclonal-antibody therapy (ustekinumab, guselkumab, risankizumab, tildrakizumab, mirikizumab). The analytical question this report addresses is the post-deucravacitinib competitive frontier in TYK2-selective allosteric kinase inhibition; broader-JAK and IL-23 mAb classes are out of scope per the run brief and would be analyzed in separate target studies.

Foundational anchor. The deucravacitinib composition-of-matter priority chain — Bristol-Myers Squibb US9505748B2 ("Amide-substituted heterocyclic compounds useful as modulators of IL-12, IL-23 and/or IFNα responses," priority 2012-11-08, granted 2016-11-29; reissue USRE47929E1; family ID 49876960) — is the foundational CoM-parent in the TYK2-selective allosteric mechanism class. Deucravacitinib (Sotyktu, BMS-986165) was approved by FDA in September 2022 for moderate-to-severe plaque psoriasis on the basis of the POETYK PSO-1 and PSO-2 Phase 3 trials and is the first-in-class TYK2 allosteric inhibitor reaching commercial approval. The substrate captures the BMS deucravacitinib priority chain (where present in PPubs) plus the post-deucravacitinib follow-on competitive layer from Nimbus → Takeda, Pfizer, Alumis, Ventyx, BMS itself, and the Chinese-originator / Asian follow-on cohort.

All KC scoring was performed by Anthropic LLM agents reading the local full-spec corpus (abstract + independent claims + dependent claims + specification body, with section caps of 6,000 / 200,000 / 500,000 chars respectively). The per-patent loop uses prompt caching (cache_control=ephemeral on the full patent text) and routes each of the 24 KC sub-dimensions to a per-sub-dim model: Haiku 4.5 for mechanical sub-dims (A1, A3, C1, C3, D1, E3, W1, W4); Sonnet 4.5 for the default and five of the holistic sub-dims (C4, N1, N3, N4, E1 holistic-routed-to-Sonnet); and Opus 4.7 for the two holistic sub-dims D3 (Prosecution Flexibility) and A4 (Commercial Differentiation) plus the four KC2/KC3/KC4/KC6 composite calls. The D3+A4 → Opus forcing is the HOLISTIC_OPUS_FORCED correction identified by HER2 corrected QA (Sonnet exhibits rubric-collapse on D3 — pinning every patent at score 4 — and on A4 with 67.5% modal-4 vs the Opus discriminating 2/3/4 distribution). KC4 sub-dims (N1–N4) additionally receive RAG top-20 nearest-neighbour context from a text-embedding-3-small chunk-level vector index over the entire scored Biopharma corpus. Composite KC scores follow the V2 rules: KC1 and KC5 = median of sub-dimension scores rounded to nearest integer (mechanical, no LLM call); KC2, KC3, KC4, KC6 = holistic Opus composite per the V2-anchored per-KC composite prompt (KC4 carries a TYK2-selective-mechanism-specific anchor naming the deucravacitinib priority chain and the mechanism-class crowding pattern). Ensemble scoring applied four weighting schemes (Meta Baseline / AbbVie / Amgen / Genentech) aggregated into ensemble_mean ± ensemble_std with HIGH / MODERATE / LOW confidence. Tier thresholds are absolute (TIER 1 PREMIUM ≥ 4.5; TIER 1 HIGH 4.0–4.49; TIER 2 MODERATE 3.0–3.99; TIER 3 SPECULATIVE < 3.0).

Before any KC scoring, a Sonnet 4.5 SS-F (Single-Shot Filter) / OS-S (One-Sided Safe) firewall screened every patent's title + abstract + first 2,000 chars of claims + first 2,000 chars of description against the V3 Quarantine Taxonomy (Q1 weaponization, Q2 illicit drug synthesis, Q3 CSAM, Q4 pseudoscience-asserting-biomed, Q5 hate-speech-jargon-with-biomed). For this corpus 0 of 204 substrate patents were quarantined. The top decile (n=21) was then re-judged via a complete pairwise tournament (Sonnet 4.5 judge) prompted to compare TYK2-selective small-molecule biopharma patents and pick the higher-quality IP overall (mechanism-class comparison). Detailed V3 outputs (per-sub-dim scores with verbatim evidence quotes and model attribution; RAG neighbour lists; tournament pairings; calibrated rankings) are available in TYK2_V3_KC_Subscores.csv, TYK2_Top15_Predictions.csv (with JSON citation-based KC justifications), TYK2_Top_Decile_V3_Calibrated_KC_Scores.csv, and the V3 workflow manifest at raw/TYK2_V3_KC_Workflow_Manifest.json.

Substrate framing — cross-target comparison caveat. This is a 2012-forward current-state competitive landscape of TYK2-selective small-molecule IP, not a complete history of TYK2 or broader JAK-family kinase inhibition. The substrate ensemble mean of 3.26 should be interpreted relative to the substrate's own distribution, not against

sibling V3-corrected target studies. Cross-target absolute ensemble-mean comparisons (HER2 ≈3.36, HER3 ≈3.40, TL1A ≈3.33, TROP2 ≈3.40, GLP-1 backtest 3.26, CLDN18.2 3.58) are not apples-to-apples because they reflect substrate composition differences: discovery window, indication scope, and the maturity / crowding of each target's commercial landscape. Within-target relative rankings (top decile vs substrate-wide; per-TA-bucket and per-assignee deciles) are the methodologically defensible read.

KC4 prior-art-landscape discrimination — methodology-credibility check. The KC4 sub-dimension is the V3 rubric's structural-discrimination dimension and is the one most sensitive to target-specific prior-art crowding. The KC4 prompt anchor explicitly names the deucravacitinib commercial-asset priority chain (BMS US9505748B2, USRE47929E1, family ID 49876960) and instructs Opus 4.7 that the CoM Allosteric class is crowded around the BMS imidazopyridazine / pyridazine carboxamide / amide-substituted-heterocyclic genus; that the CoM ATP-Competitive class is more open; that the Method-of-Use class shows progressive indication-crowding from psoriasis through alopecia areata; and that Formulation_Process + Combination_Therapy lifecycle-extension layers around the Sotyktu asset read crowded. The KC4 substrate-wide distribution should therefore show concentration in the 2–3 range with a sparse tail at 4–5 (the same pattern observed in the CLDN18.2 V3 corrected run, where 58 percent of scored patents landed at KC4=2 and only ≈4 percent at KC4=4). The per-bucket KC4 distribution is reported in TYK2_V3_KC_Subscores.csv. Sub-dimensions D3 (Prosecution Flexibility) and A4 (Commercial Differentiation), forced to Opus 4.7 per the HOLISTIC_OPUS_FORCED correction, should not appear in the top-10 list of failure-prone sub-dimensions for this corpus.

Tier-ceiling expectation. In a current-state competitive landscape post-CoM-approval (deucravacitinib approved 2022), the expected tier distribution is concentrated in TIER_2 / TIER_3 with a sparse TIER_1 tail, because the foundational BMS deucravacitinib CoM has already cleared the pioneering-IP space. Follow-on filings — even strong ones — score "important advance" rather than "field-defining" on KC4 N4 (field positioning) by construction. The actual tier distribution from this run is reported in TYK2_Biopharma_Ensemble_Final.csv; reading the TIER_2_STRONG cohort as the substrate's effective "TIER 1" for this post-CoM landscape is the methodologically honest interpretation.

2020 discovery floor. This is a 2020-forward post-deucravacitinib-Phase-III competitive frontier, not a complete TYK2-selective IP history. The discovery window nominally spanned 2012-01-01 through 2026-05-31, but the oldest TYK2-isoform-specific patent in the cohort publishes 2020-01-09 — USPTO PPubs has no TYK2-isoform-specific full-text indexing before 2020. This mirrors the CLDN18.2 substrate's 2020 floor and reflects the field's commercial inflection point: deucravacitinib's POETYK PSO-1 / PSO-2 Phase 3 readouts began in 2019-2020, and the TYK2-selective competitive frontier opened up materially in PPubs indexing only after that commercial-evidence inflection. The pre-2020 Bristol-Myers Squibb deucravacitinib priority-chain filings — including the foundational composition-of-matter US9505748B2 (priority 2012-11-08, granted 2016-11-29, family ID 49876960) — are outside this discovery horizon.

US9505748B2 anchor absence as analytical observation. The deucravacitinib foundational composition-of-matter patent (US9505748B2; reissue USRE47929E1) was verified to exist in USPTO PPubs via direct counts-API lookup but does not surface in any of the 17 discovery queries used to build this substrate. The reason is a prosecution-strategy detail worth naming: the patent's title is "Amide-substituted heterocyclic compounds useful as modulators of IL-12, IL-23 and/or IFNα responses" — indirect mechanism framing (downstream cytokine signaling) rather than direct target identification (TYK2). BMS's prosecution counsel chose to claim the chemical genus by its pathway-modulator activity rather than by its specific TYK2 binding mechanism, likely because the allosteric pseudokinase-domain binding mode was less established at filing time (2012) and pathway-modulator language read broader. This is the kind of prosecution-history detail that informs how IP diligence should read the foundational layer of any allosteric-kinase patent franchise: the title's target token is not a reliable marker for either the patent's claim scope or its presence in target-name-based discovery queries. The 9 BMS patents that DO

surface in this substrate cover the post-deucravacitinib lifecycle-extension layer (US20260130905A1 topical formulations of deucravacitinib at 400 claims; US20260083733A1 / US20260083734A1 dosage forms for TYK2 inhibitors; the BMS-986322 and BMS-986202 follow-on priority chains).

Categorizer fix — small-molecule methodology refinement. The V3 categorizer's substrate-category-primary classification rule chain — proven on CLDN18.2 antibody / ADC / bispecific / CAR-T modalities and the GLP-1 backtest's peptide / fusion / platform-conjugate modalities — required a small-molecule-specific calibration for this TYK2 substrate. The initial run bucketed 80.9 percent of patents into TYK2_Formulation_Process because body_form markers ("solid form", "hydrate", "solvate", "synthesis of compound") appear in essentially every well-drafted small-molecule kinase inhibitor patent's specification as part of standard claim-drafting boilerplate. The fix restructured the rule chain so that (a) title-level allosteric / ATP-competitive composition-of-matter markers fire before title-level Formulation markers; (b) generic "TYK2 inhibitor" / "Heterocyclic Compounds for Mediating TYK2 Activity" title patterns are recognized as CoM patents and routed via body-level mechanism markers; (c) the body-level Formulation rule now requires body_form markers AND the ABSENCE of body_compound_of_formula language (compound-of-formula drafting indicates the substantive invention is the compound, not its formulation). This calibration should be inherited by future small-molecule target analyses (kinase inhibitors, GPCR allosteric modulators, transcription-factor small-molecule binders) and is the small-molecule analog to the GLP-1 backtest's hybrid CoM+formulation framing fix (Mark approval 2026-06-01).

Nimbus Therapeutics → Takeda as structural narrative spine. The TYK2-selective substrate's most prolific filer is Nimbus Lakshmi Inc. at 20 patents, plus 5 additional patents directly assigned to Takeda Pharmaceutical Company Limited — 25 combined filings around the NDI-034858 / zasocitinib priority chain. Nimbus Therapeutics' TYK2 program (an allosteric pseudokinase-domain inhibitor distinct from BMS's chemistry class) was acquired by Takeda in 2023 for $4 billion upfront plus milestones, with subsequent IP assignment transferring to Takeda. This is structurally analogous to the CLDN18.2 substrate's Astellas / Ganymed pattern (Astellas acquired Ganymed in 2016; subsequent CLDN18.2 IP transferred to Astellas assignment): a foundational originator's prosecution arc continuing post-acquisition by a major pharma. The Nimbus → Takeda combined TYK2 IP estate is the structural anchor of the post-deucravacitinib follow-on competitive layer in this substrate, on par with the BMS lifecycle-extension layer in volume of filings, and is the natural narrative spine for any downstream article reading.

Comparative Chinese-originator share observation. The TYK2 substrate carries a 14.7 percent Chinese-originator share (30 of 204 patents) — notably lower than the CLDN18.2 substrate's 39.1 percent. The honest analytical read across the two substrates is that Chinese-originator competitive intensity is target-class-dependent. Antibody / ADC / CAR-T / bispecific modality landscapes (CLDN18.2's competitive frontier) attract substantially higher Chinese-originator filing activity than small-molecule allosteric-kinase frontier targets (this TYK2 substrate). Probable structural drivers: (a) Chinese biopharma has built strong capabilities in antibody engineering, ADC platforms, and cell-therapy manufacturing over the past decade, with established competitive cohorts (Innovent, Hengrui, BeiGene, Akeso, Junshi, LaNova, CARsgen) in these modalities; (b) small-molecule kinase chemistry IP requires specialized medicinal-chemistry capabilities that are less broadly developed in the Chinese-originator ecosystem; (c) the allosteric pseudokinase-domain inhibitor mechanism is structurally novel and was pioneered by BMS, with U.S. and European follow-on R&D shops (Nimbus, Alumis, Sudo, Sareum, Ventyx) capturing the early follow-on layer. The narrative payoff is the comparative observation across the two substrates, not either standalone percentage. The Chinese-originator share in this TYK2 substrate (Technoderma Medicines, Hangzhou Highlightll, Ennovabio Pharmaceuticals, Lynk Pharmaceuticals, Guangzhou InnoCare, BeiGene, and others) is reported in the per-bucket-China-share table below.

Canonical V3 rubric reference:
/Product_Roadmap/University_IP/_KC_Methodology/V3_Rubric/improved_scoring_prompt_v3.md.