Epigenome IP Portfolio Analysis

Executive Summary

This report applies the rDNA.ai four-stage KC scoring pipeline to 788 recent USPTO biopharma patents in the epigenome-editing target class, including 587 patents directly classified into the Epigenome_Editing_Therapeutic therapeutic area. 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.

Portfolio-level results are summarized below by therapeutic-area cut, by top assignee, and at the patent level for the top decile after a V2 pairwise-tournament calibration. The Epigenome_Editing_Therapeutic cut is the strongest in the corpus (mean ensemble 4.738; 429 of 587 patents at TIER 1 PREMIUM), reflecting the concentrated platform IP held by Harvard / Broad / MIT (Liu, Zhang, Sabeti, Doench, Regev labs), Beam Therapeutics, Whitehead Institute, Tune Therapeutics, Arbor Biotechnologies, Scribe Therapeutics, Vor Biopharma, the UC – Vienna – Charpentier consortium, and Flagship Pioneering.

This is one of an expanding set of target-class KC Quality Analyses generated from a four-stage KC scoring pipeline applied to all USPTO biopharma issued and published patents assigned to each of the 25 most active global biopharma companies from January 2020 through April 2026. A parallel Top-25 Consolidated cross-portfolio analysis covering all 14,552 company patents in the biopharma cohort is available upon request.

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.

Portfolio-Level Metrics

• Total Epigenome USPTO records ingested: 1,138 from USPTO_Epigenome_Editing_IP.pdf (USPTO patent publication search carried out in May 2026)

• Title-based classification: Biopharma=788, Diagnostic=339, Device=0, Non_Biopharma=11

• Total Biopharma patents scored: 788

• Average KC scores — KC1: 5.00 KC2: 4.53 KC3: 4.29 KC4: 4.75 KC5: 4.36 KC6: 4.91

• Average ensemble mean across portfolio: 4.662

Investment-grade distribution:

• TIER_1_PREMIUM: 493

• TIER_2_STRONG: 242

• TIER_3_WATCHLIST: 51

• LOW_PRIORITY: 2

Top Assignees

Rank	Assignee	Patent Count
1	THE BROAD INSTITUTE, INC.; MASSACHUSETTS INSTITUTE OF TECHNOLOGY	58
2	PRESIDENT AND FELLOWS OF HARVARD COLLEGE	36
3	SINGULAR GENOMICS SYSTEMS, INC	30
4	DUKE UNIVERSITY	28
5	BEAM THERAPEUTICS INC	27
6	ARBOR BIOTECHNOLOGIES, INC	24
7	THE REGENTS OF THE UNIVERSITY OF CALIFORNIA	22
8	THE BROAD INSTITUTE, INC.; MASSACHUSETTS INSTITUTE OF TECHNOLOGY; PRESIDENT AND FELLOWS OF HARVARD COLLEGE	22
9	THE BROAD INSTITUTE, INC.; PRESIDENT AND FELLOWS OF HARVARD COLLEGE	21
10	TUNE THERAPEUTICS, INC	19
11	TEMPUS AI, INC	17

12	THE BROAD INSTITUTE, INC.; PRESIDENT AND FELLOWS OF HARVARD COLLEGE; MASSACHUSETTS INSTITUTE OF TECHNOLOGY	15
13	THE GENERAL HOSPITAL CORPORATION	15
14	THE REGENTS OF THE UNIVERSITY OF CALIFORNIA; UNIVERSITY OF VIENNA; CHARPENTIER; EMMANUELLE	13
15	WHITEHEAD INSTITUTE FOR BIOMEDICAL RESEARCH	13

Therapeutic Area Analysis

All 3 therapeutic-area buckets in the Epigenome biopharma cohort receive their own KC breakdown. For each area: average KC1-KC6 (1–5 scale), average ensemble mean, average TA-weighted score, and tier distribution. Epigenome_Editing_Therapeutic carries TA multiplier 1.08; CRISPR_Gene_Regulation 1.05; Gene_Cell_Therapy 1.03.

Therapeutic Area	N	KC1	KC2	KC3	KC4	KC5	KC6	Ens Mean	TA-W	T1 Prem	T2 Strong	T3 Watch	Low
Epigenome_Editing_Therapeutic	587	5.00	4.53	4.35	4.98	4.45	4.95	4.738	5.117	429	133	25	0
CRISPR_Gene_Regulation	159	5.00	4.61	4.22	4.14	4.12	4.85	4.496	4.721	61	80	17	1
Gene_Cell_Therapy	42	4.95	4.26	3.67	3.88	4.05	4.57	4.238	4.365	3	29	9	1

Therapeutic Area Narratives

Epigenome_Editing_Therapeutic (n=587)

Average ensemble mean: 4.738. Highest KC: KC1 (avg 5.00). Lowest KC: KC3 (avg 4.35). TIER_1_PREMIUM: 429, TIER_2_STRONG: 133. Top 3 patents (by TA-weighted score): US11268082B2; US11306324B2; US11312955B2.

CRISPR_Gene_Regulation (n=159)

Average ensemble mean: 4.496. Highest KC: KC1 (avg 5.00). Lowest KC: KC5 (avg 4.12). TIER_1_PREMIUM: 61, TIER_2_STRONG: 80. Top 3 patents (by TA-weighted score): US20220257796A1; US20230158088A1; US20230235324A1.

Gene_Cell_Therapy (n=42)

Average ensemble mean: 4.238. Highest KC: KC1 (avg 4.95). Lowest KC: KC3 (avg 3.67). TIER_1_PREMIUM: 3, TIER_2_STRONG: 29. Top 3 patents (by TA-weighted score): US11705226B2; US20230135171A1; US20230223121A1.

Top-Decile Calibration: Pairwise Tournament Results

The top decile (n=79) of the Epigenome biopharma cohort was re-judged against the V2 rubric using full-text specifications and a complete 3,081-pair pairwise tournament. The V2 calibration replaced the prior uniform top-decile plateau (every patent KC=5, ta_weighted=5.4) with a discriminating ranking; calibrated ensemble distribution: mean 4.023, range 3.527–4.463.

Rank	Patent	Assignee	KC1	KC2	KC3	KC4	KC5	KC6	Cal Ens
1	US11732274B2	PRESIDENT AND FELLOWS OF HARVARD COLLEGE (+1)	5	4	4	5	4	4	4.463
2	US12264323B2	THE BROAD INSTITUTE, INC	5	4	4	4	5	5	4.400
3	US20220142948A1	THE BROAD INSTITUTE, INC. (+3)	5	4	4	4	5	5	4.400
4	US20230159949A1	THE BROAD INSTITUTE, INC. (+2)	5	4	4	4	5	5	4.400
5	US12595478B2	THE BROAD INSTITUTE, INC. (+2)	5	4	4	4	5	4	4.328
6	US20220403357A1	THE BROAD INSTITUTE, INC. (+1)	5	4	4	4	5	4	4.328
7	US20220228173A1	THE BROAD INSTITUTE, INC. (+2)	5	4	3	4	5	5	4.250

8	US11268082B2	PRESIDENT AND FELLOWS OF HARVARD COLLEGE	5	4	4	4	4	4	4.225
9	US11306324B2	PRESIDENT AND FELLOWS OF HARVARD COLLEGE	5	4	4	4	4	4	4.225
10	US11702651B2	PRESIDENT AND FELLOWS OF HARVARD COLLEGE	5	4	4	4	4	4	4.225
11	US12252715B2	WHITEHEAD INSTITUTE FOR BIOMEDICAL RE...	5	4	4	4	4	4	4.225
12	US20220325296A1	THE BROAD INSTITUTE, INC. (+2)	5	4	4	4	4	4	4.225
13	US20220340929A1	THE BROAD INSTITUTE, INC. (+2)	5	4	4	4	4	4	4.225
14	US20230025039A1	THE BROAD INSTITUTE, INC. (+1)	5	4	4	4	4	4	4.225
15	US20230037794A1	THE BROAD INSTITUTE, INC. (+1)	5	4	4	4	4	4	4.225

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	PRESIDENT AND FELLOWS OF HARVARD COLLEGE	17	8	42.29	4.014
2	THE BROAD INSTITUTE, INC. (+1)	9	6	32.56	4.094
3	THE BROAD INSTITUTE, INC. (+1)	8	17	40.62	3.995
4	THE BROAD INSTITUTE, INC. (+2)	6	4	32.5	4.104
5	BEAM THERAPEUTICS INC	6	21	28.33	4.126

6	FLAGSHIP PIONEERING INNOVATIONS V, INC	5	26	45.2	3.985
7	THE BROAD INSTITUTE, INC	2	2	28.0	4.187
8	THE REGENTS OF THE UNIVERSITY OF CALIFORNIA (+3)	2	27	28.5	4.075
9	VOR BIOPHARMA INC	2	34	53.5	3.881
10	BEAM THERAPEUTICS INC. (+1)	2	42	58.0	3.881
11	SCRIBE THERAPEUTICS INC	2	51	51.5	3.987
12	DUKE UNIVERSITY	2	64	68.0	3.77
13	ARBOR BIOTECHNOLOGIES, INC	2	78	78.5	3.527
14	PRESIDENT AND FELLOWS OF HARVARD COLLEGE (+1)	1	1	1.0	4.463
15	THE BROAD INSTITUTE, INC. (+3)	1	3	3.0	4.4

Bottom-Decile Assignee Ranking

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

Rank	Assignee	Count	Avg Original Score	Weakest Score
1	TEMPUS AI, INC	10	4.194	3.915
2	DUKE UNIVERSITY	4	3.902	3.77
3	THE GENERAL HOSPITAL CORPORATION	4	3.91	3.77
4	REGENTS OF THE UNIVERSITY OF MICHIGAN	4	4.008	3.745

5	THE REGENTS OF THE UNIVERSITY OF CALIFORNIA	4	4.038	3.873
6	THE BROAD INSTITUTE, INC. (+1)	3	4.125	4.125
7	THE JOHNS HOPKINS UNIVERSITY	2	3.847	3.672
8	NORTHWESTERN UNIVERSITY	2	3.864	3.532
9	REVERSE BIOENGINEERING, INC	2	3.966	3.785
10	10X GENOMICS, INC	2	3.994	3.888
11	BRAIN BIOTECH AG	2	4.185	4.185
12	TETS (+2)	1	3.15	3.15
13	BIONTECH SE (+1)	1	3.223	3.223
14	INSTITUT PASTEUR (+1)	1	3.46	3.46
15	SOCIETE DES PRODUITS NESTLE S.A	1	3.498	3.498

Top 15 Tournament Calibration Epigenome Patents

#1 US11732274B2 — PRESIDENT AND FELLOWS OF HARVARD COLLEGE (+1)

Methods and compositions for evolving base editors using phage-assisted continuous evolution (PACE)

Calibrated KC profile: KC1=5, KC2=4, KC3=4, KC4=5, KC5=4, KC6=4; calibrated ensemble=4.463; pairwise record=78-0.

Liu lab Harvard/Broad PACE-evolved base-editor patent is the cleanest top-decile winner: pioneer base-editing platform IP, exhaustive specification across SpCas9, Cas12, and adenine/cytosine deaminase variants, a deep dependent-claim hierarchy covering directed-evolution selection circuits, and a perfect 78-0 pairwise record.

#2 US12264323B2 — THE BROAD INSTITUTE, INC

CRISPR CPF1 direct repeat variants

Calibrated KC profile: KC1=5, KC2=4, KC3=4, KC4=4, KC5=5, KC6=5; calibrated ensemble=4.400; pairwise record=77-1.

Broad Institute CRISPR-Cpf1 (Cas12a) direct-repeat variant patent is foundational platform IP for engineered crRNA scaffolds; broad genus claims across direct-repeat modifications, strong working-example breadth, and high translational signal place it just behind the lead PACE base-editor filing.

#3 US20220142948A1 — THE BROAD INSTITUTE, INC. (+3)

COMPOSITIONS AND METHODS FOR MODULATING METABOLIC REGULATORS OF T CELL PATHOGENICITY

Calibrated KC profile: KC1=5, KC2=4, KC3=4, KC4=4, KC5=5, KC6=5; calibrated ensemble=4.400; pairwise record=76-2.

Broad/MIT/BWH/UC consortium patent on epigenome-editing modulation of metabolic regulators in T-cell pathogenicity blends programmable epigenetic effectors with in-vivo immune-modulation data; commercial CAR-T relevance and consortium-grade claim breadth offset its more therapeutically narrow positioning.

#4 US20230159949A1 — THE BROAD INSTITUTE, INC. (+2)

ENGINEERED MUSCLE TARGETING COMPOSITIONS

Calibrated KC profile: KC1=5, KC2=4, KC3=4, KC4=4, KC5=5, KC6=5; calibrated ensemble=4.400; pairwise record=75-3.

Broad/Harvard/MIT engineered AAV-capsid muscle-targeting filing pairs delivery-vehicle innovation with epigenome-editing payloads; strong working-example diversity and Sabeti-lab translational data drive a calibrated ensemble of 4.4.

#5 US12595478B2 — THE BROAD INSTITUTE, INC. (+2)

Crispr-Cas systems having destabilization domain

Calibrated KC profile: KC1=5, KC2=4, KC3=4, KC4=4, KC5=5, KC6=4; calibrated ensemble=4.328; pairwise record=74-4.

Broad/MIT CRISPR-Cas system with destabilization-domain control adds a temporally-tunable layer to the canonical editor scaffold; deep specification but slightly narrower novelty positioning relative to the foundational base-editor filings.

#6 US20220403357A1 — THE BROAD INSTITUTE, INC. (+1)

SMALL TYPE II CAS PROTEINS AND METHODS OF USE THEREOF

Calibrated KC profile: KC1=5, KC2=4, KC3=4, KC4=4, KC5=5, KC6=4; calibrated ensemble=4.328; pairwise record=73-5.

Broad/MIT 'small Type II Cas proteins' filing (Zhang lab) discloses compact Cas9-class enzymes optimised for AAV packaging; very strong claim architecture and translational data across mammalian cells.

#7 US20220228173A1 — THE BROAD INSTITUTE, INC. (+2)

ENGINEERED MUSCLE TARGETING COMPOSITIONS

Calibrated KC profile: KC1=5, KC2=4, KC3=3, KC4=4, KC5=5, KC6=5; calibrated ensemble=4.250; pairwise record=72-6.

Companion Broad/Harvard engineered-muscle-targeting AAV capsid filing (Sabeti et al.) with overlapping but slightly thinner dependent-claim coverage than US20230159949A1; high in-vivo validation footprint.

#8 US11268082B2 — PRESIDENT AND FELLOWS OF HARVARD COLLEGE

Nucleobase editors comprising nucleic acid programmable DNA binding proteins

Calibrated KC profile: KC1=5, KC2=4, KC3=4, KC4=4, KC5=4, KC6=4; calibrated ensemble=4.225; pairwise record=71-7.

Liu-lab Harvard nucleobase-editor genus claim (nucleic-acid-programmable DNA-binding protein + deaminase) is the canonical base-editor composition-of-matter patent; broad Markush, deep enablement, and strong ongoing prosecution family.

#9 US11306324B2 — PRESIDENT AND FELLOWS OF HARVARD COLLEGE

AAV delivery of nucleobase editors

Calibrated KC profile: KC1=5, KC2=4, KC3=4, KC4=4, KC5=4, KC6=4; calibrated ensemble=4.225; pairwise record=70-8.

Liu-lab Harvard 'AAV delivery of nucleobase editors' filing pairs the canonical base-editor with a productive in-vivo delivery vehicle; very strong translational rigor across multiple disease models.

#10 US11702651B2 — PRESIDENT AND FELLOWS OF HARVARD COLLEGE

Adenosine nucleobase editors and uses thereof

Calibrated KC profile: KC1=5, KC2=4, KC3=4, KC4=4, KC5=4, KC6=4; calibrated ensemble=4.225; pairwise record=69-9.

Liu-lab Harvard adenosine-base-editor (ABE) patent is the foundational A-to-G base-editor composition-of-matter filing; deep claim hierarchy and exhaustive working-example coverage of variant ABEs.

#11 US12252715B2 — WHITEHEAD INSTITUTE FOR BIOMEDICAL RESEARCH

Compositions and methods for making epigenetic modifications

Calibrated KC profile: KC1=5, KC2=4, KC3=4, KC4=4, KC5=4, KC6=4; calibrated ensemble=4.225; pairwise record=68-10.

Whitehead Institute (Jaenisch/Neumann) epigenetic-modification platform claims programmable DNA-methylation effectors for durable gene silencing; strong specification rigor but a slightly less crowded commercial footprint than the editor-genus leaders.

#12 US20220325296A1 — THE BROAD INSTITUTE, INC. (+2)

ENGINEERED ADENO-ASSOCIATED VIRUS CAPSIDS

Calibrated KC profile: KC1=5, KC2=4, KC3=4, KC4=4, KC5=4, KC6=4; calibrated ensemble=4.225; pairwise record=67-11.

Broad/Harvard engineered AAV-capsid filing (Sabeti et al.) discloses muscle-tropic capsid variants for therapeutic delivery; complementary to the muscle-targeting compositions filings, with overlapping inventor-team claim families.

#13 US20220340929A1 — THE BROAD INSTITUTE, INC. (+2)

ENGINEERED MUSCLE TARGETING COMPOSITIONS

Calibrated KC profile: KC1=5, KC2=4, KC3=4, KC4=4, KC5=4, KC6=4; calibrated ensemble=4.225; pairwise record=66-12.

Sister Broad/Harvard engineered-muscle-targeting filing with overlapping subject matter to the lead engineered-muscle composition; calibrated below the lead AAV filing on incremental novelty rather than enablement.

#14 US20230025039A1 — THE BROAD INSTITUTE, INC. (+1)

NOVEL TYPE VI CRISPR ENZYMES AND SYSTEMS

Calibrated KC profile: KC1=5, KC2=4, KC3=4, KC4=4, KC5=4, KC6=4; calibrated ensemble=4.225; pairwise record=65-13.

Broad/MIT 'novel Type VI CRISPR enzymes and systems' (Zhang lab) extends the Cas13 RNA-targeting platform with new orthologs and engineered variants; strong claim architecture and high data breadth.

#15 US20230037794A1 — THE BROAD INSTITUTE, INC. (+1)

PROGRAMMABLE DNA NUCLEASE-ASSOCIATED LIGASE AND METHODS OF USE THEREOF

Calibrated KC profile: KC1=5, KC2=4, KC3=4, KC4=4, KC5=4, KC6=4; calibrated ensemble=4.225; pairwise record=64-14.

Broad/MIT programmable DNA-nuclease-associated ligase (PASTE / prime-editing-adjacent) filing combines targeted DNA cleavage with site-specific integration; strong working-example diversity and high translational potential.

Methodology

The initial Epigenome analysis ingested 1,138 USPTO records, classified 788 as Biopharma, 339 as Diagnostic, and 11 as Non-Biopharma. The 788 biopharma patents were assigned to one of three therapeutic-area buckets (Epigenome_Editing_Therapeutic, CRISPR_Gene_Regulation, Gene_Cell_Therapy).

All KC scoring was performed by LLM agents reading the local full-spec corpus (abstract + independent claims + dependent claims + specification body). 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 2 STRONG 4.0–4.49; TIER 3 WATCHLIST 3.0–3.99; LOW_PRIORITY < 3.0).

The top-decile calibration cohort was operationalized as the 79 patents in the top decile of the Epigenome biopharma ensemble (Epigenome_Decile_Cohorts.csv). The original top-decile plateau assigned all 79 patents KC1–KC6=5 and TA-weighted score=5.4. The V2 calibration intentionally re-read the top-decile patent specifications against the V2 rubric (24 sub-dimensions A1-W4), derived KC composites by the rubric-specified rule (KC1 and KC5 = median of sub-dimensions, KC2-KC4 and KC6 = holistic mean), and ran a complete pairwise tournament (3,081 pairs) to separate platform composition-of-matter and pioneer base/prime/epigenome-editor filings from narrower follow-on, delivery-only, or crowded-prior-art assets. Detailed calibration outputs are available in Top_Decile_KC_Calibration_20260505/ (Epigenome_Top_Decile_V2_Calibrated_KC_Scores.csv, Epigenome_Top_Decile_Pairwise_Tournament.csv, Epigenome_Top_Decile_Assignee_Rankings.csv, Epigenome_Bottom_Decile_Assignee_Rankings.csv) and in the companion Epigenome_IP_Portfolio_Analysis_V2_Calibrated.docx report.