KIF18A as a Therapeutic Target in Anti-Aging / Age-Related Degenerative Disease — Clinical Translation Assessment

13 August 2026

Trial/dataset identifiers verified against retrieved sources; other figures are as reported by the curated skill and were not number-gated.

Target-disease evaluation · KIF18A (kinesin family member 18A, UniProt Q8NI77, NCBI Gene 81930) · Queried indication: anti-aging / age-related degenerative disease / dual-purpose (oncology + geroscience) · Date: 2026-08-13

1 Executive Summary

The whole report on one scannable page — the finding, the basis for it and the evidence behind them.

Verdict — adjudicating the two-to-one disagreement across the three internal reports: Reports 2 and 3 are correct, and Report 1 overstates the case. There is **no human clinical evidence** — of any phase — that a selective KIF18A inhibitor (or any drug with an identical or adjacent mechanism of action) is safe, effective or robust for anti-aging, age-related degenerative disease, or a dual-purpose (oncology + geroscience) indication. The entire KIF18A clinical enterprise is oncology, aimed at chromosomally unstable (CIN-high) tumors, and it is still early: the most advanced asset is Phase 1/2. **Confidence: HIGH.**

Four grounded observations drive this verdict:

1. **Zero aging trials.** Every registered KIF18A-inhibitor trial retrieved (10 programs, internal trials dataset + ClinicalTrials.gov) is oncology. None targets aging, senescence, neurodegeneration or any age-related degenerative disease. Most advanced phase = **Phase 1/2** (VLS-1488, NCT05902988; ATX-295, NCT06799065). No Phase 3 exists.
2. **PandaOmics scores KIF18A at zero for aging.** For the disease "aging" (EFO_0022597), KIF18A's **Attention Score = 0.000** and **Relevance = 0.000**; the target does not appear among aging's 2362 differentially expressed genes (q<0.05). By contrast, KIF18A's PandaOmics indication list is entirely oncology (neoplasm, cancer, breast, hepatocellular, colorectal, liver) plus infertility — aging is not in its top 50 indications.

3. **The mechanistic chain in Report 1 is not established for KIF18A.** The proposed pathway (KIF18A inhibition → micronuclei → cGAS-STING → clearance of aneuploid/senescent cells → reduced inflammaging) is assembled from adjacent, non-KIF18A literature. A direct PubMed search for "KIF18A micronuclei cGAS-STING" returns **no results** — no paper links KIF18A inhibition to cGAS-STING in any context, let alone aging.
4. **The rationale contains an internal contradiction and a pharmacological mismatch.** Report 1's thesis needs cGAS-STING activation to be beneficial, but the geroscience consensus is that cGAS-STING activation is a **primary driver of inflammaging and neurodegeneration** (PMID 42556484, PMID 42412280) — i.e., chronic KIF18A inhibition would be expected to raise STING tone and plausibly accelerate inflammaging. Separately, KIF18A is a **mitosis-restricted** motor; the post-mitotic and senescent (growth-arrested) cells that dominate aged tissue barely express it, so an anti-mitotic agent has little to act on there.

KIF18A remains a **credible, differentiated oncology target** for CIN-high tumors (PMID 38151625, PMID 39747049). The recommendation is to pursue it there and to treat the anti-aging / dual-purpose narrative as **not supported by current evidence and mechanistically counter-indicated** — a No-Go for a geroscience program until (and unless) direct data replace the current inferential chain.

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2 Methodology

Data sources: **NCBI Gene, UniProt, Ensembl, PandaOmics (Insilico Medicine), ChEMBL, RCSB PDB, AlphaFold, STRING, Reactome, PubMed, the internal Insilico Curated Clinical Trials Dataset, and ClinicalTrials.gov**, plus FreePatentsOnline / Google Patents for the patent landscape. Trial identifiers, PMIDs and patent numbers were taken verbatim from tool results logged to `outputs/citations.jsonl`; none were written from memory.

Workflow: (i) resolved KIF18A gene/protein identity and PandaOmics scores for the disease "aging" (disease_id 12202, EFO_0022597) and for KIF18A's ranked indications; (ii) mapped the real KIF18A clinical/trial landscape via `query_trials_db` and `clinicaltrials_search`; (iii) ran targeted PubMed reviews for KIF18A × aging / senescence / neurodegeneration / cGAS-STING, and for the anti-mitotic comparator class; (iv) gathered structural (PDB, AlphaFold), interaction (STRING), pathway (Reactome), compound (ChEMBL) and patent evidence. Three independent research workers (trial landscape, aging-evidence literature, comparator/precedent) supplied cross-checked syntheses.

The three attached internal reports (kif18a_anti_aging.md; kif18a_indication_prioritization_micheal_skill_v2.html; kif18a_indication_prioritization_base_pandaclaw.md) were **not retrievable in this session** (no

documents present in uploads). This assessment therefore relies on the verbatim conclusions and structure quoted in the brief, independently re-tested against live tool data. Where the reports disagree, the adjudication below rests on the tool evidence, not on any single report's stated grade.

Terminology follows the brief: "**selective KIF18A inhibitor**" throughout (never "pan-KIF18A"); KIF18A's nearest paralog KIF18B is only 36.4% identical (KIF25 27.6%, KIF3B 27.2%), so **kinome selectivity**, not paralog breadth, is the design goal. Ratings use ALL-CAPS `HIGH/MODERATE/LOW` for judgments and Title Case for source-native measurements.

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3 Target Biology

3.1 Identity, domains and structure

ATTRIBUTE	VALUE	SOURCE
Gene / Entrez ID	KIF18A / 81930	NCBI Gene
Locus	11p14.1 (chromosome 11)	NCBI Gene
UniProt / length	Q8NI77 / 898 aa	UniProt
Family	Kinesin-8 (kinesin superfamily), "Generic protein" (PandaOmics)	UniProt / PandaOmics
Motor (catalytic) domain	~ residues 11–355 (ATP hydrolysis, microtubule binding)	per brief; UniProt function
Molecular function	Microtubule plus-end-directed, microtubule-**depolymerizing** kinesin; reduces amplitude of preanaphase kinetochore oscillations, slows poleward movement in anaphase → suppresses chromosome movement and drives congression to the metaphase plate	UniProt
Key interactors (stabilizes)	CENPE–BUB1B complex at kinetochores in early mitosis	UniProt

ATTRIBUTE	VALUE	SOURCE
Experimental structures	7 PDB entries: 3LRE, 7RSI, 5OAM, 5OCU, 5OGC, 9YMG, 9DI0	RCSB PDB
Predicted structure	AlphaFold model available for Q8NI77	AlphaFold

KIF18A is a **mitotic motor**, not a chromatin-modifying enzyme; no epigenetic/senotherapeutic/MYST-family framing applies. Its function is required essentially only in **dividing** cells.

3.2 Pathway role

Reactome annotates KIF18A within kinesin/microtubule-motor biology (pathway R-HSA-376239, "Kinesins", accessed 2026-08-13). Its cellular role is confined to mitotic spindle dynamics — chromosome congression and the control of kinetochore oscillation (Stumpff & Wordeman, PMID 17470346; Gardner et al., PMID 18513970; Mayr et al., PMID 22102900; Huang et al., PMID 19625775; Serpico et al., PMID 39610707).

3.3 Interaction network (STRING, native 0–1 confidence)

PARTNER	CONFIDENCE	NATURE / SIGNIFICANCE
DLGAP5 (HURP)	0.945	Spindle/kinetochore; modulates KIF18A function (PMID 21924616) — HIGH
TUBB2B	0.939	β-tubulin; substrate track for the motor — HIGH
KIF11 (Eg5)	via network (KIF11↔KIF2C 0.968; KIF11↔KIF14 0.930)	Co-clustered mitotic kinesin; the archetypal drugged spindle motor — HIGH
CENPE, NUF2, CDC20, KIF2C, KIF14, KIF15	0.93–0.98 (mutual)	Kinetochore/SAC and mitotic-motor module

The network is a tight **mitotic-apparatus module** — every high-confidence neighbor is a cell-division protein, reinforcing that KIF18A biology is proliferation-restricted.

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4 Disease-Specific Evidence

4.1 Expression evidence in aging (PandaOmics)

The queried indication is aging (disease_id 12202, EFO_0022597; 383 datasets, 12616 samples in PandaOmics).

DATASET / ANALYSIS	RESULT FOR KIF18A	SIGNIFICANCE
Aging differential-expression meta-analysis (2362 DEGs at q<0.05)	**KIF18A not present in the DEG set**	Not differentially expressed with age at q<0.05
PandaOmics golden global-expression (aging)	Not available in this workspace (golden expression dataset not loaded)	Not evaluable
Combined	**No age-associated KIF18A expression signal**	**Absent**

Interpretation: there is no per-dataset log2FC/p-value table to report for KIF18A in aging because KIF18A does not surface as a significant DEG in the aging meta-analysis. This is itself an evidence point: the target shows no expression dysregulation with age. (Consistent with KIF18A being proliferation-restricted — aged tissue is enriched for post-mitotic/senescent cells that do not express mitotic motors.)

4.2 PandaOmics target scores — KIF18A in "aging"

DIMENSION	SCORE (0–1)	READ
Attention Score (the mandated disease-relevance metric)	**0.000**	No AI-prioritized relevance to aging
Relevance (AI Core)	0.000	No relevance signal
Credibility-adjusted attention index	0.000	No credible attention
Funding	0.000	No aging funding signal
Matrix factorization	0.334	Weak latent association
Expression (omics)	0.156	LOW
Knockouts / Overexpression / Mutations / Disease Sub-modules	0.000 each	No genetic/perturbation link to aging

DIMENSION	SCORE (0–1)	READ
Causal inference	0.466	Modest, generic
Pathways (iPanda)	0.571	Generic pathway co-membership
Interactome Community	0.894	HIGH — but reflects mitotic-hub connectivity, not aging biology
LLM Druggability	0.716	Tractable small-molecule target
LLM Safety	**0.133**	**LOW safety score — high on-target toxicity concern**
LLM Novelty	0.333	Low novelty as an aging idea

Because the skill ranks indications by **Attention Score**, and KIF18A's Attention Score for aging is **0.000**, aging does not qualify as a KIF18A indication. The only above-baseline omics scores (Interactome Community 0.894, Pathways 0.571) are driven by KIF18A's dense mitotic-network membership, not by any aging-specific evidence.

4.3 KIF18A's actual ranked indications (PandaOmics)

RANK	DISEASE	RELEVANCE	ATTENTION	THERAPEUTIC AREA
1	neoplasm	1.00	1.00	Oncology
2	cancer	0.99	1.00	Oncology
3	breast cancer	0.89	0.86	Oncology
4	hepatocellular carcinoma	0.33	0.90	Oncology
5	colorectal cancer	0.21	0.72	Oncology
6	liver cancer	0.31	0.80	Oncology
8	infertility	0.79	0.50	Reproduction

Disclosure (no cherry-picking): aging is not the queried target's leading indication — it is not in the top 50 at all. The top indications are oncology; the sole non-cancer entry (infertility) reflects KIF18A's germ-cell/meiotic role, not a geroscience benefit. The literature signal is the same: searches for "KIF18A aging" and "KIF18A senescence" return only cancer cell-biology and egg/meiotic-aneuploidy papers (PMID 39475646, PMID 39006445; note PMID 37708299 is a colorectal-cancer paper that merely appears in the journal Aging (Albany NY) — its content is oncology, not aging biology). A search for "KIF18A neurodegeneration" returns no results.

5 MOA Analysis

On-target MOA (established, oncology): selective small-molecule inhibition of the KIF18A motor domain arrests chromosome congression and mitotic progression. Cancer cells with chromosomal instability / aneuploidy — which rely on KIF18A to cluster extra centrosomes and dampen kinetochore oscillations — undergo mitotic catastrophe, while diploid cells are relatively spared. This CIN-selective vulnerability is well documented (Payton et al., Nat Cancer 2024, PMID 38151625; Phillips et al., Nat Commun 2025, PMID 39747049; Cohen-Sharir et al., Nature 2021, PMID 33505028; Gliech et al., EMBO J 2024, PMID 38279026; JAK1-loss sensitization, PMID 41591363). In CRC with a CIN phenotype, KIF18A inhibition can also trigger antitumor immunity and enhance PD-1 blockade (Liu et al., PMID 40175357).

Proposed anti-aging MOA (Report 1) — status: not established for KIF18A. The chain is:

KIF18A inhibition → chromosome mis-segregation → **micronuclei** → cytosolic dsDNA → **cGAS-STING** activation → immune clearance of aneuploid/senescent cells → reduced **inflammaging**.

Each arrow is individually plausible from general CIN biology, but **none has been demonstrated for KIF18A**:

- Direct searches "KIF18A micronuclei cGAS-STING" and "KIF18A cGAS STING inflammation" return **no results** — the micronuclei→cGAS-STING step is imported from generic CIN literature, not shown for KIF18A.
- No study links KIF18A inhibition to senescent-cell clearance or to any aging phenotype in vivo.

Two decisive problems with the anti-aging MOA:

1. **Directional contradiction on cGAS-STING.** The thesis is anti-aging by activating cGAS-STING. But the geroscience consensus is that cGAS-STING activation **drives** inflammaging, SASP and neurodegeneration (Wei et al., "cGAS-STING in age-related pathophysiology," PMID 42556484; Ma et al., "dysfunctional mitochondria in microglia drive cognitive aging and neurodegeneration via cGAS-STING," PMID 42412280). The therapeutic direction pursued for inflammaging is STING **inhibition**, not activation. A KIF18A inhibitor would be expected to **increase** cytosolic DNA/STING tone — plausibly accelerating inflammaging rather than relieving it. What is beneficial in oncology (STING-driven antitumor immunity) does not transpose to aging, where the same signal is deleterious.
2. **Cell-cycle mismatch.** KIF18A acts only in mitosis. Aged tissue is dominated by **post-mitotic and senescent (growth-arrested)** cells that do not divide and express little KIF18A. An anti-mitotic agent cannot act on non-cycling cells — the very population the thesis wants to clear. The somatic mosaic aneuploidy that accumulates with age largely resides in these non-dividing cells, outside KIF18A's window of action.

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6 Druggability Assessment

CRITERION (0–10)	SCORE	ASSESSMENT
Structural tractability	9	7 experimental PDB structures + AlphaFold; defined motor-domain pocket (incl. the α4-helix allosteric site, PMID 38410188)
Known small-molecule chemmatter	9	Multiple clinical inhibitors (sovilnesib/AMG-650, VLS-1488, ATX-295, GenSci-122, GH2616, MEN2501, HS387); ChEMBL targets CHEMBL4523403, CHEMBL5291576
Selectivity headroom	8	Nearest paralog KIF18B only 36.4% identical → kinome-selective design achievable; clinical compounds reported selective
Ligandability of pocket	8	Allosteric α4-helix / motor pocket validated as druggable
Oral exposure	8	Several inhibitors are oral (VLS-1488, ATX-295, GenSci-122, sovilnesib)
Biomarker for patient selection	7	CIN / aneuploidy score, chromosome-instability signatures (oncology)
Genetic validation (disease)	3 (aging) / 8 (oncology)	Strong for CIN-cancers; **null for aging** (Attention 0.000)
Assay availability	8	Mitotic-arrest, micronucleus, ATPase assays established
On-target safety window	4	Mitosis-essential; LLM Safety 0.133; germ-cell/marrow risk
Overall developability	7 (oncology) / 2 (aging)	Highly druggable molecule; **no druggable aging hypothesis**

Summary: KIF18A is a **highly druggable protein** with validated chemistry — but druggability of the protein is not evidence for the aging indication. For aging the target-disease link scores essentially zero.

7 On-Target Toxicity & Safety

DIMENSION	RISK	BASIS
Knockout lethality	MODERATE	Kif18a-mutant mice are viable but show **germinal cell aplasia / male infertility** from impaired chromosome congression (PMID 20981276) — a clear on-target reproductive phenotype
Essential proliferating-tissue function	MODERATE–HIGH	Mitosis-essential; on-mechanism toxicity expected in bone marrow, gut, skin, germline (class base rate below)
Paralog cross-reactivity	LOW (designable)	KIF18B 36.4%, KIF25 27.6%, KIF3B 27.2% identity → kinome selectivity is achievable, not breadth
Immune-system effects	MODERATE	Micronuclei/cGAS-STING induction can be pro-inflammatory — an asset in oncology, a **liability in aging**
Reproductive toxicity	HIGH (chronic use)	Direct germ-cell phenotype in mice
CNS effects	LOW (adults)	Little CNS mitosis in adults; but STING activation in microglia is pro-neurodegenerative (PMID 42412280)
PandaOmics LLM Safety (aging context)	LOW score (0.133)	Model-flagged safety concern

Chronic-dosing caveat (decisive for anti-aging): every prior mitotic-motor/spindle drug was dosed **intermittently, in cancer patients, for limited durations**, and was still limited by **myelosuppression/ neutropenia** (see Competitive Landscape). An anti-aging indication requires dosing **healthy or minimally-symptomatic older adults for years** — an exposure profile with **no tolerability precedent** in this class and a materially higher bar for cumulative antiproliferative and reproductive toxicity.

8 Competitive Landscape

8.1 KIF18A inhibitor clinical landscape — 100% oncology

Every registered KIF18A-inhibitor trial (internal trials dataset + ClinicalTrials.gov) targets cancer. **No aging, senescence, or age-related degenerative-disease trial exists.**

REGISTRY ID	DRUG (sponsor)	PHASE	STATUS	INDICATION	ENROLMENT
NCT04293094	AMG 650 / sovilnesib (Amgen → Volastra)	Phase 1	Completed	Advanced solid tumors	66
NCT06084416	Sovilnesib (Volastra)	Phase 1b	Active, not recruiting	High-grade serous ovarian (CIN-high)	120
NCT05902988	VLS-1488 (Volastra), oral	Phase 1/2	Recruiting	Advanced solid tumors	not reported
NCT06799065	ATX-295, oral	Phase 1/2	Open	Solid tumors incl. HGSOC	not reported
NCT06772415	GenSci-122, oral	Phase 1	Open	Advanced solid tumors	not reported
NCT06329206	GH2616	Phase 1a/1b	Open	Advanced solid tumors	not reported
NCT07260513	GH2616	Phase 1	Closed	Advanced solid tumors	not reported
NCT07226427	MEN2501 (Menarini)	Phase 1	Open	Platinum-resistant ovarian	not reported
NCT07092748	HS387	Phase 1	Open	Advanced solid tumors incl. NSCLC	not reported
701018 (internal ID; no NCT)	HW221043	Phase 1	Planned	Advanced solid tumors	not reported

Most advanced phase: Phase 1/2. No Phase 3, no approval, no efficacy readout in aging. Aging/geroscience trials: **none found.** (Note: "sabatolimab" is a TIM-3 antibody unrelated to KIF18A; "VLS-1487" has no registered trial.)

8.1.1 Adjacent-MOA precedent — mitotic-motor / spindle inhibitors (all oncology, none approved)

AGENT	TARGET	MAX PHASE (retrieved)	INDICATION	OUTCOME
Ispinesib (SB-715992)	KIF11/ Eg5	Phase 2 (e.g. NCT00354250, NCT00089973)	Multiple solid tumors	Negative as monotherapy; discontinued
Filanesib (ARRY-520)	Eg5	Phase 2 (AfFIRM NCT02092922)	Multiple myeloma	No approval; discontinued
Litronesib (LY2523355)	Eg5	Phase 1 (PMID 28097385)	Solid tumors	Phase 1 only
AZD4877	Eg5	Phase 1 (PMID 21638123)	Solid/lymphoid	Phase 1 only
Alisertib (MLN8237)	Aurora A	Phase 3 (PTCL)	Lymphoma, solid tumors	Phase 3 **failed**; multiple terminations
Volasertib (BI 6727)	PLK1	Phase 3 (AML)	AML/MDS, NSCLC	Phase 3 **failed**

Base rate: across the anti-mitotic class, **zero approvals** and **zero programs in aging/senescence/ degenerative disease** — the mechanism has no geroscience precedent whatsoever. Dose-limiting toxicity across the class is **myelosuppression/neutropenia**, intrinsic on-mechanism pharmacology (class review PMID 16022179). KIF18A is differentiated only by its claimed CIN-selectivity, which — if it holds in humans — is what could spare normal diploid marrow; that claim is exactly what the class base rate stress-tests.

8.2 Patent landscape (illustrative, newest priority first)

PATENT / PUBLICATION	ASSIGNEE (as printed)	SCOPE
WO2024039829A1 / AU2023324826A1	(2022 priority)	Inhibitors of KIF18A and uses thereof
WO2024153217A1	(2023 priority, CN)	Inhibitors of KIF18A and uses thereof
EP4524135A4 / WO2023217230A1	Chinese biotech (2022 priority)	Kinesin-KIF18A inhibitors and uses
EP3897852A1	(KIF18A inhibitors)	Composition-of-matter
WO2021026098A1	incl. Volastra Therapeutics (spiro-indoline chemotype)	KIF18A inhibitors

PATENT / PUBLICATION	ASSIGNEE (as printed)	SCOPE
WO2021211549A1 / US20230151432A1	(KIF18A + CDK4/6)	KIF18A inhibitors for neoplastic disease / CDK4/6-resistant tumors
WO2020132648A1 / JP2022514268A	Amgen Inc.	Heteroaryl amides as KIF18A inhibitors
US20220281843A1	(KIF18A inhibitors)	Modulating KIF18A; claims cover cancer, inflammation, ciliopathies

The patent estate is **oncology-focused** (several explicitly "for treatment of neoplastic diseases"); one broad filing (US20220281843A1) nominally mentions inflammation/ciliopathies, but no aging/degenerative claim or supporting data was found. Competitive density is high (Amgen/Volastra plus multiple Chinese biotechs), which matters for oncology freedom-to-operate, not for an aging thesis.

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9 Strategy Options

1. **[Recommended] Pursue KIF18A in oncology; do not open a geroscience program.** Focus on CIN-high indications (HGSOC, CIN breast/CRC) where genetic validation, biomarker (CIN/aneuploidy score) and clinical precedent exist. Confidence HIGH.
2. **[Conditional] Keep aging as a "watch," not a program.** Re-evaluate only if direct data emerge — specifically: (a) a demonstrated KIF18A-inhibition → micronuclei → cGAS-STING link in a normal-cell/aging model, (b) evidence that immune clearance of induced-aneuploid cells outpaces senescent-cell accumulation in an aged, immunosenescent host, and (c) a chronic-dosing tolerability model. Absent these, No-Go.
3. **[Reject] Dual-purpose "oncology + geroscience" positioning.** The oncology benefit (STING-driven immune activation, killing of dividing CIN cells) and the aging harm (STING-driven inflammaging, no substrate in non-dividing aged cells) point in **opposite** directions. Marketing a single KIF18A inhibitor as both is not supported and is mechanistically self-contradictory — this is the specific claim Reports 2 and 3 reject, correctly.
4. **[Alternative geroscience path, if the goal is aneuploidy/senescence]** senolytics or improved mitotic fidelity/reprogramming are the evidenced directions (e.g., PMID 30795536), and STING inhibition is the inflammaging direction (PMID 42556484) — none of which is a KIF18A inhibitor.

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10 Challenges, Limitations & Opportunities

Challenges / limitations

- **Evidence Level 0 for aging:** no human clinical, and no direct preclinical KIF18A-aging, data. PandaOmics Attention Score 0.000; not an aging DEG.
- **Mechanistic contradiction:** cGAS-STING activation is pro-inflammaging; the anti-aging thesis requires it to be beneficial.
- **Cell-cycle mismatch:** mitosis-restricted target vs. post-mitotic/senescent aged tissue.
- **Chronic-dosing toxicity:** class DLT is myelosuppression; germ-cell aplasia on target; no long-term tolerability precedent.
- **Analytic limitation:** the three source reports could not be opened this session; conclusions were re-derived from live data and match Reports 2 & 3. The PandaOmics golden global-expression dataset for aging was not loadable in this workspace (KIF18A's absence from the 2362-DEG set is the substitute evidence).

Opportunities

- KIF18A is a **highly druggable, well-validated oncology target** with a rich, selective chemotype landscape and clear CIN biomarker strategy.
- The **immune-activating** facet (micronuclei→STING) that is a liability in aging is an asset in oncology (combinations with PD-1, PMID 40175357) — the right home for the mechanism.

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11 Conclusions

Adjudicating the two-to-one split: **Reports 2 and 3 are supported by the evidence; Report 1's "moderate-to-strong" anti-aging grade is not.** Selective KIF18A inhibitors — and every adjacent-MOA (mitotic-motor / spindle) agent — have **no human clinical evidence of safety, efficacy or robustness for anti-aging, age-related degenerative disease, or a dual-purpose oncology + geroscience indication.** All clinical development (10 programs, up to Phase 1/2) is oncology; PandaOmics assigns KIF18A a zero Attention Score for aging; the proposed mechanism is an unproven chain of imported inferences that additionally **contradicts** geroscience consensus on cGAS-STING and **mismatches** KIF18A's mitosis-restricted biology to non-dividing aged tissue.

Recommendation: advance KIF18A as a CIN-selective oncology target; classify the anti-aging / dual-purpose indication as No-Go pending direct, currently-absent evidence. Confidence HIGH.

Not medical advice; supports research and portfolio decisions only.

12 References

Consolidated source, registry and record identifiers.

Clinical trials (internal trials dataset / ClinicalTrials.gov): NCT04293094 (AMG 650/sovilnesib, Ph1, completed, n=66); NCT06084416 (sovilnesib, Ph1b, HGSOC, n=120); NCT05902988 (VLS-1488, Ph1/2); NCT06799065 (ATX-295, Ph1/2); NCT06772415 (GenSci-122, Ph1); NCT06329206 & NCT07260513 (GH2616, Ph1); NCT07226427 (MEN2501, Ph1); NCT07092748 (HS387, Ph1); internal ID 701018 (HW221043, Ph1, planned). Comparator class: NCT00354250, NCT00089973 (ispinesib); NCT02092922 (filanesib); NCT02721875 (volasertib, terminated).

Literature (PMID): 38151625 (Payton, Nat Cancer 2024 — small-molecule KIF18A inhibition, CIN vulnerability); 39747049 (Phillips, Nat Commun 2025 — selective KIF18A inhibitor); 33505028 (Cohen-Sharir, Nature 2021 — aneuploidy vulnerability); 38279026 (Gliech, EMBO J 2024 — APC/C weakening); 41591363 (JAK1-loss sensitization); 40175357 (Liu — antitumor immunity + PD-1, CRC CIN); 41543111 (Truong, review — KIF18A cancer trials); 38410188 (α4-helix therapeutic site); 20981276 (Kif18a-mutant male germ-cell aplasia); 20595236 (KIF18A in breast carcinogenesis); 17470346, 18513970, 19625775, 22102900, 21924616, 39610707 (KIF18A/kinesin-8 mitotic biology); 39475646, 39006445 (kinesin motor variants & egg aneuploidy); 42556484 (cGAS-STING in age-related pathophysiology); 42412280 (microglial cGAS-STING in cognitive aging/neurodegeneration); 30795536 (mitotic competence / senescence review); 28097385, 21638123, 24077982, 16022179 (Eg5/anti-mitotic class toxicity precedent).

Other identifiers: UniProt Q8NI77; NCBI Gene 81930; Ensembl KIF18A; PDB 3LRE, 7RSI, 5OAM, 5OCU, 5OGC, 9YMG, 9DI0; AlphaFold AF-Q8NI77; ChEMBL CHEMBL4523403, CHEMBL5291576; Reactome R-HSA-376239 (accessed 2026-08-13); PandaOmics disease "aging" EFO_0022597. Patents per §8.2 (FreePatentsOnline / Google Patents).

13 Appendix — Data provenance

Saved artifacts: `outputs/KIF18A_indications.json`, `outputs/pandaomics_targets_aging.json`, `outputs/KIF18A_aging_degs.json`, `outputs/citations.jsonl`, and worker syntheses under `outputs/workers/{landscape,aging_evidence,comparator}/findings.md`. All trial IDs, PMIDs and patent numbers copied verbatim from tool outputs logged in `outputs/citations.jsonl`.