cGAS-STING — V4 Target Opportunity Report (Public Edition)

Whitespace & Trajectory, in one decision-first view

Target: cGAS-STING innate-immune DNA-sensing pathway — cGAS (CGAS/MB21D1; UniProt Q8N884) + STING (STING1/TMEM173; UniProt Q86WV6) **Date:** 2026-07-22 · **Substrate:** a full-landscape patent-family set (incl. the pre-2020 foundational tail); **101 on-pathway** families after claim-scope screening. **What this is for:** to let an inventor or BD&L reader *see where the defensible room is and where the field is going* — a whitespace/trajectory signal.

> **Read-me (the guardrails, once):** This is **candidate generation and a whitespace/trajectory signal — NOT a freedom-to-operate (FTO) opinion.** "Whitespace" = absence of *strong structural claim coverage*, which is necessary-but-not-sufficient for opportunity. Structural overlap and sequence identity are directional **lower bounds**. Verify any specific family before relying on it.
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> **Public edition note.** This is the public edition of the cGAS-STING V4 Target Opportunity Report. It presents the whitespace and trajectory reads that accompany the article. The underlying patent-craftsmanship (KC) strength scoring, per-family score tables, machine-readable knowledge graph, and raw scored inputs are part of the internal analyst deliverable and are not reproduced here; the strength layer is relative-ordering, calibration-pending work and is deliberately not published as a ranking.

PART I — ACT ON THIS

1. Actionable summary — where to build

Ranked opportunities, each with the reason it is open and the standing claims to design around. Detail in §2 (whitespace), §3 (the actionable chemical core), §4 (trajectory).

#	Opportunity	Status	Why it's actionable	Watch / design around
1	**STING trafficking / palmitoylation inhibitor** — autoimmune	**OPEN** (0 families)	Mechanistically distinct from the crowded pocket binders; sits next to a *populated* non-CDN-inhibitor neighbor, so it is a real gap, not an artifact	No blocking genus in-corpus; confirm vs. academic palmitoylation art (e.g., C-178/H-151 class) outside the corpus

#	Opportunity	Status	Why it's actionable	Watch / design around
2	**CDN-pocket STING *antagonist*** — autoimmune	**OPEN / near-open**	The single family in this cell is itself **lapsed** → the direction is unclaimed *and* undefended	The maintained *agonist* CDN core is adjacent chemistry, not a direct block
3	**cGAS DNA-binding-surface inhibitor**	**OPEN** (0 families)	A mechanistic alternative to the crowded catalytic-site race; the catalytic genus does not reach the DNA-binding surface	Design around the cGAS-catalytic genus (median recall ~0.33 — see §3)
4	**ENPP1 inhibitor** — IO	**Contestable now**	Genus-broad (recall **0.582**, the highest of any cell) but only **1 of 5** families is a live grant — the *grants* have not consolidated	A same-applicant continuation cluster is filing here; move before grants issue
5	**Non-systemic / non-CDN STING agonist** (delivery-formulated)	**Opening**	4 of 5 lapsed foundational patents are STING agonists → the original broad systemic-CDN genus is no longer defended	Maintained core: Aduro, InvivoGen, ImmuneSensor CDN estates (expiries 2033-2038)
6 *(speculative)*	**STING or cGAS degrader (PROTAC)**	OPEN*	No degrader claimed anywhere in the corpus	*`degrader` is unpopulated corpus-wide — treat as a hypothesis prompt; verify against a dedicated degrader search before relying on it (see §2 caveat)
—	**cGAS-catalytic occupancy inhibitor**	**AVOID**	COVERED & crowded: 18 families, 9 live	The consolidated multi-sponsor catalytic-inhibitor

#	Opportunity	Status	Why it's actionable	Watch / design around
	(generic scaffold)		grants, 4 defended scaffold lanes	estates

The one-sentence read: the open, defensible room is on the **inhibitor / trafficking / degrader** side of *STING* and the **DNA-binding / degrader** side of *cGAS* — the autoimmune-directed *mechanistic alternatives* the field is pivoting toward but has not yet fenced — plus a **time-limited ENPP1** window before its broad genera mature into grants.

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2. Whitespace map — the open cells

The landscape was projected onto a scope grid (mechanism-node × direction × modality × indication). A cell is a **whitespace candidate** when it is *scientifically reachable* but *structurally thin*: few on-pathway families, no broad **live-granted** genus, and/or coverage held only by lapsing patents.

Verdict rule: OPEN = 0 on-pathway families · THIN = ≤2 families, no broad live genus · PARTIAL = coverage but no broad live-granted genus · COVERED = broad live-granted genus present.

mechanism cell	verdict	on-path families	live grants	genus recall (N)
STING trafficking / inhibitor	**OPEN**	0	0	—
cGAS DNA-binding / inhibitor	**OPEN**	0	0	—
CDN-pocket / antagonist	**THIN — & lapsed**	1	0 (1 lapsed)	—
STING-degradation / degrader	OPEN*	0	0	—
cGAS-catalytic / degrader	OPEN*	0	0	—
downstream TBK1/IRF3 / inhibitor	OPEN	0	0	—
ENPP1 / inhibitor	contestable	5	1	0.582 (5)
non-CDN allosteric / inhibitor	COVERED	11	3	0.528 (7)
non-CDN allosteric / agonist	COVERED	6	2	0.536 (4)
CDN-pocket / agonist	COVERED / **decaying**	14	10 (+4 lapsed)	0.365 (11)
cGAS-catalytic / inhibitor	**COVERED**	18	9	0.326 (12)

*degrader caveat: the degrader direction is unpopulated across the **entire** corpus (on- and off-pathway). The two degrader cells are "open" partly by corpus/axis construction — they are the weakest of the open calls and should be verified with a dedicated degrader-corpus search. The trafficking-inhibitor, DNA-binding, and CDN-pocket-antagonist cells are better-grounded because they sit adjacent to* populated* neighboring cells.

Read: open cells cluster on **STING-trafficking-inhibitor, cGAS-DNA-binding-inhibitor, and CDN-pocket-antagonist** — autoimmune-directed mechanistic alternatives. The agonist/IO side is either covered-and-crowded (cGAS-catalytic inhibitor is the real core) or covered-and-decaying (CDN-pocket agonist).

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3. The actionable chemical core — the genus-bearing families

Small-molecule / chemical-genus families are the most actionable subset for an inventor, because their scope is defined by a compiled Markush **genus** whose **breadth** (recall, a lower bound) tells you how much analog space is fenced. Of the genus-bearing families, most are on-pathway small-molecule chemotypes; median `family_best` genus recall across the small-molecule set is **~0.41** — i.e. compiled claims capture ~40% of the enumerable analog space they gesture at, leaving material *in-scaffold* room even in "covered" cells.

What this means where you'd build:

- **cGAS-catalytic inhibitor (COVERED, but diversifying — median recall 0.326).** Four distinct scaffold lanes, no single genus dominating: **quinoline**, **indazole**, **pyridine-pyrrolidine**, **other-heterocycle**. Crowded — but recall ~0.33 means each lane still has analog headroom, and the **DNA-binding-surface** alternative (§2 #3) is entirely open.
- **ENPP1 inhibitor (contestable — recall 0.582, highest of any cell, but 1/5 live-granted).** The scaffolds are well-drafted but the *grants* have not consolidated; a same-applicant continuation cluster shows high structural similarity (INDETERMINATE membership). **This is the clearest time-limited window in the portfolio** — broad genera, immature grants.
- **Non-CDN STING inhibitor (COVERED — recall 0.528; 8 of 11 pending).** Actively consolidating. Filing here now means entering a fast-filling cell — the trafficking-inhibitor alternative is the cleaner play.
- **CDN-pocket agonist (COVERED / decaying — recall 0.365).** The foundational genera are moderate-breadth and partly lapsing (§4). The maintained core is the design-around constraint; **non-systemic / delivery-formulated** agonist chemistry is the opening (§2 #5).

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4. Trajectory — where this target is going

Composed from filing velocity × direction × modality × entrant type, on **real filing dates** (all 101 on-pathway families dated; no proxy).

era	dominant modality	direction (agonist : inhibitor)	entrants
pre-2018	CDN (9)	**8 : 1**	US pharma/academic
2018-2021	CDN (7) + first small-molecule (9) + non-CDN agonist (5) + biologic (5)	21 : 8	+ first China (2), Korea (1)
2022-2026	**small-molecule heterocycle (33 + 12 named-scaffold)**	**9 : 39**	37 company, 12 academic, 4 China, 3 Korea

Trajectory statement: *cGAS-STING is transitioning from a lapsing first-wave systemic-CDN* ***STING-agonist / IO*** *foundation toward (i) a crowded, well-drafted, multi-scaffold small-molecule* ***cGAS-catalytic-inhibitor*** *race for* ***autoimmune*** *indications — the current center of gravity, accelerating 2021→2024 — and (ii) an emerging* ***ENPP1-inhibitor*** *and* ***non-CDN STING-inhibitor*** *frontier (non-CDN inhibitor filings build through 2025). Genuine whitespace concentrates in the* ***STING-trafficking-inhibitor, cGAS-DNA-binding-inhibitor, and CDN-pocket-antagonist*** *cells. Entrants broaden from a US-pharma/academic core to include China- and Korea-origin filers, though the count is still modest (China 2→4, Korea 1→3).*

The decisive dynamic — the agonist foundation is being abandoned. Five foundational STING patents are **LAPSED or DISCONTINUED for non-payment** — 4 CDN-pocket *agonist* + 1 CDN-pocket *inhibitor*, the latter discontinued as recently as 2026-07-20. The original broad systemic-CDN genus is no longer defended (freedom expands for non-systemic/delivery-formulated agonist chemistry designing around a maintained 2033-2038 core), while the cGAS-**inhibitor** core is entirely fresh (2021-2026 filings) and accreting. **Direction of travel: agonist→inhibitor, IO→autoimmune, systemic-CDN→small-molecule + targeted-delivery.**

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5. Lapse / decay timeline — the temporal signal under §4

The public trajectory turns on which foundational estates are being abandoned versus maintained (legal-status facts, not quality scores):

patent	node / direction	event	date
US-10047115	CDN-pocket agonist	LAPSED (non-payment)	2022-10-11
US-10450341	CDN-pocket agonist	LAPSED (non-payment)	2023-12-19
US-9549944	CDN-pocket **inhibitor**	LAPSED (non-payment)	2025-03-25
US-9724408	CDN-pocket agonist	LAPSED (non-payment)	2025-10-07
US-9994607	CDN-pocket agonist	DISCONTINUATION	2026-07-20

Maintained core (survives; design-around targets): Aduro US-9770467 (→2033), US-9695212 (→2033); InvivoGen US-10011630 (→2035), US-11730817 (→2038);

ImmuneSensor US-10519188 (→2038); Aduro non-CDN US-10738056 (→2038, broad genus recall 0.629).

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6. Combination adjacencies + cross-class transfer

- **Combination interest:** cGAS-STING is being co-claimed with checkpoint (anti-LAG-3/PD-1), innate-checkpoint (SIRPα, CD47), **DDR inhibitors** (ATM, Chk1, DNA-PK), cytokines (IL-18, APRIL-TACI), and cell therapy (CAR). **Unclaimed rational pairs:** cGAS/STING-*inhibitor* × DDR for autoimmune (the DDR co-claims are all agonist/oncology-directed); ENPP1-inhibitor × checkpoint.
- **Cross-class transfer (candidate generation; lower bounds):** scaffolds whose Markush genus reaches into cGAS-STING space but were filed for other purposes — transfer hypotheses: proven chemistry, structurally adjacent to a cGAS-STING node, not yet claimed *for* the pathway. (All INDETERMINATE-driven — candidate generation, not FTO.)

PART II — METHOD & LIMITS (public summary)

How the reads were built

- **Discovery** on both pathway nodes across **all four jurisdictions** (US/EP/WO/CN), then a **full-landscape assembly including the pre-2020 foundational anchors** (cGAMP, CDN, STING), whole-family.
- **Scope binning** onto four externally-grounded axes (literature + Wikidata SPARQL) — mechanism-node, direction, modality/chemotype, indication — *not* derived from the patent set; each family carries an LLM claim-scope `scope_evidence` string.
- **A load-bearing on/off-pathway screen:** only **101 of 126 families** genuinely claim a cGAS-STING mechanism; the rest co-mention the pathway but claim something else (SIRPα/CD47 antibodies, DDR inhibitors, CAR constructs, radiotherapy scheduling) and are held out of the whitespace/trajectory denominator (retained only as combination signal). Treating raw hit counts as coverage would overstate the estate by ~25%.
- **Structural genus/scope layer** over the genus-bearing families (median small-molecule `family_best` recall ~0.41; overlap INDETERMINATE-dominated — candidate generation), plus **legal-status timelines** for the lapse/decay read and **real filing dates** for the trajectory (no proxy).
- **Independent adversarial review** of both the strength read and the whitespace/trajectory read by impartial reviewers with full data/script access; headline integrity fixes (a genus-recall lookup bug, a filing-year proxy replaced with real dates, an agonist/inhibitor mislabel, an entity-origin misclassification) were applied before release.

Limits — read before relying

- **Not FTO.** Whitespace = absence of *strong structural claim coverage* (necessary-not-sufficient). Structural overlap/genus recall are lower bounds. An OPEN cell is a hypothesis prompt, not clearance.
- **`degrader` is unpopulated corpus-wide** — the two degrader cells are "open" partly by axis/corpus construction; weakest of the open calls (verify with a dedicated degrader search).
- **The denominator is operator-defined** (the scope ontology); different axes → different whitespace. **Classification is a model read** (the 101/25 split and per-family bins are LLM claim-scope reads) emphasizing cell-level patterns over single-family calls.
- **Corpus-bounded & US-anchored.** Whitespace is relative to the ingested families; ex-US members materialize at bibliographic tier (full-text analysis not yet run); genuinely un-filed art is invisible by construction.

This public edition presents the cGAS-STING whitespace and trajectory reads. Every whitespace/trajectory number is computed on the 101 on-pathway families on real filing dates. Candidate generation, NOT freedom-to-operate.