WFS1 Molecular Docking — Candidate Shortlist

Variant **R558C** · pocket 33 · POCKET UNREVIEWED · generated 2026-08-27 22:14 UTC

Read this before the table

This document prioritises bench work. It does not establish that any compound binds wolframin. Every number below is a prediction from a scoring function.

1. POCKET 33 WAS NOT REVIEWED BY A HUMAN. This run was forced. Every candidate below inherits that: the site itself is unconfirmed.
2. DiffDock confirmation was NOT run, so the spec's 'DiffDock confidence > 0.5' secondary filter is INACTIVE - not passed. These are single-engine Vina scores with no orthogonal confirmation.
3. CONFORMER SENSITIVITY, MEASURED ON THIS RUN: 698 molecules were present as both a parent and a salt form, giving an internal replicate (identical molecule, identical seed and box, different starting 3D conformer). Median score difference 0.034 kcal/mol, 95th percentile 0.425, worst case 1.485. Differences below roughly 0.425 kcal/mol are not meaningful.
4. Vina affinity is a scoring-function ESTIMATE, not a measured binding constant. Its standard error (~2-3 kcal/mol) exceeds the gap between most adjacent ranks, so treat this as an unordered shortlist rather than a ranked order.
5. Vina's raw affinity scales with molecular size, so larger ligands score better almost regardless of fit. Ligand efficiency (-affinity per heavy atom) is reported alongside and is the fairer comparison; a shortlist read on affinity alone will be biased toward the heaviest compounds in the library.
6. The receptor is rigid: induced fit and sidechain rearrangement are not modelled.
7. Docking was performed against the wild-type AlphaFold model. It does not account for any local remodelling the variant itself causes.
8. This is a computational prediction intended to prioritise bench work. It is not evidence of binding.

Target

Variant	R558C
Receptor	AlphaFold AF-O76024-F1 (WFS1 / wolframin, 890 aa), rigid
Residue	ARG558 (pLDDT 84.56)
Pocket	33 · druggability 0.000 · 195 A^3 · mean pLDDT 87.0
Distance to variant	5.51 A (does not line the residue)
Pocket lining	LYS424, ILE427, PRO428, CYS429, SER430, GLU550, SER551, THR552
Reviewed by	NOT REVIEWED

Top 20 candidates

Ranked by Vina affinity (most negative first) over 1566 scored compounds. DiffDock secondary filter: **INACTIVE**.

#	Compound	Vina kcal/mol	LE per atom	DiffDock	FDA	MW	Chaperone mechanism
1	BICTEGRAVIR SODIUM	-7.42	0.232	not run	yes	448	-
2	CAPMATINIB	-7.42	0.239	not run	yes	412	-

#	Compound	Vina kcal/mol	LE per atom	DiffDock	FDA	MW	Chaperone mechanism
3	DEXAMETHASONE SODIUM PHOSPHATE	-7.35	0.230	not run	yes	470	-
4	FLUOCINONIDE	-7.30	0.209	not run	yes	495	-
5	DOLUTEGRAVIR SODIUM	-7.20	0.240	not run	yes	418	-
6	OXACILLIN	-7.16	0.256	not run	yes	401	-
7	CLOXACILLIN	-7.13	0.246	not run	yes	436	-
8	OXYPHENISATIN ACETATE	-7.10	0.237	not run	yes	401	-
9	PREDNISOLONE TEBUTATE	-7.09	0.215	not run	yes	459	-
10	IDARUBICIN HYDROCHLORIDE	-7.08	0.197	not run	yes	498	-
11	CABOTEGRAVIR SODIUM	-7.08	0.244	not run	yes	404	-
12	PREDNISOLONE SODIUM PHOSPHATE	-7.05	0.235	not run	yes	438	-
13	OLAPARIB	-7.02	0.219	not run	yes	434	-
14	NALFURAFINE	-7.02	0.201	not run	yes	477	-
15	TADALAFIL	-6.99	0.241	not run	yes	389	-
16	EPLERENONE	-6.99	0.233	not run	yes	414	-
17	FLUDROCORTISONE ACETATE	-6.98	0.233	not run	yes	422	-
18	FLUMETHASONE PIVALATE	-6.96	0.199	not run	yes	495	-
19	GLIPIZIDE	-6.95	0.224	not run	yes	446	-
20	AVAPRITINIB	-6.94	0.188	not run	yes	499	-

The same run, ranked by ligand efficiency

Vina's raw affinity rewards heavy atoms, so the table above is biased toward the largest compounds in the library. Ligand efficiency (-affinity per heavy atom) corrects for that and gives a materially different order. Neither list is the right answer on its own; compounds appearing high in both are the safer bets. Restricted to molecules with at least 10 heavy atoms, below which the metric is meaningless.

#	Compound	Vina	LE	Atoms	Chaperone
1	ALLOPURINOL	-4.68	0.468	10	-
2	MERCAPTOPURINE	-4.55	0.455	10	-
3	ACETAZOLAMIDE	-5.71	0.439	13	-
4	ISOSORBIDE	-4.38	0.438	10	-
5	PHENICARBAZIDE	-4.81	0.437	11	-
6	GLUTAMINE	-4.36	0.436	10	-
7	MAGNESIUM TRISILICATE	-4.78	0.435	11	-
8	COUMARIN	-4.78	0.435	11	-
9	SALICYLIC ACID	-4.33	0.433	10	-
10	ETIDRONATE DISODIUM	-4.76	0.432	11	-
11	ISONIAZID	-4.32	0.432	10	-
12	FAVIPIRAVIR	-4.74	0.431	11	-
13	POTASSIUM BITARTRATE	-4.31	0.431	10	-
14	BUFORMIN	-4.73	0.430	11	-
15	THIOGUANINE	-4.70	0.428	11	-

Mechanism-tagged compounds (all, regardless of rank)

Compounds manually tagged in the ER-stress / chaperone / ER-calcium literature. A tag is a literature association asserted by a person, not evidence of binding to WFS1. Shown with full-ranking position so a poor score is as visible as a good one.

Rank	Compound	Vina	Mechanism
50	SITAGLIPTIN PHOSPHATE	-6.73	metabolic / beta-cell: DPP-4 inhibitor; beta-cell relevance, not a folding mechanism.
391	DONEPEZIL HYDROCHLORIDE	-5.98	sigma-1 agonist: Acetylcholinesterase inhibitor with reported sigma-1 receptor agonism.
458	TAURURSODIOL	-5.88	bile acid / ER stress: TUDCA; bile-acid derivative associated with reduced ER stress and...
568	URSODIOL	-5.74	bile acid / ER stress: UDCA; parent bile acid of TUDCA, associated with ER stress modulation.
825	DANTROLENE SODIUM	-5.38	ER calcium (RyR): Salt form of dantrolene; same mechanism class.
1116	RILUZOLE	-4.98	glutamate modulation: Neuroprotective agent; adjacent literature only, not an ER-stress...
1176	IBUDILAST	-4.88	PDE / neuroinflammation: Phosphodiesterase inhibitor investigated in neurodegeneration...
1297	FLUVOXAMINE MALEATE	-4.65	sigma-1 agonist: SSRI with sigma-1 receptor agonism; sigma-1 is an ER chaperone at the MAM...
1316	SODIUM PHENYLBUTYRATE	-4.61	chemical chaperone: 4-PBA; chemical chaperone / HDAC inhibitor, widely used to relieve ER...
1384	METFORMIN HYDROCHLORIDE	-4.46	metabolic / beta-cell: Relevant to the diabetes component of Wolfram syndrome rather than to...

Reproducibility

Run ID	1478c9c9a483
Engine	AutoDock Vina v1.2.7 · exhaustiveness 16 · seed 42 · --cpu 1 per process (multi-CPU Vina is not deterministic)
Library	version 0.1.0-dev · 1566 compounds scored
Ligands docked	2480
Started	2026-08-27T07:01:19+00:00

RareResearch.AI · WFS1 Molecular Atlas docking extension · compound data from ChEMBL (CC BY-SA 3.0, EMBL-EBI) · structure from AlphaFold DB (EMBL-EBI). Full run manifest with input hashes and tool versions accompanies this report.