Target–Drug Landscape Dossier

Compiled June 25, 2026 · Sources: ChEMBL, PubChem, ClinicalTrials.gov, company filings & peer-reviewed literature

About this project

This dossier is one entry in a target–drug landscape catalogue. For each biological target of interest, the goal is to capture, on a single reference sheet: (1) a concise target profile (what the protein is and why it is being drugged), (2) the approved drugs acting on it, (3) the clinical-stage pipeline with development phase, and (4) where no approved or clinical asset exists, the leading preclinical or literature ('journal') compounds. Each chemical entity is accompanied by its 2D structure rendered from canonical SMILES.

This entry profiles BRD4 across both pharmacological modalities aimed at it: occupancy (bromodomain) inhibitors and targeted protein degraders (PROTACs, molecular glues, chaperone-mediated degraders). Most agents are pan-BET; BRD4-selectivity is noted where established.

Target profile — BRD4 (Bromodomain-containing protein 4)

Field	Value
Target name	Bromodomain-containing protein 4 (BRD4); BET family member (UniProt O60885)
Gene	BRD4 — chromosome 19p13.12; NCBI Gene 23476
Class	Epigenetic 'reader'. BET (Bromodomain & Extra-Terminal) family — two tandem bromodomains (BD1, BD2) plus an ET domain; paralogues BRD2, BRD3 and testis-specific BRDT. Not an enzyme in the conventional sense (an intrinsic HAT/atypical-kinase activity is reported but contested).
Ligands / mechanism	Binds acetyl-lysine marks on histones (H3K27ac; H4K5/8/12/16ac) via conserved bromodomain asparagines; recruits P-TEFb (CDK9–cyclin T1) to phosphorylate RNA Pol II and drive transcriptional elongation. Concentrates at super-enhancers that sustain MYC and other oncogenes.
Expression	Ubiquitous; nuclear / chromatin-associated; remains bound to chromatin through mitosis ('epigenetic bookmarking').

Field	Value
Function	Transcriptional co-activator / elongation factor coupling histone acetylation to output of growth- and survival-driving genes (notably MYC).
Disease rationale	Oncology is the anchor. NUT carcinoma is defined by the BRD4–NUT fusion oncogene (t(15;19)). Hematologic malignancies (AML, myelofibrosis) depend on BRD4 via MYC/BCL2 and NF-κB-driven cytokine programs; selected solid tumors (castration-resistant prostate cancer; ASCL1-driven SCLC). Targeted DEGRADATION is pursued over occupancy to also remove BRD4's non-bromodomain scaffolding functions and achieve deeper, more durable knockdown — a lower-dose / wider-therapeutic-window benefit is hypothesised but not yet demonstrated clinically. A separate cardiovascular / anti-inflammatory hypothesis (BD2-selective apabetalone) reached Phase 3 but FAILED its primary endpoint.
Class liability	Dose-limiting thrombocytopenia is the universal, on-target toxicity of BET inhibitors (BET/GATA1-dependent suppression of megakaryopoiesis), alongside GI toxicity and fatigue, across structurally distinct agents. BD2-selectivity (ABBV-744, NUV-868, apabetalone) has reduced but not eliminated it. This liability is a core driver of interest in degraders and tumor-selective approaches.
Approval status	No BET/BRD4 inhibitor and no BRD4/BET degrader is approved anywhere as of June 2026 — all assets are investigational. Closest to approval: pelabresib (pan-BET inhibitor) in myelofibrosis — MANIFEST-2 met its spleen-volume endpoint but missed the symptom endpoint and is NOT filed; a leukemic-transformation imbalance prompted a new pivotal trial (MANIFEST-3). The only clinical-stage dedicated BRD4 degrader is RNK05047 (Ranok) — a chaperone-mediated 'CHAMP' degrader, not a PROTAC — in Phase 1/2. (Note: vepdegestrant/DEG-471 is an FDA-filed PROTAC but degrades the estrogen receptor, not BRD4, and is excluded.)

Clinical-stage BRD4 / BET agents (inhibitors & degraders)

Compound (code)	Developer	Modality	Route	Phase / status	Lead indicatio
Pelabresib (CPI-0610 / DAK539)	a global pharmaceutical company (ex-a BET-focused	Pan-BET inhibitor	Oral	Phase 3 active. MANIFEST-2 met spleen endpoint (SVR35 66% vs 35%) but missed	Myelofib (+ ruxolit

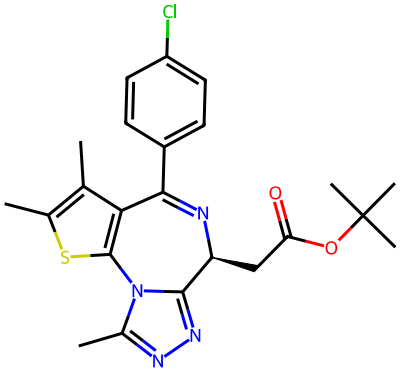
Compound (code)	Developer	Modality	Route	Phase / status	Lead indicatio
	developer / MorphoSys)			symptom endpoint (TSS50); not filed; new pivotal MANIFEST-3 recruiting (2026)	
ZEN-3694	a clinical-stage developer	Pan-BET inhibitor	Oral	Phase 2b active; FDA Fast Track (NUT carcinoma, 2025)	mCRPC (enzaluta NUT carcinom
a global pharma-986158	a global pharmaceutical company	Pan-BET inhibitor	Oral	Phase 1/2 active (pivoted to myelofibrosis)	Myelofib multiple myeloma
INCB057643	Incyte	Pan-BET inhibitor	Oral	Phase 1/2 active (LIMBER program)	Myelofib MPN
ABBV-744	a global pharmaceutical company	BD2-selective inhibitor	Oral	Phase 1b active (MF, + ruxolitinib/navitoclax); AML arm terminated. DLTs still thrombocytopenia/anemia	Myelofib mCRPC
EP31670 (NEO2734)	Epigenetix	Dual BET + CBP/p300 inhibitor	Oral	Phase 1 recruiting	Solid tun NUT carcinom CMML
Apabetalone (RVX-208)	Resverlogix	BD2-selective inhibitor	Oral	Phase 3 completed — BETonMACE MISSED primary MACE endpoint (HR 0.82, p=0.11); development funding-stalled	Cardiova (post-AC type-2 diabetes
RNK05047 (CHAMP-1)	Ranok Therapeutics	BRD4 degrader — chaperone-mediated (CHAMP), not a PROTAC	IV	Phase 1/2 recruiting (NCT05487170). Only BRD4-selective degrader in the clinic	Advance solid tum DLBCL
Birabresib (OTX-015 / MK-8628)	Oncoethix → Merck	Pan-BET inhibitor	Oral	Discontinued (~2017) — limited single-agent efficacy	NUT carcinom AML, DL

Compound (code)	Developer	Modality	Route	Phase / status	Lead indicatio
Molibresib (a global pharmaceutical company525762)	a global pharmaceutical company	Pan-BET inhibitor	Oral	Discontinued — modest efficacy, thrombocytopenia ~51%	NUT carcinom NHL, bre
Trotabresib (CC-90010)	a global pharmaceutical company → a global pharma	Pan-BET inhibitor (CNS-penetrant)	Oral	Discontinued 2024 (strategic) despite documented BBB penetration	Glioblast
Mivebresib (ABBV-075)	a global pharmaceutical company	Pan-BET inhibitor	Oral	Discontinued — myelofibrosis study halted at n=1; thrombocytopenia	AML, sol tumors
NUV-868	Nuvation Bio	BD2-selective inhibitor	Oral	Discontinued 2024 (risk-benefit; Phase 2 declined)	Ovarian, pancreat mCRPC,
RO6870810 (TEN-010)	a global pharmaceutical company	Pan-BET inhibitor	SC	Discontinued — combo study terminated (immune-related AEs)	NUT carcinom ovarian,

Modality 'pan-BET' = binds BRD2/3/4 (and BRDT); 'BD2-selective' = selective for the second bromodomain. MF = myelofibrosis; MPN = myeloproliferative neoplasm; AML = acute myeloid leukaemia; NHL = non-Hodgkin lymphoma; DLBCL = diffuse large B-cell lymphoma; mCRPC = metastatic castration-resistant prostate cancer; SCLC = small-cell lung cancer; TNBC = triple-negative breast cancer; NUT = nuclear-protein-in-testis (midline) carcinoma; CMML = chronic myelomonocytic leukaemia; MACE = major adverse cardiovascular events; BBB = blood–brain barrier. Additional discontinued/dormant BET inhibitors not tabulated: INCB054329, PLX51107, FT-1101 (CC-95775), BI 894999, a global pharmaceutical company2820151, ODM-207, PLX2853.

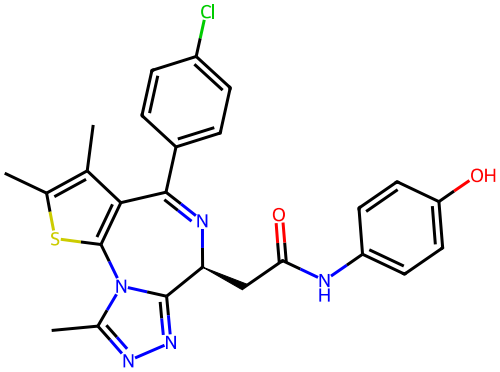
Chemical structures

Structures below are rendered from canonical SMILES retrieved and re-verified against PubChem and ChEMBL (molecular formula confirmed by the Astinova platform for every entry). Shown: the foundational tool inhibitor (+)-JQ1, the clinically disclosed BET inhibitors, and five disclosed tool degraders/PROTACs. The clinical degrader RNK05047 has no publicly disclosed structure; the inhibitor codes ZEN-3694, a global pharma-986158, INCB057643 and EP31670 are likewise not curated in public small-molecule databases and are omitted.



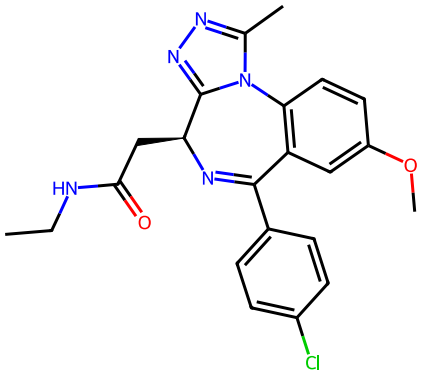
(+)-JQ1 (tool inhibitor)

C23H25ClN4O2S · MW 457.0 · ChEMBL: CHEMBL1957266



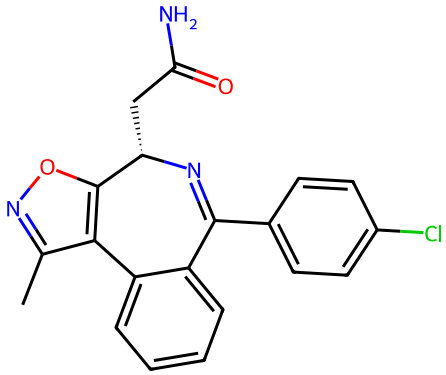
Birabresib (OTX-015)

C25H22ClN5O2S · MW 492.0 · ChEMBL: CHEMBL3581647



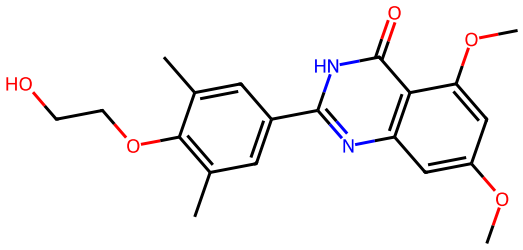
Molibresib (a global pharmaceutical company525762)

C22H22ClN5O2 · MW 423.9 · ChEMBL: CHEMBL1232461



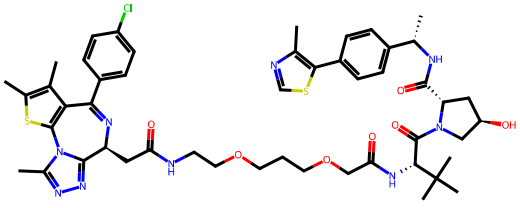
Pelabresib (CPI-0610)

C20H16ClN3O2 · MW 365.8 · ChEMBL: CHEMBL4303404



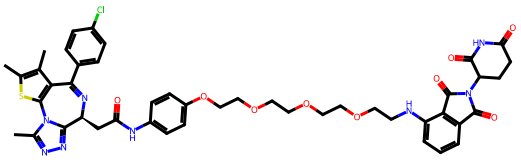
Apabetalone (RVX-208)

C20H22N2O5 · MW 370.4 · ChEMBL: CHEMBL2393130



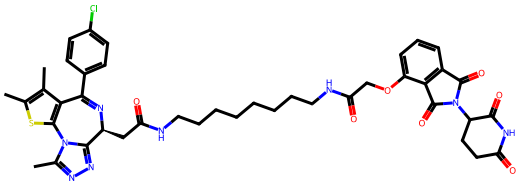
DEG-771 (VHL PROTAC)

C49H60ClN9O7S2 · MW 986.7 · ChEMBL: CHEMBL4215078



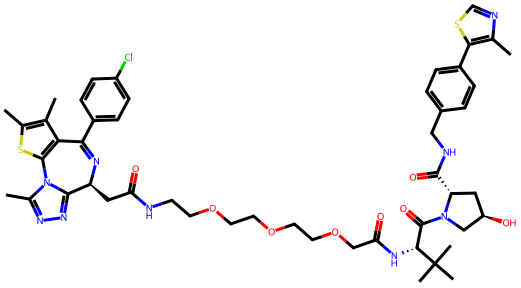
DEG-825 (CRBN PROTAC)

C46H47ClN8O9S · MW 923.4 · ChEMBL: CHEMBL4226052



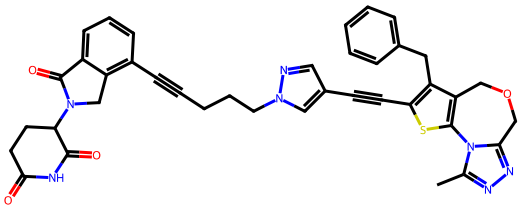
dBET6 (CRBN PROTAC)

C42H45ClN8O7S · MW 841.4 · ChEMBL: CHEMBL4303781



MZ1 (VHL PROTAC, BRD4-pref.)

C49H60ClN9O8S2 · MW 1002.7 · ChEMBL: CHEMBL4226570



QCA570 (CRBN PROTAC)

C39H33N7O4S · MW 695.8 · PubChem CID: 134348221

Preclinical & journal (literature) compounds

Targeted BRD4 degradation is, as of mid-2026, overwhelmingly a preclinical / tool-compound field — the molecules below defined the chemistry and validated that removing BRD4 protein (rather than merely blocking its bromodomains) drives deeper MYC suppression and, in models, tumor regression. The E3 ligase recruited is noted (VHL or CRBN; one intramolecular molecular glue). (+)-JQ1 is included as the foundational bromodomain probe from which most of these degraders were built.

Compound	Origin · E3 ligase	Note (primary reference)
(+)-JQ1	Bradner / Knapp · n/a (inhibitor)	First-in-class, selective BET bromodomain inhibitor; the chemical probe that validated BET as a drug target and the warhead for most BET PROTACs. Filippakopoulos et al., Nature 2010 (PMID 20871596).
DEG-771	a protein-degradation company / Crews (Yale) · VHL	Pan-BET PROTAC; first to show tumor regression in castration-resistant prostate cancer models, outperforming BET inhibition. Raina et al., PNAS 2016;113(26):7124 (PMID 27274052).
DEG-825	Crews / a protein-degradation company · CRBN (pomalidomide)	OTX-015-based BRD4 PROTAC; rapid, sustained BRD4 degradation in Burkitt lymphoma. Lu et al., Chem Biol 2015;22(6):755 (PMID 26051217).
dBET1	Bradner / Winter (Dana-Farber) · CRBN	First JQ1–phthalimide degrader; established 'phthalimide conjugation' for in-vivo target degradation. Winter et al., Science 2015;348(6241):1376 (PMID 25999370).
dBET6	Bradner / Winter · CRBN	Improved, cell-permeable BET degrader used to show BET proteins act as master elongation factors. Winter et al., Mol Cell 2017;67(1):5 (PMID 28673542).
MZ1	Ciulli (Dundee) · VHL	First PROTAC with preferential BRD4 (over BRD2/3) degradation, from JQ1 + VHL ligand. Zengerle, Chan & Ciulli, ACS Chem Biol 2015;10(8):1770 (PMID 26035625).
AT1	Ciulli (Dundee) · VHL	Structure-guided, highly BRD4-selective PROTAC; the accompanying MZ1–VHL–BRD4(BD2) ternary crystal structure explained cooperative selectivity. Gadd et al., Nat Chem Biol 2017;13(5):514 (PMID 28288108).
QCA570	S. Wang (Michigan) · CRBN	Exceptionally potent (picomolar) BET degrader; complete tumor regression in leukemia xenografts. Qin et al., J Med Chem 2018;61(15):6685 (PMID 30019901).
ZBC260 / BETd-260	S. Wang (Michigan) · CRBN	Picomolar BET degrader capable of tumor regression. Zhou et al., J Med Chem 2018;61(2):462 (PMID 28339196).
macroPROTAC-1	Ciulli (Dundee) · VHL	Macrocyclized MZ1 analogue; rigidified ternary complex with improved degradation selectivity. Testa

Compound	Origin · E3 ligase	Note (primary reference)
		et al., Angew Chem Int Ed 2020;59(4):1727 (PMID 31746102).
IBG1	Ciulli (Dundee) + Winter (CeMM) · DCAF16/11	Intramolecular bivalent 'glue' degrading BRD4/BRD2 via a novel DCAF16/DCAF11 mechanism (not classic VHL/CRBN recruitment). Hsia et al., Nature 2024;627(8002):204 (PMID 38383787).

Key sources

ChEMBL & PubChem (compound records, SMILES, formulae — all structures the Astinova platform-verified) · ClinicalTrials.gov (NCT05487170 RNK05047; NCT04603495 MANIFEST-2; NCT07357727 MANIFEST-3; NCT04986423 ZEN-3694; NCT04817007 a global pharma-986158; NCT04279847 INCB057643; NCT04454658 ABBV-744; NCT02586155 BETonMACE) · Rampal et al., Nature Medicine 2025 (MANIFEST-2, PMID 40065169) · Ray et al., JAMA 2020 (BETonMACE) · Faivre et al., Nature 2020 (ABBV-744 BD2-selective) · Filippakopoulos et al., Nature 2010 (JQ1) · Raina et al., PNAS 2016 (DEG-771) · Lu et al., Chem Biol 2015 (DEG-825) · Winter et al., Science 2015 (dBET1) & Mol Cell 2017 (dBET6) · Zengerle et al., ACS Chem Biol 2015 (MZ1) · Gadd et al., Nat Chem Biol 2017 (AT1) · Qin et al., J Med Chem 2018 (QCA570) · Zhou et al., J Med Chem 2018 (ZBC260) · Testa et al., Angew Chem Int Ed 2020 (macroPROTAC-1) · Hsia et al., Nature 2024 (IBG1) · Ranok / a global pharmaceutical company / Resverlogix / Nuvation company disclosures (2022–2026) · review: 'An updated patent review of BRD4 degraders' (PMC11427152). Development phases reflect information available at the compile date and may change.