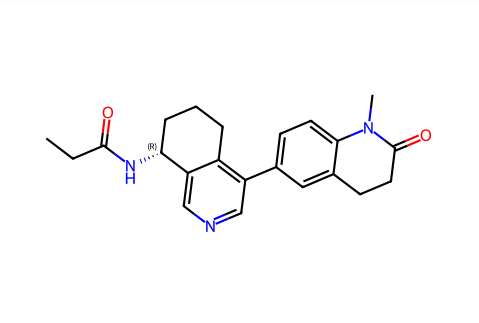
Baxdrostat (Baxfendy™) — Drug Intelligence Dossier

Compiled: 2026-05-23 · **Trigger event:** FDA approval, 2026-05-18 **Innovator:** AstraZeneca plc (asset acquired via CinCor Pharma, Feb 2023; originally developed at F. Hoffmann-La Roche) **Status:** Approved NME

INN: baxdrostat | **Brand (US):** Baxfendy™ | **CAS:** 1428652-17-8 | **ChEMBL:** CHEMBL4113975 | **MW:** 363.5 g/mol

NDA #: TBD — to be confirmed on Drugs@FDA (NDA number not yet published in openFDA at compile time) | **Approval:** 2026-05-18



API structure

`CCC(=O)N[C@@H]1CCCc2c(-c3ccc4c(c3)CCC(=O)N4C)cncc21`

t½: 26–31 h (supports once-daily dosing) · **Tmax:** 0.5–2 h (rapid absorption)

1. Identity & Molecular Profile

Field	Value
INN	baxdrostat
Brand (US)	BAXFENDY
CAS	1428652-17-8
UNII	NF3P9Z8J5Y
ChEMBL	CHEMBL4113975
KEGG	D12789
PubChem CID	71535962
Molecular formula	C22H25N3O2
MW (free base)	363.5 g/mol
IUPAC	N-[(8R)-4-(1-methyl-2-oxo-3,4-dihydroquinolin-6-yl)-5,6,7,8-tetrahydroisoquinolin-8-yl]propanamide
SMILES	`CCC(=O)N[C@@H]1CCCc2c(-c3ccc4c(c3)CCC(=O)N4C)cncc21`
InChIKey	VDEUDSRUMNAXJG-LJQANCHMSA-N
Ro5 violations	0 (cLogP 3.56, PSA 62.30 Å², HBD 1, HBA 3, RTB 3)
QED	0.91

Structural class & SAR background: Convergent synthesis disclosed in WO 2014/135561 (Roche). Eastern fragment: 1-methyl-6-bromo-3,4-dihydroquinolin-2(1H)-one (INT-2) → pinacolboronate (INT-3, via Pd/B2pin2 Miyaura). Western fragment: (R)-8-aminotetrahydroisoquinoline scaffold, Boc-protected (INT-5), 4-bromide for coupling. Late-stage convergence: Suzuki C–C coupling at THIQ-C4/DHQ-C6 (→ INT-7), TFA Boc deprotection (→ INT-8),...

Pharmacology snapshot

Target	Activity (ChEMBL pChEMBL)	Selectivity
Cytochrome P450 11B2, mitochondrial	EC50 = 14.0 nM	—
Cytochrome P450 11B1, mitochondrial	EC50 = 980.0 nM	—

PK summary: - t½: 26–31 h (supports once-daily dosing) - Tmax: 0.5–2 h (rapid absorption) - Steady-state PD: Plasma aldosterone reduced 51–73% on day 10 of MAD; no meaningful effect on cortisol (selectivity confirmed clinically) - Food effect: Minimal expected (no specific food-effect language in

BaxHTN protocol); QD oral

2. Patent Landscape & Exclusivity

2.1 Key patent filings

Patent / Application	Type	Assignee	Filed	Expiry (~)	Key Claims & FTO Strategy
WO 2014/135561 A1 (US 9,458,135 B2; EP 2,964,628 B1)	Composition of matter	F. Hoffmann-La Roche AG	2014-03-05 (priority 2013-03-08)	~Mar 2034 nominal + up to 5 yr PTE → effective LoE 2036–2039	Generic Markush and specific compound claims on dihydroquinoline-2-one CYP11B2/CYP11B1 inhibitors including baxdrostat (worked example). The blocking COM patent — cannot design around the API itself. **FTO solution:** wait for expiry, or compete on non-infringing process, polymorph, formulation, or method-of-use.
US 9,353,081 B2 (NZ 620652 B2 family)	Composition (parent family)	F. Hoffmann-La Roche AG	2012-09-14	~Sep 2032 nominal	Earlier bicyclic dihydroquinoline-2-one derivatives — broader Markush than WO 2014/135561, may also read on baxdrostat. **FTO check:** confirm whether baxdrostat falls within the genus scope; if so, this is the earliest priority filing and the controlling expiry for COM.
WO 2025/125513 A1	Combination / use	AstraZeneca Ireland Limited	2024-12-12	~Dec 2044 nominal	Fixed-dose combination of an SGLT2 inhibitor (dapagliflozin) and baxdrostat for chronic kidney disease and HF. Method-of-treatment claim. **FTO impact:** not blocking for a generic baxdrostat monotherapy; potential blocker for FDC competitors. Filed alongside Phase 3 NCT06268873 / NCT06742723 / NCT06677060.
MX 2025/001406 A	Method of treatment	Cincor Pharma Inc (now AstraZeneca)	2025-02-04	~Feb 2045 nominal	Treating hypertension with baxdrostat (use claim). Secondary indication patent — unlikely to add exclusivity in major markets where the NCE/COM dominates. Mexico-only; check WO / US counterparts.
WO 2025/002335 A1	Crystal form (third-party)	Suzhou Crystallization Pharma Co., Ltd	2024-06-28	~Jun 2044 nominal (if granted)	Specific crystalline polymorph of baxdrostat with claimed XRPD / DSC fingerprint — a generic-facing filing that does **NOT** extend AZ's exclusivity. **FTO impact for AZ:** none on monotherapy; potential opposition target. **FTO solution for generics:** target a different polymorph (Form II/III, amorphous, or HPMC-AS spray-dried dispersion).
CN 117247371 B	Process (third-party)	Shanghai Xianghui Pharma Technology Co.	2023-09-18	~Sep 2043 nominal	Specific preparation method of baxdrostat. Third-party Chinese filing — does **NOT** extend AZ's exclusivity. **FTO solution:** if AZ's CMO uses a non-overlapping route this is irrelevant; for non-AZ manufacturers, design around (different chirality-setting step, different coupling order).
WO 2024/222814 A1 (CN 118852196 A; CN 118852103 A)	Composition (competitor family)	Changchun GeneScience Pharmaceuticals Co., Ltd	2024-04-25	~Apr 2044 nominal	Generic Markush on related CYP11B2 inhibitor scaffolds — competitor chemistry, not baxdrostat itself. **Competitive intelligence:** signals Chinese players entering the ASI space; track for FTO conflicts on AZ's follow-on ASIs.
EP 4 711 361 A1	Composition (competitor)	Jiangsu Deyuan Pharmaceutical Co., Ltd	2024-05-11	~May 2044 nominal	Nitrogen-containing heterocyclic compounds. **FTO check:** confirm whether claims encompass baxdrostat or close analogues.
Process patent(s) — Roche/AZ (expected, not yet identified)	Process	F. Hoffmann-La Roche AG / AstraZeneca AB	~2017–2020 (typical 3–5 yr after COM)	~2037–2040 nominal	**Expected but not yet identified** — typical originator pattern. Likely covers chirality-setting step (transaminase / chiral hydrogenation), specific Suzuki conditions (Pd source, ligand, base), Pd scavenging. **Action:** monitor Espacenet / PATENTSCOPE with assignee = Hoffmann-La Roche, AstraZeneca, CinCor, CinRx + IUPAC keywords.
Polymorph patent — Roche/AZ (expected, not yet identified)	Polymorph	F. Hoffmann-La Roche AG / AstraZeneca	~2018–2024	~2038–2044 nominal	**Expected before NDA approval (mid-2025) but not yet identified.** Will claim specific Form (likely Form I) with XRPD 2θ peaks, DSC endotherm, hygroscopicity range. The fact that Suzhou Crystallization Pharma filed WO 2025/002335 suggests originator polymorph filing exists. **Action:** retrieve from Espacenet once granted.
Formulation patent — AZ (expected, not yet identified)	Formulation	AstraZeneca AB	~2022–2024	~2042–2044 nominal	**Expected; not yet identified.** Likely tablet excipient composition for 1/2 mg immediate-release. **Action:** monitor once FDA label posts on DailyMed; cross-check excipient list.

2.2 US regulatory exclusivities

Exclusivity	Expiry	Para IV gate	Applies?
NCE (new chemical entity)	2031-05-18	2030-05-18	Yes — baxdrostat is a new molecular entity
Orphan-drug exclusivity	—	—	Not granted (HTN is not a rare disease); may apply if primary aldosteronism (NCT07007793) gets orphan designation in 2028
Pediatric exclusivity (+6 mo)	TBD	TBD	TBD — pediatric study plan (PSP) likely filed with NDA; +6 mo gates on existing patent/exclusivity if granted
Patent Term Extension (PTE, 35 USC §156)	up to 5 yr extension on COM patent	—	Likely — typical for full-cycle NMEs; clock starts at FDA approval (2026-05-18). Calculation uses 1/2 NDA review time + IND clock; expect 3–5 yr extension on US 9,458,135 → effective LoE 2037–2039

2.3 ANDA / Paragraph IV monitoring calendar

- Approval date: **2026-05-18**
- Para IV ANDA window opens: **2030-05-18 (NCE +4 yr)**
- NCE exclusivity ends: **2031-05-18 (NCE +5 yr)**
- COM patent nominal expiry: **~Mar 2034 (US 9,458,135)**
- Effective LoE (with PTE): **~2037–2039 effective LoE (PTE 3–5 yr)**
- Likely first Para IV filers: Aurobindo, Lupin, Hetero, MSN, Glenmark

Date	Event
2030-05-18	First Para IV ANDA window opens — start monitoring FDA Para IV first-applicant list
2031-05-18	NCE exclusivity ends — additional generic filings possible
2034-03 (nominal)	COM patent (US 9,458,135) nominal expiry — earliest generic launch absent PTE
2037–2039	Effective LoE after PTE; realistic generic entry window

2.4 SureChEMBL patent–compound cross-references

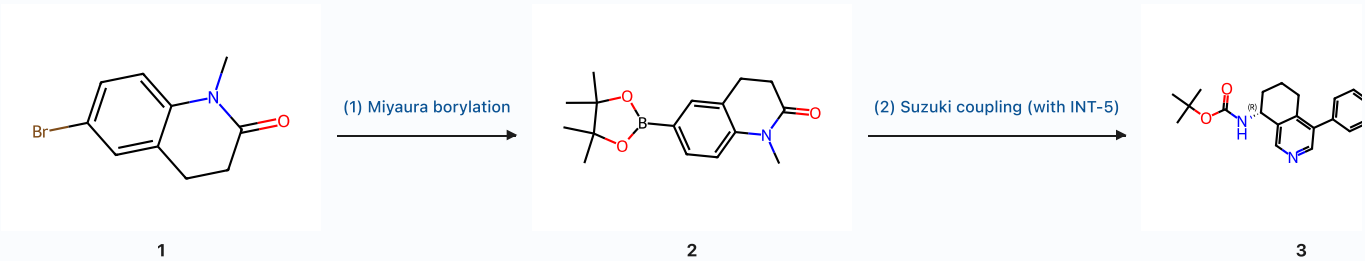
No SureChEMBL xref via ChEMBL. Manual search: SureChEMBL (InChIKey) · SureChEMBL (free-text) · Lens.org chemistry.

---

3. Synthesis Route of the Originator

Convergent synthesis disclosed in WO 2014/135561 (Roche). Eastern fragment: 1-methyl-6-bromo-3,4-dihydroquinolin-2(1H)-one (INT-2) → pinacolboronate (INT-3, via Pd/B2pin2 Miyaura). Western fragment: (R)-8-aminotetrahydroisoquinoline scaffold, Boc-protected (INT-5), 4-bromide for coupling. Late-stage convergence: Suzuki C–C coupling at THIQ-C4/DHQ-C6 (→ INT-7), TFA Boc deprotection (→ INT-8), propionoylation with propionyl chloride / Et3N (→ baxdrostat). Chirality-setting step is the key process-IP question; Roche likely uses asymmetric reductive amination or transaminase on the THIQ-C8 ketone (specific route in patent working examples — not yet disclosed in open primary literature).

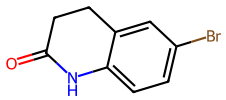
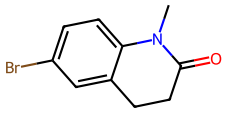
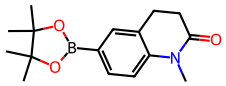
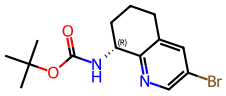
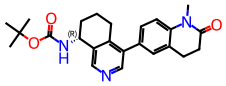
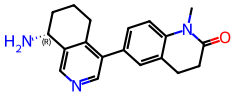
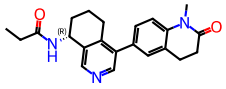
Scheme. 4-step convergent route[a]



[a]Reagents and conditions: (1) B2pin2 (1.2 eq), PdCl2(dppf) (3 mol%), KOAc (3 eq), 1,4-dioxane, 90 °C, 6 h; (2) (R)-INT-5 [tert-butyl (4-bromo-5,6,7,8-tetrahydroisoquinolin-8-yl)carbamate] (1.0 eq), Pd(PPh3)4 (5 mol%), Na2CO3 (aq), dioxane/H2O 4:1, 85 °C, 12 h; (3) TFA / CH2Cl2 1:1, 0 °C → rt, 1 h; (4) Propionyl chloride (1.1 eq), Et3N (2 eq), CH2Cl2, 0 °C → rt, 2 h.

Stand-alone (print-friendly) version: `baxdrostat_synthesis_scheme.html`.

3.1 Key intermediates

Label	Structure	Name	Sourcing / role
INT-1		6-bromo-3,4-dihydroquinolin-2(1H)-one	Commodity, Chinese/Indian CMOs; ~$50–100/kg at scale
INT-2		1-methyl-6-bromo-3,4-dihydroquinolin-2(1H)-one	N-methylation (NaH/MeI) of INT-1; trivial scale-up
INT-3		Eastern pinacolboronate	Miyaura borylation; commodity B2pin2 + Pd cat
INT-5		(R)-Boc-4-bromo-tetrahydroisoquinolin-8-amine	Western fragment — chirality-setting step; **PROCESS-IP-CRITICAL**. Likely asymmetric routes: enzymatic transaminase, chiral hydrogenation (Rh/Ir-bisphosphine), or classical resolution
INT-7		(R)-Boc-protected biaryl	Suzuki product of INT-3 + INT-5; Pd-residual control to ≤10 ppm per ICH Q3D
INT-8		(R)-Penultimate free amine	TFA / DCM Boc removal of INT-7; quantitative
API		Baxdrostat (free base)	Propionoylation of INT-8 with propionyl chloride / Et3N

3.2 Process IP-critical considerations

For non-infringing process scoping, focus IP clearance on:

- the **chirality-setting step** on the THIQ-C8 amine (asymmetric reductive amination, transaminase, or classical resolution) — Roche/AZ process IP almost certainly claims this;
- the **Suzuki C–C coupling step** between INT-3 boronate and INT-5 aryl bromide (Pd source, ligand, base, solvent, Pd-residual control);
- the **polymorph / salt / crystallization** of the free base API.

4. Crystal Forms, Salts, and Solid-State Profile

- **API in approved drug product:** free base (per AZ press release; confirm via DailyMed once label posted)
- **Strengths approved:** Tablets 1 mg and 2 mg (BaxHTN dosing)
- **Third-party polymorph activity:** WO 2025/002335 (Suzhou Crystallization Pharma) filed Form A — a generic-facing filing; does **NOT** extend AZ's exclusivity
- **Originator polymorph filing:** expected before NDA approval but not yet identified in PATENTSCOPE — monitor Espacenet

4.1 Available experimental protein structures (RCSB PDB)

PDB ID	Target	Title	Resolution (Å)	Method	Released
7E7F	Cytochrome P450 11B2, mitochondrial	Human CYP11B1 mutant in complex with metyrapone	1.4	X-RAY DIFFRACTION	2022-01-05
8UQF	Cytochrome P450 11B2, mitochondrial	Crystal structure of designed cortisol-binding...	1.52	X-RAY DIFFRACTION	2024-11-20
6ITQ	Cytochrome P450 11B2, mitochondrial	Crystal structure of cortisol complexed with...	1.526	X-RAY DIFFRACTION	2019-07-24
3PB9	Cytochrome P450 11B1, mitochondrial	Crystal structure of the catalytic domain of...	1.12	X-RAY DIFFRACTION	2011-02-02
5S8M	Cytochrome P450 11B1, mitochondrial	XChem group deposition -- Crystal Structure of...	1.2	X-RAY DIFFRACTION	2021-01-13
7E7F	Cytochrome P450 11B1, mitochondrial	Human CYP11B1 mutant in complex with metyrapone	1.4	X-RAY DIFFRACTION	2022-01-05

For SAR / docking and ligand-bound forms relevant to polymorph analysis.

---

5. Clinical & Regulatory Profile

5.1 Approved indication

- **Approval date (US):** 2026-05-18
- **NDA number:** TBD — to be confirmed on Drugs@FDA (NDA number not yet published in openFDA at compile time)
- **Brand (US):** Baxfendy™
- **Indication:** Add-on therapy for adults with hypertension not adequately controlled by other antihypertensives (per BaxHTN, NCT06034743)
- **Dosage form / strength:** Oral tablets, 1 mg and 2 mg, once daily
- **Review pathway:** NDA Priority Review accepted Dec 2025; approval May 18, 2026; no AdComm convened

5.2 Pivotal trial

BaxHTN (NCT06034743, n=796) — Flack et al., NEJM 2025 (DOI 10.1056/NEJMoa2507109)

Official title: A Randomised, Double-Blind, Placebo-Controlled, Parallel Group Study to Assess the Efficacy and Safety of Baxdrostat in Participants With Uncontrolled Hypertension on Two or More Medications Including Participants With Resistant Hypertension

Design: Phase III, multicentre, randomised, double-blinded, placebo-controlled, parallel group, 1 mg / 2 mg / placebo QD oral · **Start:** 2023-11-22 · **Primary completion:** 2025-05-21 · **Final completion:** 2025-10-10 · **Sites:** 263 across 29 countries

Countries: US, UK, Germany, France, Italy, Spain, Canada, Japan, South Korea, Australia, India, Argentina, Brazil, South Africa, Turkey, plus 14 others (full list in raw/clinicaltrials.json)

Key inclusion criteria: - Age ≥ 18 yr - Mean seated SBP 140–<170 mmHg at screening (≥135 at baseline) - Uncontrolled HTN (2 antihypertensives, incl. diuretic) OR Resistant HTN (≥3 antihypertensives, incl. diuretic) - eGFR ≥ 45 mL/min/1.73m² - Serum K^+ 3.5–<5.0 mmol/L

Key exclusion criteria: - Mean seated SBP ≥170 or DBP ≥110 mmHg - Secondary HTN (renal artery stenosis, pheochromocytoma, Cushing's, coarctation, untreated thyroid) - NYHA class IV heart failure - Persistent atrial fibrillation - Serum Na^+ <135 mmol/L

Endpoint	Result
Placebo-corrected ΔSBP (1 mg) at wk 12	**−8.7 mmHg**
Placebo-corrected ΔSBP (2 mg) at wk 12	**−9.8 mmHg (absolute −15.7 mmHg)**
Hyperkalemia (>5.5 mmol/L) — baxdrostat (clinically used threshold)	**~12%**
Hyperkalemia (>5.5 mmol/L) — placebo	**~3%**
Hyperkalemia (>6.0 mmol/L) — 1 mg (severe threshold)	**2.3%**
Hyperkalemia (>6.0 mmol/L) — 2 mg	**3.0%**
Hyperkalemia (>6.0 mmol/L) — placebo	**0.4%**
Treatment discontinuation rate (baxdrostat arms)	**~2% (low)**
Cortisol suppression / adrenal insufficiency	**None observed (selectivity confirmed in vivo)**

Secondary endpoints: - Change from baseline in seated SBP for 2 mg in resistant-HTN subpopulation @ wk 12 - Change from baseline in seated SBP for 1 mg in resistant-HTN subpopulation @ wk 12 - Change from baseline in seated DBP for 2 mg @ wk 12 - Change from baseline in seated DBP for 1 mg @ wk 12 - Proportion achieving seated SBP <130 mmHg (1 mg and 2 mg) @ wk 12 - Change from randomised-withdrawal baseline (wk 24) in seated SBP for 2 mg @ wk 32

Label requirements: - Baseline serum K^+ and Na^+ before initiating - Periodic K^+ and Na^+ monitoring during treatment - Dose adjustment / discontinuation if K^+ >5.5 mmol/L

5.2.1 Supportive trial — Bax24

Bax24 (NCT06168409, n=218) — Qureshi AJ et al., Cardiovasc Drugs Ther 2026 (DOI 10.1007/s10557-026-07887-2)

Endpoint	Result
24-h ambulatory SBP reduction (baxdrostat)	**−16.6 mmHg**
Placebo-corrected 24-h ABPM SBP reduction	**−14.0 mmHg (p<0.001)**

Among the largest 24-h ABPM SBP reductions reported in contemporary resistant-HTN trials

5.2.2 AstraZeneca Phase 3 baxdrostat program

Trial	Name	Indication	n	Sites	Primary completion	Status
NCT06034743	BaxHTN	Uncontrolled / resistant HTN	796	263	2025-05-21	Completed (pivotal)
NCT06168409	Bax24	Resistant HTN, 24-h ABPM	218	102	2025-08-17	Completed
NCT06344104	BaxAsia	Asian uncontrolled / resistant HTN	326	93	2025-11-24	Completed
NCT06268873	(CKD+HTN)	CKD + HTN with dapagliflozin	2554	565	2028-02-24	Active, not recruiting
NCT06742723	(CKD outcomes)	CKD renal outcomes with dapagliflozin	5000	759	2029-12-18	Recruiting

AstraZeneca currently sponsors 5 Phase-3 baxdrostat trials totalling 8,892 enrolled / planned (BaxHTN 796 ✓, Bax24 218 ✓, BaxAsia 326 ✓, CKD+HTN dapa 2,554, CKD outcomes dapa 5,000). Largest of these (CKD outcomes NCT06742723) runs at 759 trial sites globally.

5.3 Label-expansion pipeline (ClinicalTrials.gov live)

Total trials matching this intervention: **20**.

Phase 3 — 7 trials

Trial	Condition	n	Status	Primary completion	Sponsor
NCT06677060	Heart Failure	11300	RECRUITING	2029-12-17	AstraZeneca
NCT06742723	Chronic Kidney Disease and Hypertension	5000	RECRUITING	2029-12-18	AstraZeneca
NCT06268873	Chronic Kidney Disease and Hypertension	2554	ACTIVE_NOT_RECRUITING	2028-02-24	AstraZeneca
NCT06034743	Uncontrolled Hypertension; Resistant Hypertension	796	COMPLETED	2025-05-21	AstraZeneca
NCT06344104	Uncontrolled Hypertension; Resistant Hypertension	326	COMPLETED	2025-11-24	AstraZeneca
NCT07007793	Primary Hyperaldosteronism	250	RECRUITING	2028-02-18	AstraZeneca
NCT06168409	Resistant Hypertension	218	COMPLETED	2025-08-17	AstraZeneca

Phase 2 — 4 trials

Trial	Condition	n	Status	Primary completion	Sponsor
NCT04519658	Resistant Hypertension	275	COMPLETED	2022-06-14	CinCor Pharma, Inc.
NCT05137002	Uncontrolled Hypertension	249	COMPLETED	2022-09-13	CinCor Pharma, Inc.
NCT07222917	Chronic Kidney Disease and Hypertension	218	RECRUITING	2027-05-24	AstraZeneca
NCT06336356	Uncontrolled Hypertension	48	COMPLETED	2024-12-04	AstraZeneca

Phase 1 — 9 trials

Trial	Condition	n	Status	Primary completion	Sponsor
NCT05500820	Hypertension	56	COMPLETED	2020-04-03	AstraZeneca
NCT05966324	Hypertension	41	COMPLETED	2022-09-20	AstraZeneca
NCT05470725	Hypertension	33	COMPLETED	2021-04-30	AstraZeneca
NCT06194032	Healthy Participants	28	COMPLETED	2024-05-13	AstraZeneca
NCT06657105	Healthy Participants	22	COMPLETED	2025-02-03	AstraZeneca
NCT05961397	Hypertension	20	COMPLETED	2022-04-15	AstraZeneca
NCT06357520	Healthy Participants	14	COMPLETED	2024-06-17	AstraZeneca
NCT05963009	Hypertension	14	COMPLETED	2020-04-29	AstraZeneca

5.4 Key peer-reviewed literature

According to PubMed, the following recent peer-reviewed records are most relevant:

- Qureshi AJ et al., *Cardiovasc Drugs Ther* 2026 — Baxdrostat and Aldosterone Synthase Inhibitors: A New Class for Treatment-resistant Hypertension (PMID 42126470) — *Direct baxdrostat review with updated BaxHTN + Bax24 numbers used in §5.2*
- Gallo G et al., *Eur Heart J Suppl* 2026 — Aldosterone synthesis inhibitors in resistant hypertension: the BaxHTN trial (PMID 42099482) — *ASI class review centred on BaxHTN*
- Cherney DZI et al., *Diabetes Obes Metab* 2026 — Effects of Vicadrostat/Empagliflozin in People With Chronic Kidney Disease: Metabolic Subgroup Analyses (PMID 42086479) — *Competitor (vicadrostat / BI 690517) Ph2 CKD subgroup data used in §7.4*
- Gill OA et al., *Dose Response* 2026 — Optimal Dose of Lorundrostat in Uncontrolled Hypertension: A Dose Response Meta-Analysis (PMID 42130914) — *Competitor (lorundrostat) meta-analysis used in §7.4*
- Schnell O et al., *Cardiovasc Diabetol* 2026 — CVOT Summit Report 2025: advances along the cardiovascular-kidney-metabolic disease continuum (PMID 42092956) — *Highlights baxdrostat (BaxHTN) and finerenone + empagliflozin (CONFIDENCE) — CKM positioning*
- Parisien-La Salle S et al., *Endocrinol Metab Clin North Am* 2026 — Evaluation and Management of Primary Aldosteronism (PMID 42067270) — *Confirms ASIs as new option for PA — supports §5.2 label-expansion thesis (NCT07007793)*
- Todua I et al., *Am J Med* 2026 — Management of salt-sensitive hypertension in clinical settings (PMID 42103091) — *Salt-sensitive HTN as a target sub-population; ASIs noted*
- Mohagaonkar S et al., *Br J Pharmacol* 2026 — Atrial natriuretic peptide counteracts aldosterone secretion by preventing acute angiotensin II-induced... (PMID 42116793) — *Mechanistic background — ANP/cGMP/PDE2A pathway opposing aldosterone*

5.5 Endpoint landscape across Phase 3 resistant-HTN trials

Across 30 Phase-3 resistant-HTN trials analysed (ClinicalTrials.gov v2 MCP): the canonical primary endpoint is change-from-baseline in seated office SBP at week 12. Secondary endpoints centre on DBP, 24-h ABPM, and the proportion achieving SBP <130 mmHg. BaxHTN's 2-mg arm (–15.7 mmHg absolute / –9.8 placebo-corrected) and Bax24's –14.0 mmHg placebo-corrected 24-h ABPM are positioned at the high end of the class.

---

6. PK / ADME / Safety profile

6.1 Pharmacokinetics & metabolism

Property	Value
Half-life (t½)	26–31 h (supports once-daily dosing)
Tmax	0.5–2 h (rapid absorption)
Primary metabolism	CYP3A4 (inferred from itraconazole DDI study NCT06357520; itraconazole = potent 3A4 inhibitor)
PD marker (aldosterone suppression)	Plasma aldosterone reduced 51–73% on day 10 of MAD; no meaningful effect on cortisol (selectivity confirmed clinically)
Food effect	Minimal expected (no specific food-effect language in BaxHTN protocol); QD oral
Hepatic impairment	Likely dose adjustment in moderate–severe (CYP3A4 substrate); specific study pending
Renal impairment	Small molecule (MW 363); not dialyzable; expect modest clearance reduction at low eGFR but CKD development program (NCT06268873) ongoing
QT/QTc study	NCT06194032 — thorough QT/QTc (Phase 1), negative at therapeutic and supratherapeutic doses
^{14}C-AME (mass balance)	NCT05961384 — ^{14}C-baxdrostat mass balance (completed; full report not yet published)

DDI / interaction flags: - Strong CYP3A4 inhibitors: Ketoconazole, ritonavir, clarithromycin — expect dose-reduction / contraindication language - Strong CYP3A4 inducers: Rifampin, phenytoin, carbamazepine, St. John's wort — expect reduced efficacy warning - Transporter: MATE1 / MATE2-K inhibition IC_{50} ~1.3–2.7 µM (per Selleck data) — clinically relevant for metformin renal clearance

6.2 Safety profile & pharmacovigilance priorities

Most frequent AEs: - Hyperkalemia (dose-dependent) - Hyponatremia - Hypotension - Dizziness

Rare signals to monitor: - Adrenal insufficiency (theoretical at supratherapeutic doses) - Muscle spasms - Drug-induced hyperkalemia in patients on RAAS-blockers

Postmarketing priorities: - Rare adrenal events in elderly - Hyperkalemia outcomes in combination with ACEi/ARB/MRA - Long-term effect on plasma renin activity

---

7. Commercial Outlook & Competitive Landscape

7.1 Market context

Metric	Value
US adults with uncontrolled HTN despite ≥2 medications	~23 million (AZ)
Global HTN prevalence	~1.4 billion (WHO)
Global antihypertensive market 2024	USD 23.9 B (Global Market Insights)
Global antihypertensive market 2034	USD 35.5 B (4.1% CAGR)

7.2 Peak-sales forecasts (USD)

Source	Forecast	Note
AstraZeneca (management guidance)	**>$5 B peak**	Stated alongside AZ's $80 B 2030 revenue target
Leerink Partners	**up to $10 B**	Bull case — HTN + CKD + HF multi-indication success
UBS	**~$4 B peak**	58% PoS in their pre-approval PharmaValues model
GlobalData	**$89 M US 2035**	Conservative outlier — likely under-models class adoption

Dispersion finding: ~100× spread between GlobalData ($89 M US 2035) and Leerink ($10 B). Reflects disagreement on (a) payer willingness vs. generic spironolactone, (b) CKD/HF Phase 3 readouts (2028–2029), (c) FDC-with-dapagliflozin opportunity. Triangulate your own model.

7.3 Demand drivers

Tailwinds - ~50% of HTN patients uncontrolled on ≥2 drugs (PATHWAY-2 baseline) - Spironolactone aldosterone-targeting precedent established; ASI is cleaner (no anti-androgen / gynecomastia, no MR off-target) - First-in-class FDA label; NEJM pivotal publication; strong KOL voice ("we have been waiting...") - Multi-indication ladder: CKD, HF prevention, primary aldosteronism (each adds $1–3 B optionality if positive) - AZ commercial muscle (Farxiga sales force overlap)

Headwinds - Generic spironolactone <$0.20/day + finerenone are entrenched 4th-line options - Hyperkalemia monitoring burden (K^+ + Na^+) raises cost-of-care - Payer pushback expected: cost-vs-benefit hurdle high vs. cheap incumbents - Lorundrostat (Mineralys) + vicadrostat (Boehringer) within 1–2 yrs of follow-on entry - US IRA negotiation eligibility: 9–11 yr post-approval → price pressure ~2035–2037

7.4 Comparator / competitive class

Asset	Code	Sponsor	Mechanism	Selectivity	Stage	IP cliff
Lorundrostat	MLS-101	Mineralys Therapeutics	Aldosterone synthase inhibitor (CYP11B2)	~100× vs. CYP11B1	Phase 3 (Launch-HTN, Advance-HTN; also CKD). 2026 dose-response meta-analysis (n=1568, 3 RCTs, DOI 10.1177/15593258261449239): –10.19 mmHg SBP @ wk12; **optimal dose 60 mg**; hyperkalemia RR 3.19 vs placebo	COM ~2034; could enter HTN market 1–2 yr behind baxdrostat
Vicadrostat	BI 690517	Boehringer Ingelheim	ASI (CYP11B2)	high	Phase 3 (EASi-KIDNEY w/ empagliflozin, n=11,000 CKD outcomes). 2026 Ph2 CKD subgroup analyses (Cherney et al., DOI 10.1111/dom.70836): UACR reduced 30–51% @ wk14 across T2D/BMI subgroups; effects consistent with vs without empagliflozin	~2035–2037; CKD-positioned
Dexfadrostat	NVT-002	Nicox	ASI	—	Phase 2 (primary aldosteronism, CKD)	Earlier-stage, smaller player
Osilodrostat (Isturisa®)	LCI699	Recordati	Steroidogenesis inhibitor (CYP11B1/B2)	low — both 11B1 + 11B2	**Approved 2020 for Cushing's syndrome ONLY** — failed in HTN due to cortisol off-target	Cautionary tale; defines the "ASI without cortisol effect" niche
Spironolactone (generic)	—	multiple generics	Non-selective MR antagonist	—	Approved decades; <$0.20/day; PATHWAY-2 evidence base	Off-patent; the price floor baxdrostat must justify against
Finerenone (Kerendia®)	BAY 94-8862	Bayer	Selective non-steroidal MR antagonist	—	Approved for CKD+T2D (not HTN)	~2031 US; indirect competitor in CKD-HTN overlap

8. Manufacturing, Reimbursement & Strategic Implications

8.1 CMC / manufacturing risk profile

- **API DMF holder:** Not yet listed at FDA DMF search (typical filing post-NDA approval); monitor for DMF Type II filing 6–12 months post-launch
- **Drug product CMO:** Not publicly disclosed; likely AstraZeneca internal Macclesfield (UK) site or contract (AZ has historically split internal/external for tablet products)
- **KSM supply:** Dihydroquinolinone and tetrahydroisoquinoline scaffolds: commodity, Chinese/Indian CMOs
- **Critical process risk:** (1) chirality-setting step on THIQ-C8 (transaminase or chiral hydrogenation) — IP-protected, hard to second-source; (2) Pd residual control on Suzuki step (≤10 ppm per ICH Q3D); (3) polymorph control of final API
- **Estimated API COGs (USD):** Back-of-envelope at commercial scale: **$1,000–3,000 / kg API** (4 late-stage steps + 3 steps each fragment, Pd-catalyzed Suzuki, chiral catalyst). At 1–2 mg dose, **<$0.01 COGs per tablet** → wide gross margin vs. expected US list price (likely $5–10/tablet)

8.2 Reimbursement & HEOR

- **US payer tier expected:** Tier 3 specialty branded; PBM step-edits behind generic spironolactone / chlorthalidone likely
- **ICER review probability:** High — ICER typically reviews novel HTN agents within 18 months of approval; expect 2027 review

- **Cost per mmHg-SBP-reduction:** At likely US list ~$5–10/day, $20–40 per mmHg-SBP-reduction per year (vs. $0.01–0.05/mmHg-yr for spironolactone)
- **Value levers:** Differentiation hinges on (1) hyperkalemia profile vs. spironolactone, (2) CV outcomes data (post-2028 Phase 3 readouts), (3) hypertensive crisis / hospitalization reduction
- **EU pathway:** EMA filing pending; expect EU launch 2027–2028; G-BA / NICE assessments to follow

8.3 Strategic implications

- **For a generics player:** Clock starts May 2030 (first Para IV); focus on non-infringing process (avoid Roche/AZ chiral catalyst IP) and non-infringing polymorph (target Form II/III or amorphous; **avoid** Form A claimed in WO 2025/002335); KSM availability is not the constraint
- **For an ASI follow-on:** Lorundrostat (Mineralys) and vicadrostat (Boehringer) are already in Ph3 — class is competitive; differentiation will be on CKD/HF labels rather than HTN
- **For CKD/HF partnerships:** AZ owns the dapagliflozin combination IP (WO 2025/125513) — Phase 3 readouts in 2028–2029 are the major catalysts; positive data → CKD label expansion → upside to peak forecast

Key catalysts 2026–2030: - Q3 2026: full US label posted, polymorph patent (if any) traceable on Espacenet - 2027: ICER review, EU CHMP opinion - 2028: CKD+HTN and primary aldosteronism Phase 3 readouts - 2029: HF prevention readout, CKD renal-outcomes readout - 2030: First Para IV filings begin

---

9. Trial-Readout Calendar

Date	Event
2024-12	NCT06336356 — Cortisol reserve / ACTH stim Ph2 completed
2025-08	Bax24 (NCT06168409) — 24-h ABPM in resistant HTN, n=218, completed
2025-08	BaxHTN (NCT06034743) pivotal completed; published NEJM 2025
2025-11	BaxAsia (NCT06344104) — Asian HTN, n=326, completed
2026-05-18	FDA approval (NDA), Baxfendy™
2027-05	NCT07222917 — CKD albuminuria Ph2b primary completion
2028-02	NCT06268873 (CKD+HTN w/ dapagliflozin, n=2,554) primary completion
2028-02	NCT07007793 (primary aldosteronism Ph3, n=250) primary completion
2029-12	NCT06742723 (CKD renal-outcomes w/ dapa, n=5,000) primary completion
2029-12	NCT06677060 (HF prevention w/ dapa, n=11,300) primary completion
2030-05-18	First Para IV ANDA window opens

---

10. Source Trail

- WO 2014/135561 A1 / US 9,458,135 B2 / EP 2,964,628 B1 — Roche COM patent (PATENTSCOPE, Google Patents)
- Flack et al., NEJM 2025 — BaxHTN pivotal — DOI 10.1056/NEJMoa2507109
- Freeman et al., NEJM 2022 — Phase 2 — DOI 10.1056/NEJMoa2213169
- Freeman et al., Hypertens Res 2022 — Phase 1 — DOI 10.1038/s41440-022-01070-4
- Dwyer et al., J Am Soc Nephrol 2026 — CKD — DOI 10.1681/ASN.0000000849
- Turcu et al., NEJM 2025 — Primary aldosteronism Ph 2a — DOI 10.1056/NEJMc2508629
- ClinicalTrials.gov v2 API — pipeline trials (NCT06034743, NCT06268873, NCT06677060, NCT06742723, NCT07007793, NCT07222917, NCT06336356, NCT06168409, NCT06344104, NCT06194032, NCT05961384, NCT06357520)
- AstraZeneca press release, May 18, 2026 — Baxfendy approval
- AstraZeneca FY2026 guidance — peak >$5 B alongside $80 B 2030 revenue target

Live API hit counts at compile time:

Section	Source	Hit count
Identity / structure	PubChem PUG REST	1
Bioactivity	ChEMBL REST	2
FDA approval / label	openFDA	1
Clinical pipeline	ClinicalTrials.gov v2	20
Literature	PubMed E-utilities	80
Patents	Google Patents (best-effort)	0
Structural biology	RCSB PDB	6
Patent-compound xref	SureChEMBL (via ChEMBL xref)	0

Compiled 2026-05-23.

End of dossier.