Crystal's Perspective: Polymorph Patent Landscape of 28 FDA-Approved Small Molecule Drugs in 2024

In 2024, the U.S. Food and Drug Administration (FDA) approved a total of 50 new drugs [1], including 34 new molecular entities (NMEs). Among these, 28 were classified as small molecule drugs. An analysis of their administration routes and dosage forms shows that 4 were liquid formulations (comprising 3 injectable solutions and 1 oral solution), 2 were suspensions (1 inhalation and 1 oral), and 22 were solid or semi-solid formulations. The solid/semi-solid group includes 20 solid oral dosage forms and 2 gel-based formulations. A detailed summary is presented in Table 1.

Table 1. Overview of the 34 New Molecular Entities Approved by the FDA in 2024

No.	Drug Name	Active Ingredient	Originator Company	Indication	Target	Type	Formulation
1	Zelsuvmi	Berdazimer	Ligand Pharmaceuticals	Local contagious molluscum	Topically applied nitric oxide (NO) releasing agent	Small molecule	Topical gel
2	Exblifep	Cefepime, enmetazobactam	Allecra Therapeutics	Complicated urinary tract infection	Combination of cefepime and enmetazobactam	Small molecule, combination	Injection
3	Exblifep	Letibotulinumtoxin A-wlbg	Hugel Inc.	Moderate to severe glabellar lines	Acetylcholine release inhibitor and neuromuscular blocking	Toxin	Injection
4	Rezdiffra	Resmetirom	Madrigal Pharmaceuticals	Non-alcoholic steatohepatitis (MASH)	PPAR agonist	Small molecule	Oral solid
5	Tryvio	Aprocitentan	Idorsia Pharmaceuticals	Hypertension	Treatment-resistant hypertension	Small molecule	Oral solid
6	Duvyzat	Givinostat	Italfarmaco SpA	Duchenne muscular dystrophy (DMD)	Histone deacetylase (HDAC) inhibitor	Small molecule	Oral solution
7	Winrevair	Sotatercept-csrk	Merck	Pulmonary arterial hypertension	IIA-type activin receptor (ActRIIA) fusion protein	Protein-based drug	Lyophilized powder for injection
8	Vafseo	Vadadustat	Akebia Therapeutics	Anemia in chronic kidney disease	Hypoxia-inducible factor prolyl hydroxylase (HIF-PHD) inhibitor	Small molecule	Oral solid
9	Voydeya	Danicopan	AstraZeneca	Paroxysmal nocturnal hemoglobinuria (PNH)	PNH inhibitor	Small molecule	Oral solid

No.	Drug Name	Active Ingredient	Originator Company	Indication	Target	Type	Formulation
10	Zevtera	Ceftobiprole medocaril sodium	Basilea Pharmaceutica	Bloodstream and skin infections, community-acquired pneumonia	Cephalosporin antibiotic	Small molecule	Intravenous infusion
11	Anktiva	Nogapendekin alfa inbakicept-pmin	Altor Bioscience Corp	Bladder cancer	IL-15 superagonist complex	Protein-based drug	Intravesical infusion
12	Ojemda	Tovorafenib	Viracta Therapeutics Inc	Pediatric low-grade gliomas	Selective type II RAF kinase inhibitor	Small molecule	Oral solid
13	Xolremdi	Mavorixafor	Sanofi	WHIM syndrome	Selective CXCR4 antagonist	Small molecule	Oral solid
14	Rytelo	Imetelstat	Geron Corp.	Myelodysplastic syndrome (MDS)	Telomerase inhibitor	Oligonucleotide	Intravenous infusion
15	Iqirvo	Elafibranor	Genfit SA	Primary biliary cholangitis	PPAR agonist	Small molecule	Oral solid
16	Sofdra	Sofpironium	Bodor Laboratories Inc	Primary axillary hyperhidrosis	Anticholinergic agent	Small molecule	Topical gel
17	Ohtuvayre	Ensifentrine	Verona Pharma	Chronic obstructive pulmonary disease	PDE3 and PDE4 inhibitor	Small molecule	Inhalation suspension
18	Leqselvi	Deuruxolitinib	Taiho Pharmaceutical	Severe alopecia areata	JAK inhibitor	Small molecule	Oral solid
19	Voranigo	Vorasidenib	Servier	Grade 2 gliomas	IDH1/2 inhibitor	Small molecule	Oral solid
20	Yorvipath	Palopegteriparatide	Ascendis Pharma	Hypoparathyroidism	Long-acting PTH precursor	Peptide	Injection
21	Livdelzi	Seladelpar	Gilead	Primary biliary cholangitis (PBC)	PPARδ agonist	Small molecule	Oral solid
22	Lazcluze	Lazertinib	Janssen/Yuhan	Non-small cell lung cancer	EGFR TKI	Small molecule	Oral solid
23	Miplyffa	Arimoclomol	Zevra Therapeutics	Niemann-Pick disease type C	Heat shock protein co-inducer	Small molecule	Oral solid
24	Aqneursa	Levacetylleucine	IntraBio	Niemann-Pick disease type C	Modified amino acid	Small molecule	Oral suspension

No.	Drug Name	Active Ingredient	Originator Company	Indication	Target	Type	Formulation
25	Cobenfy	Xanomeline and trospium chloride	BMS	Schizophrenia	Muscarinic receptor agonist	Small molecule, combination	Oral solid
26	Itovebi	Inavolisib	Genentech	Metastatic breast cancer	PI3Kα inhibitor	Small molecule	Oral solid
27	Orlynvah	Sulopenem, etzadroxil, probenecid	Iterum Therapeutics	Uncomplicated urinary tract infection (uUTI)	Combination antibiotics	Small molecule	Oral solid
28	Revuforj	Revumenib	Syndax Pharmaceuticals	Acute leukemia	Menin inhibitor	Small molecule	Oral solid
29	Attruby	Acoramidis	BridgeBio	TTR amyloidosis	TTR stabilizer	Small molecule	Oral solid
30	Rapiblyk	Landiolol	AOP Orphan Pharmaceuticals	Supraventricular tachycardia	Adrenergic receptor antagonist	Small molecule	Injection
31	Crenessity	Crinecerfont	Neurocrine Biosciences	Classic congenital adrenal hyperplasia (CAH)	CRF type 1 receptor antagonist	Small molecule	Capsules and oral solution
32	Ensacove	Ensartinib	Xcovery Holdings, Inc	ALK-positive NSCLC	ALK inhibitor	Small molecule	Capsules
33	Tryngolza	Olezarsen	Ionis	Familial chylomicronemia syndrome	ASO-GalNAc3 conjugate	Antisense oligonucleotide	Subcutaneous injection
34	Alyftrek	Vanzacaftor, tezacaftor, deutivacaftor	Vertex	Cystic fibrosis	Vanza triple therapy	Small molecule, triplet	Oral solid

An analysis of the patent strategies associated with the 22 solid and semi-solid formulation drugs revealed that 15 products—including those with pending applications—have incorporated polymorph patents. This represents approximately 68% of all small-molecule drugs in this category. Further details are provided in Table 2.

Table 2. Overview of Polymorph Patent Strategies for 22 Solid and Semi-Solid Small Molecule Drugs Approved by the FDA in 2024

No.	Drug Name	Active Ingredient	Originator Company	Patent Status
1	Zelsuvmi	Berdazimer	Ligand Pharmaceuticals	Not found
2	Exblifep	cefepime, enmetazobactam	Allecra Therapeutics	Granted

No.	Drug Name	Active Ingredient	Originator Company	Patent Status
3	Tryvio	aprocitentan	Idorsia Pharmaceuticals	Granted
4	Vafseo	vadadustat	Akebia Therapeutics, Inc.	Granted
5	Voydeya	danicopan	AstraZeneca	Granted
9	Ojemda	tovorafenib	Viracta Therapeutics Inc	Granted
7	Xolremdi	mavorixafor	Sanofi	Not found
8	Iqirvo	elafibranor	Genfit SA	Substantive examination
9	Sofdra	sofpironium	Bodor Laboratories Inc	Granted
10	Leqselvi	deuruxolitinib	Taiho Pharmaceutical	Not found
11	Voranigo	vorasidenib	Servier	Granted
12	Livdelzi	seladelpar	Gilead	Granted
13	Lazcluze	lazertinib	Janssen/Yuhan	Granted
14	Miplyffa	arimoclomol	Zevra Therapeutics	Not found
15	Cobenfy	xanomeline and trospium chloride	BMS	Not found
16	Itovebi	inavolisib	Genentech	Granted
17	Orlynvah	sulopenem etzadroxil, probenecid	Iterum Therapeutics	Disclosed crystalline form in compound patent
18	Revuforj	revumenib	Syndax Pharmaceuticals	Not found
19	Attruby	acoramidis	BridgeBio	Granted
20	Crenessity	crinecerfont	Neurocrine Biosciences	Substantive examination
21	Ensacove	ensartinib	Xcovery Holdings, Inc	Granted
22	Alyftrek	vanzacaftor,tezacaftor, and deutivacaftor	Vertex	Not found

For the 15 small-molecule drugs identified above with originator-filed polymorph patent strategies, we further analyzed the expiration dates of their compound and polymorph patents, as well as the time intervals between them. The findings are summarized in Table 3. Two products with polymorph patents still under regulatory examination were excluded from the statistical analysis. In one case (Orlynvah), polymorph-related claims were disclosed within the compound patent itself. Among the remaining 12 products, all originator polymorph patents expire later than their corresponding compound patents, with time gaps exceeding one year. Notably, 9 of these products exhibit a gap of three years or more, and 6 show a gap of at least five years. Of particular interest, **Sofdra** achieved an exceptional 13-year extension of exclusivity through its polymorph patent strategy.

Table 3. Comparative Analysis of Compound and Polymorph Patents for 13 Small Molecule Drugs

No.	Drug Name	Compound Patent	Compound Patent Expiry	Crystal Form Patent	Crystal Form Patent Expiry Date[3]	Patent Term Difference	Remarks
1	Exblifep	US7687488B2	2027-12-3	US11124526B2	2034-11-7	~7 years	-
2	Tryvio	US8324232B2	2029-9-21	US20200002317A1	2038-2-26	~8.5 years	-
3	Vafseo	US8940773B2	2027-6-26	US9987262B2	2034-11-14	~7 years	-
4	Voydeya	US9796741B2	2035-2-25	US11814363B2	2039-11-23	~4.5 years	-
5	Ojemda	US8293752B2	2031-8-4	US10426782B2	2035-6-23	~4 years	-
6	Sofdra	US8628759B2	2026-11-13	US11584715B2	2040-5-22	~13.5 years	-
7	Voranigo	US9579324B2	2034-7-11	US11345677B2	2039-1-16	~4.5 years	-
8	Livdelzi	US7301050B2	2025-8-2	US7709682B2	2026-9-13	1 year	-
9	Lazcluze	US9593098B2	2035-10-13	US11981659B2	2038-4-18	~2.5 years	-
10	Itovebi	US8343955B2	2030-9-27	US11028100B2	2038-4-26	~7.5 years	-
11	Orlynvah	US7795243B2	2029-6-3	US7795243B2	2029-6-3	NA	Disclosed crystalline form
12	Attruby	US9642838B2	2033-3-14	US11919865B2	2038-5-27	~5 years	-
13	Ensacove	US8551995B2	2029-2-9	US9126947B2	2031-11-29	~2.5 years	-

Among the 13 products analyzed (including Orlynvah), two representative cases were selected for in-depth discussion to illustrate how innovative pharmaceutical companies leverage polymorph patent strategies to extend product lifecycles. The approval of these two drugs marks a significant milestone, as both exhibit strong therapeutic potential and are anticipated to capture substantial market share.

Voranigo®

Voranigo® (vorasidenib), developed by Servier, is approved for the postoperative treatment—including biopsy, subtotal resection, or gross total resection—of grade 2 astrocytoma or oligodendroglioma harboring isocitrate dehydrogenase (IDH) 1 or 2 mutations in patients aged 12 years and older. It is the first and only FDA-approved targeted therapy specifically indicated for IDH-mutant grade 2 gliomas. Voranigo® exerts its therapeutic effect by selectively inhibiting mutant IDH1/2 enzyme activity, thereby suppressing disease progression in IDH-mutant gliomas. The FDA approval, announced by Servier on August 6, 2024, represents a significant advancement in the treatment landscape for diffuse gliomas.

The active pharmaceutical ingredient in the commercial product is a co-crystal of vorasidenib hemicitrate hemihydrate. The compound patent (US9579324B2) is set to expire on July 11, 2034. In contrast, the polymorph patent (US11345677B2), which discloses the citric acid co-crystal form, extends protection until January 16, 2039. This polymorph patent strategy effectively provides an additional 4.5 years of exclusivity beyond the expiration of the compound patent.

Sofdra®

Sofdra® (sofpironium), developed by Bodor Laboratories Inc., is a topical gel approved for the treatment of primary axillary hyperhidrosis in patients aged 9 years and older. As the first FDA-approved new molecular entity specifically for this indication, Sofdra® addresses a substantial unmet medical need—hyperhidrosis ranks as the third most prevalent dermatological condition following acne and atopic dermatitis. Existing treatment options range from topical therapies to systemic medications and surgical procedures, each associated with varying degrees of efficacy and adverse effects. As a locally applied anticholinergic agent, Sofdra® minimizes systemic exposure while achieving meaningful reductions in sweat production and maintaining favorable tolerability in clinical trials. Prior to Sofdra®, the only FDA-approved topical anticholinergic for hyperhidrosis was glycopyrronium tosylate (Qbrexza), approved in 2018. FDA approval of Sofdra® was announced by Botanix on June 18, 2024.

The commercial product contains crystalline sofpironium. The compound patent (US8628759B2) is set to expire on November 13, 2026, whereas the polymorph patent (US11584715B2), which discloses multiple crystalline forms (Form A, MN, MJ, CO, and B), extends protection until May 22, 2040. This polymorph patent strategy affords an exceptional 13.5-year extension of market exclusivity beyond the expiration of the compound patent.

Summary

A review of data from the past six years (Table 4) shows that, although the number of approved small-molecule drugs in 2024 declined slightly compared to the previous year, the proportion of solid and semi-solid formulations remained consistent with historical trends. Notably, 60% to 80% of newly approved innovative small-molecule drugs continue to incorporate polymorph patent strategies—underscoring the growing importance of crystal form research in pharmaceutical development.

This trend is driven by two key factors. First, polymorphic properties play a critical role in determining a drug's bioavailability, stability, and manufacturability—all of which are central to regulatory evaluation and approval. Second, well-constructed polymorph patents serve as effective intellectual property barriers against generic entry, thereby prolonging market exclusivity and enhancing commercial value.

Table 4. Trends in Polymorph Patent Protection Among FDA-Approved New Small Molecule Drugs (2019–2024)

Year	2019	2020	2021	2022	2023	2024
FDA-Approved New Drugs	48	53	50	37	55	50
Small Molecule Drugs	32	34	31	17	38	28
Solid/Semi-Solid Dosage Forms	26	20	23	15	24	22
Originator Polymorph Patents	17	12	16	10	20	15
% of Solid/Semi-Solid Drugs with Originator Polymorph Patents	65%	60%	70%	67%	83%	68%

References and Notes

[1] FDA. Novel Drug Approvals 2024. Available at: https://www.fda.gov/drugs/novel-drug-approvals-fda/novel-drug-approvals-2024
[2] Compound patent expiration dates are based on the Orange Book-listed expiration date: https://www.accessdata.fda.gov/scripts/cder/ob/index.cfm
[3] For granted patents, expiration dates are determined based on official records published by the relevant authorities.
[4] The expiration gap is calculated as: Polymorph patent expiration date – Compound patent expiration date.