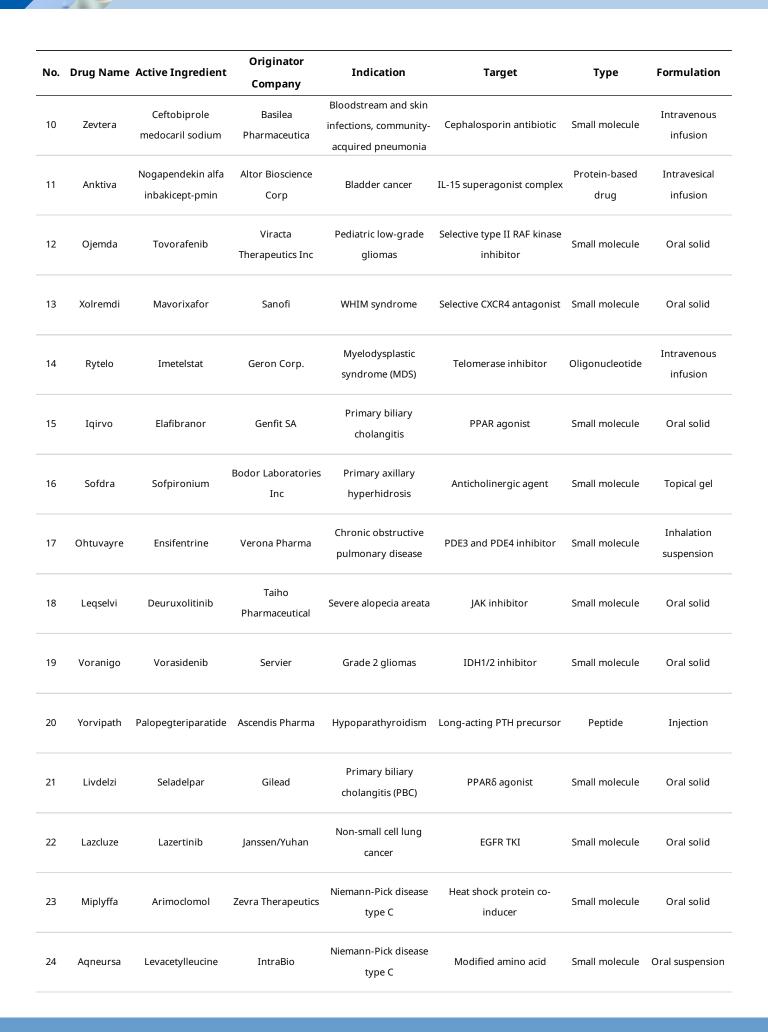
Crystal's Perspective: Polymorph Patent Landscape of 28 FDA-Approved Small Molecule Drugs in 2024

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	Туре	Formulation	
1	Zelsuvmi	Berdazimer	Ligand Pharmaceuticals	Local contagious Topically applied nitric molluscum oxide (NO) releasing age		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	



Ensartinib

Olezarsen

Vanzacaftor,

tezacaftor,

deutivacaftor

Inc

Ionis

Vertex

32

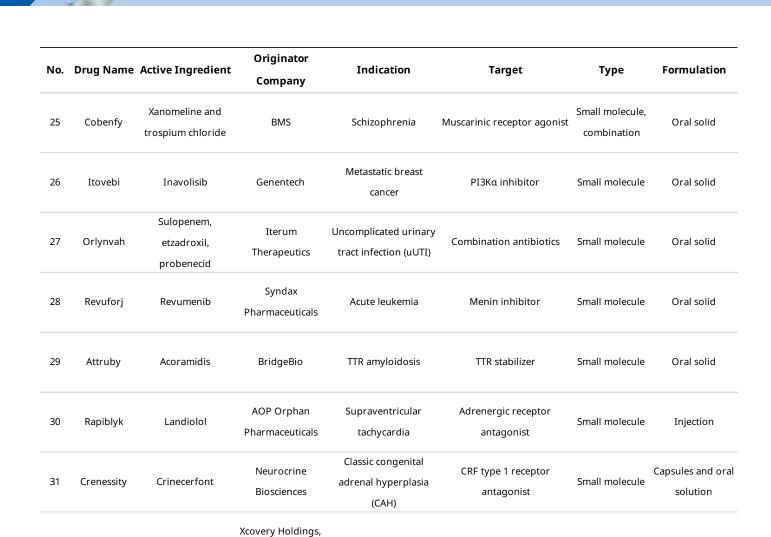
33

34

Ensacove

Tryngolza

Alyftrek



ALK-positive NSCLC

Familial

chylomicronemia

syndrome

Cystic fibrosis

ALK inhibitor

ASO-GalNAc3 conjugate

Vanza triple therapy

Small molecule

Antisense

oligonucleotide

Small molecule,

triplet

Capsules

Subcutaneous

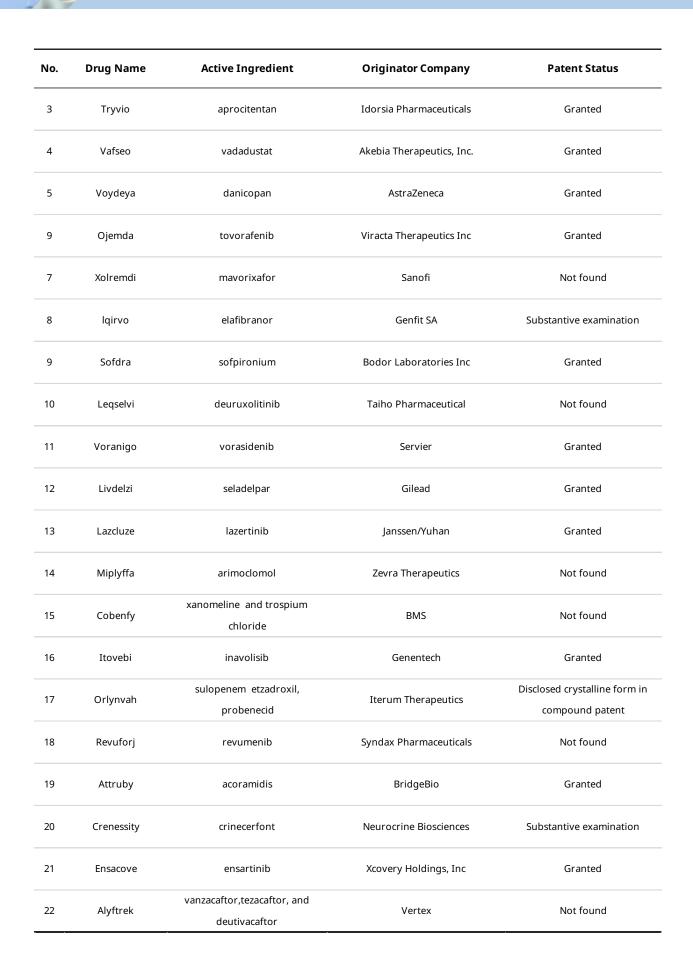
injection

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



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

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N.c.	Drug Name	Compound	Compound	Crystal Form	Crystal Form Patent	Patent Term	
No.		Patent	Patent Expiry	Patent	Expiry Date[3]	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.