The Patent Cliff and Company Strategies

Pullan's Pieces #227 July 2026

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The patent cliff is one of the drivers for deal making. I show here over $300M in blockbuster drugs with Loss of Exclusivity (LOE) from 2023 to 2032. In the U.S. market, 423 branded drugs are expected to lose exclusivity (LOE) between 2026 and 2030, comprising 316 small molecules and 105 biologics (RBC Capital Market Research, Jul 5, 2026).

Loss of exclusivity is not the same as patent expiration or first approval of a generic or biosimilar. The FDA can approve a generic or biosimilar before the patent expiration, as the competitor would like to launch immediately once there is freedom to operate, but it often takes years to settle patent disputes. Of course, the patent expirations can be complex as there are generally multiple patents. The first biosimilar for Humira was approved in 2016 but the launch was in 2023, due to the patent thicket created by Abbvie, with patenting on MOU across an ever-expanding list of indications, devices, formulation, and manufacturing. **The effective LOE is when broad competition can impact sales.**

Blockbusters with LOE from 2023 to 2032 sorted by company

LOE	Generic name	Brand	Company	Primary target / indication	peak sales) $M	peak year	% sales that year	co sales in 2025 $M
2023 (effective)	Adalimumab	Humira	AbbVie	TNF-α; RA, psoriasis, IBD	21	2022	36%	61
2032	Risankizumab	Skyrizi	AbbVie	IL-23; psoriasis, IBD	32	2032	33%	61
2032	Upadacitinib	Rinvoq	AbbVie	JAK1; RA, IBD, dermatology	17	2032	18%	61
2027	Ibrutinib	Imbruvica	AbbVie	BTK; hematologic cancers	4.3	2021	8%	61
2025–26	Denosumab	Prolia	Amgen	RANKL; osteoporosis, oncology	4.4	2025	12%	37
2030–31	Etanercept	Enbrel	Amgen	TNF-α; RA, psoriasis	5.3	2019	21%	37
2027	Enzalutamide	Xtandi	Astellas / Pfizer	AR; prostate cancer	6.3	2026	42%	14
2025	Dapagliflozin	Farxiga	AstraZeneca	SGLT2; diabetes, HF, CKD	8.4	2025	14%	59
2032	Osimertinib	Tagrisso	AstraZeneca	EGFR; NSCLC	9.3	2031	10%	59
2025	Rivaroxaban	Xarelto	Bayer	Factor Xa; anticoagulant	5.6	2021	11%	51
2026	Apixaban	Eliquis	BMS	Factor Xa; anticoagulant	8	2025	17%	48
2028	Nivolumab	Opdivo	BMS	PD-1; oncology	10	2025	21%	48
2027	Dulaglutide	Trulicity	Eli Lilly	GLP-1; diabetes	7.4	2022	26%	65
2032	Bictegravir/FTC/TAF	Biktarvy	Gilead	HIV	17	2032	39%	29
2025	Rivaroxaban	Xarelto	J&J	Factor Xa; anticoagulant	2.5	2022	7%	94
2027	Ibrutinib	Imbruvica	J&J	BTK; hematologic cancers	2.6	2021	10%	94
2023	Ustekinumab	Stelara	J&J	IL-12/23; psoriasis, IBD	10.9	2023	13%	94
2029	Daratumumab	Darzalex	J&J	CD38; multiple myeloma	20	2028	17%	94
2028	Pembrolizumab	Keytruda	Merck	PD-1; oncology	32	2026	46%	65
2028	HPV vaccine	Gardasil 9	Merck	HPV prevention	8.9	2023	15%	65
2025	Sacubitril/valsartan	Entresto	Novartis	Neprilysin/ARB; heart failure	7.8	2024	16%	57
2029	Secukinumab	Cosentyx	Novartis	IL-17A; psoriasis, SpA	7.9	2028	13%	57
2032 (device)	Semaglutide	Ozempic	Novo Nordisk	GLP-1; diabetes, obesity	19	2025	41%	46
2026	Tofacitinib	Xeljanz	Pfizer	JAK; RA, IBD	2.5	2021	3%	63
2027	Palbociclib	Ibrance	Pfizer	CDK4/6; breast cancer	5.4	2021	14%	51
2032	Pneumococcal conjugate	Prevnar 20	Pfizer	Pneumococcal prevention	6.5	2025	10%	63
2024	Aflibercept	Eylea	Regeneron (Bayer)	VEGF; retinal disease	6.3	2022	52%	14
2027	Ocrelizumab	Ocrevus	Roche	CD20; multiple sclerosis	9.7	2028	11%	76
2029–31	Dupilumab	Dupixent	Sanofi (Regeneron)	IL-4/13; atopic dermatitis, asthma	28	2030	37%	53
2032	Vedolizumab	Entyvio	Takeda	α4β7 integrin; IBD	6.8	2027	24%	29

Most drugs on the list- Abbvie and J&J

Abbvie has 4 drugs on the list (Humira, Skyrizi, Rinvoq and Imbruvica). J&J has 4 drugs (Xarelto, Imbruvica, Stelara, Darzalex) on the list, Pfizer has 3 (Xeljanz, Ibrance, Prevnar).

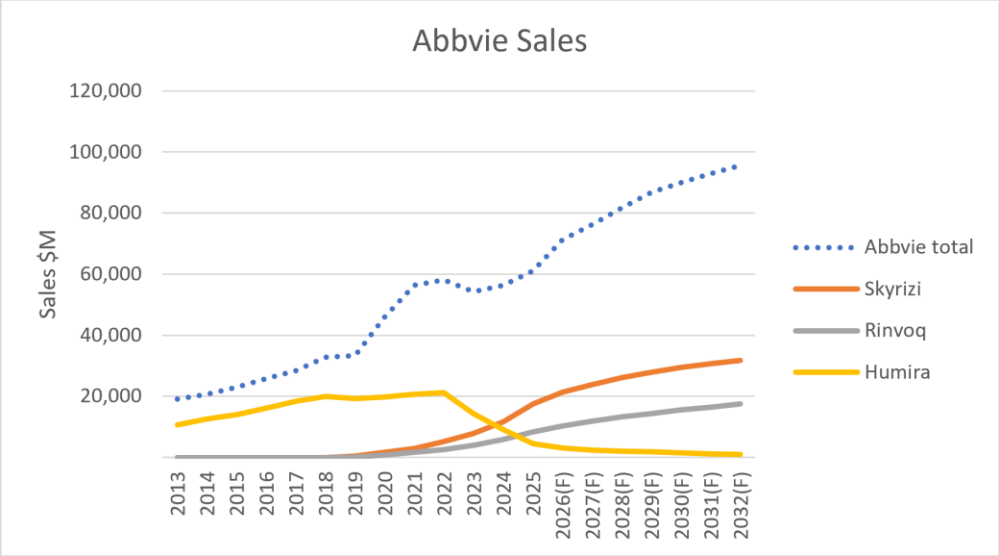
Most sales subject to LOE - Abbvie followed by Merck

The total of the peak sales (in various years) for 4 drugs for Abbvie is $74B, the largest sales at risk for LOE in the period of 2023 to 2032. Merck has the 2nd most sales at risk with $41B for peak sales of Keytruda. J&J has $36B peak sales at risk.

Biggest % of total company sales- Regeneron

On the list for Regeneron is Eylea that represented 52% of Regeneron sales at the time of its peak in 2022.

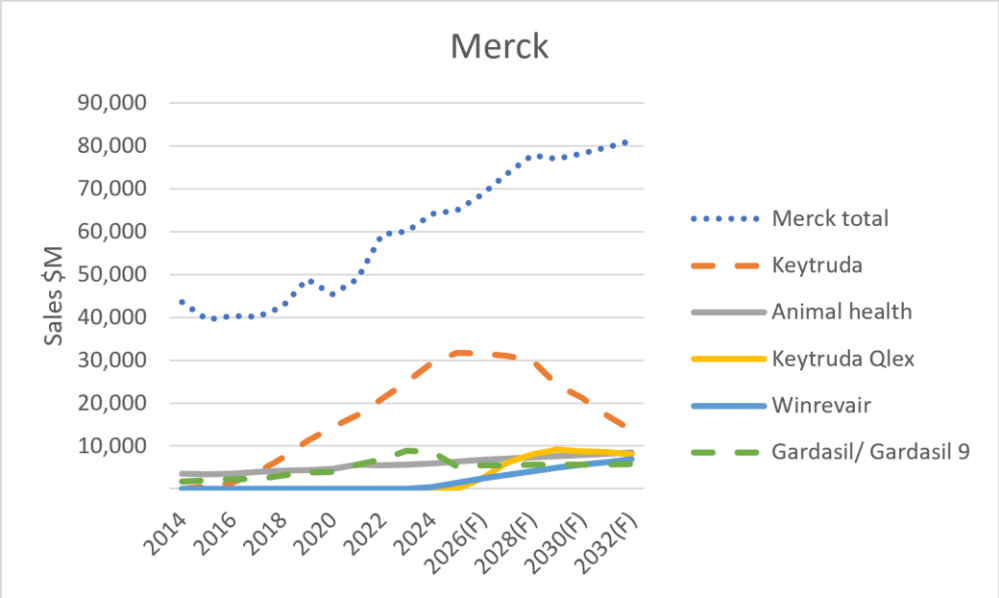
Abbvie Sales- Humira replaced by Skyrizi (from a deal) and Rinvoq, now facing LOE in 2032.



Rinvoq was an Abbvie originated drug.

- Skyrizi came at Phase 3 in psoriasis to Abbvie in a $595M deal with Boehringer Ingelheim in 2016.

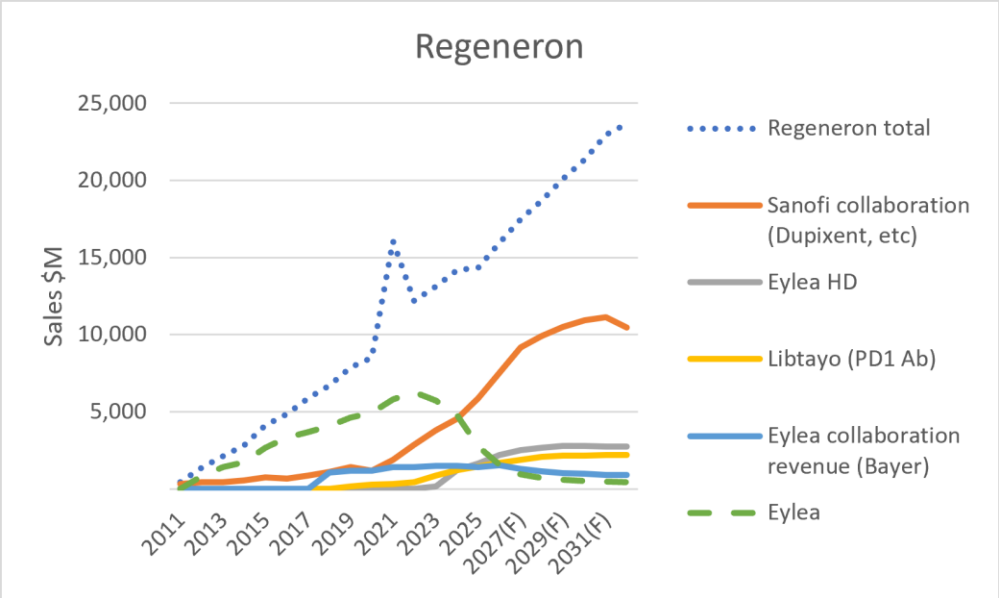
Merck LOE of Keytruda offset by animal health, Keytruda Qlex formulation and a drug from an acquisition.



Merck's Life Cycle Management strategy for Keytruda included a subcutaneous formulation with a device (Keytruda Qlex) as well as the establishment of Keytruda as a backbone in oncology combinations and moving into earlier lines of treatment. But the growth in sales after the Keytruda sales peaked is due to multiple drugs and to the animal health business revenues.

- Winrevair (the PAH drug) was part of the $11.5B acquisition of Acceleron in 2021.

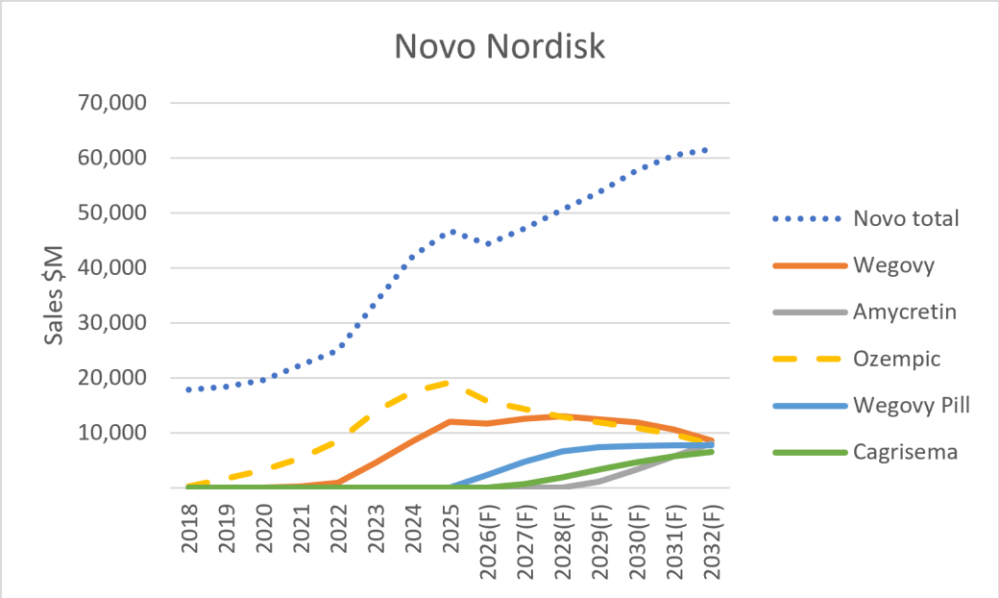
Regeneron LOE for Eylea was more than replaced by Sanofi collaboration revenues.



- The Sanofi Regeneron deal back in 2007 provided Regeneron revenue (not booked sales) from Dupixent and other antibodies.

Regeneron also created a high dose form Eylea HD with a device and new patents. The blip upward in 2021 was the COVID Ab cocktail.

Novo Nordisk sales of Ozempic after LOE are being replaced by other obesity drugs from internal research.



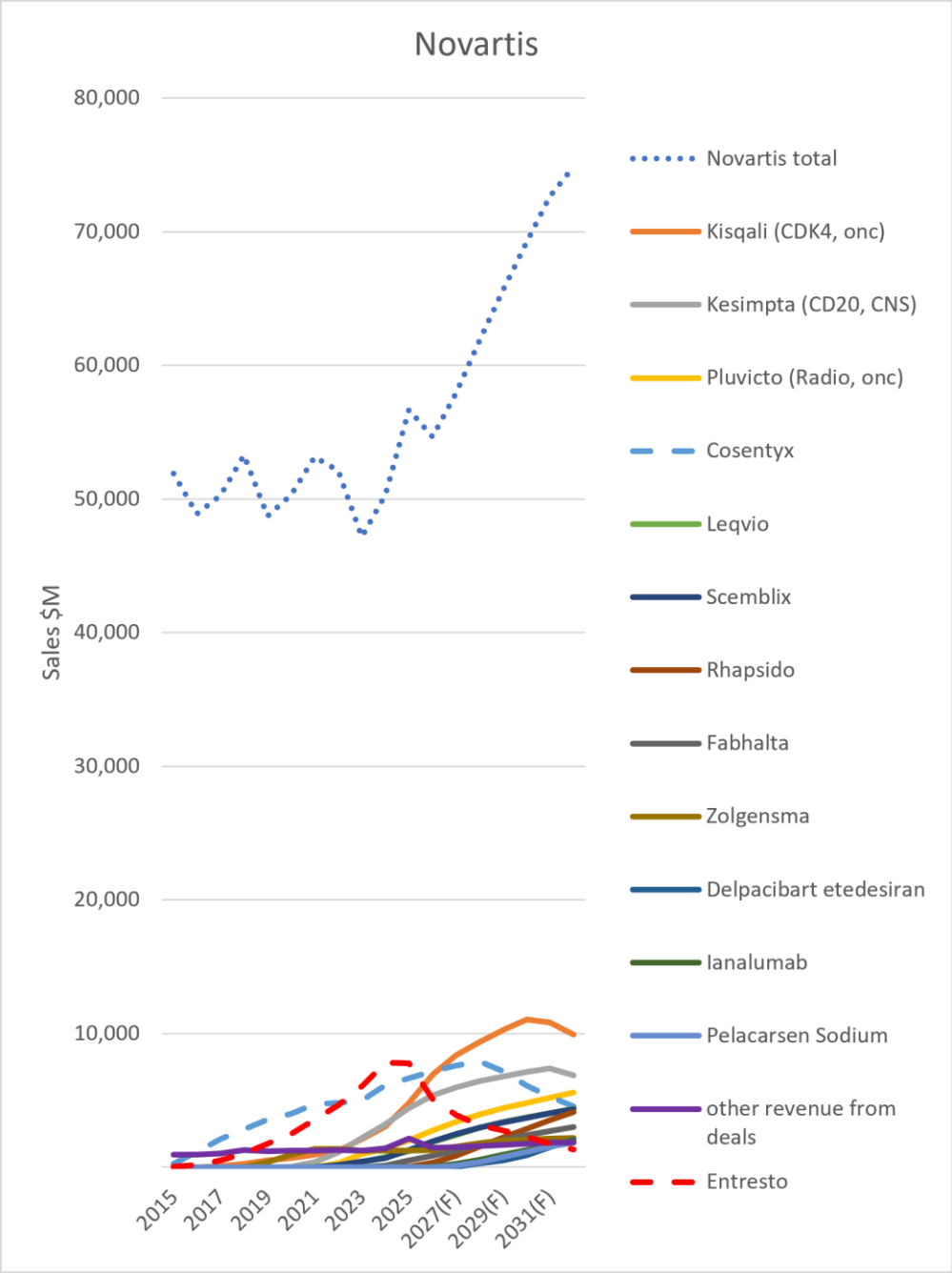
Novo's Wegovy is the same semaglutide molecule as Ozempic but is a higher dose for obesity versus diabetes and in a different device.

Amycretin is also a Novo discovery combining GLP1 and amylin functions in one molecule.

- The Wegovy pill relies on an absorption enhancer licensed from Emisphere in 2007 (attempting oral insulin) and Novo Nordisk went on to acquire Emisphere in 2020 for $1.8B

Cagrisema is the combination of semaglutide with a long-acting amylin and was internally discovered.

Novartis sales were more uneven, but the forecast is for rapid growth from a number of drugs

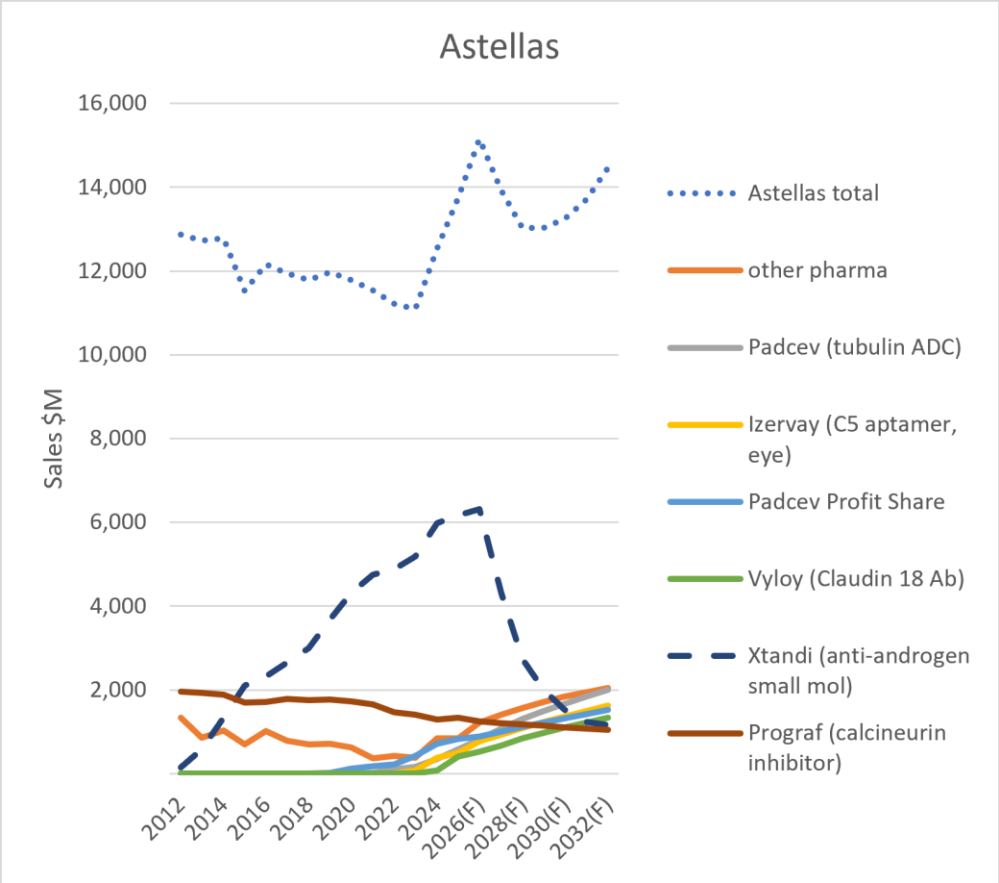


Novartis has just returned to growth. No single product dominates Novartis sales. Entresto at its peak in 2024 was 16% of Novartis sales. Cosentyx at its forecast peak in 2028 is forecast to be 13% of Novartis sales.

The drugs providing new growth came from deals.

- Kisqali was created in a research collaboration with Astek Pharmaceuticals that started in 2005.
- Kesimpta was created by Genmab and partnered first with GSK, who then partnered with Novartis in 2015. The Ab was approved in CLL but in late-stage development for MS.
- Pluvicto, the Lu-177 PSMA radioligand peptide conjugate, was acquired at Phase 3 as the lead asset in a 2015 acquisition Endocyte for $2.1B.

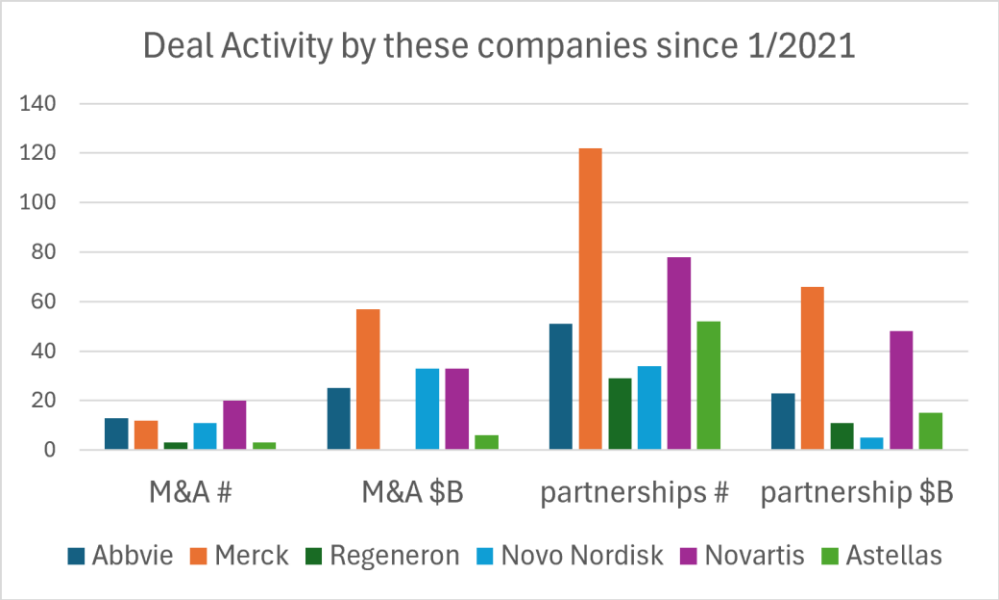
Astellas Xtandi LOE impact just beginning to be replaced by collaborations and new drugs



Astellas sales come from "other pharma" which is a mix of sales of Astellas products with other partners, as well from a mix of drugs.

- Pacdev (the anti-tubulin ADC) came from a SeaGen collaboration signed in 2007 with an Agensys Ab that came in the acquisition of Agensys in 2007.
- Izervay, the C5 aptamer for ophthalmology came in the 2023 acquisition of Iveric Bio for $5.8B.
- Vyloy, the claudin 18 Ab, came with the $1.3B acquisition of Ganymead in 2016. Prograf (tacrolimus) had LOE back in 2009 but continues to contribute to the Astellas sales.

Looking at deal activity for these LOE examples?



For this subset of companies facing LOEs:

- Merck (orange) has done a lot of strategic partnerships and licenses for big announced deal values and has done a high value of M&A deals. Since 2021, Merck has expanded its late-stage pipeline with deals, and split oncology into a separate unit (Fierce)

- Novartis (purple) has also been very active despite facing only a smaller % of sales to be lost in LOE. However, Entresto and Cosentyx were the biggest products until LOEs. Now, it deals in the past 5 years includes the $12B acquisition of Avidity. The CEO says they are looking to target mainly smaller deals while remaining open to larger deals (WSJ, July 21).

Tim Opler and Stifel say in their July 7th newsletter:

"In the past 18 months pharma has spent approximately $165 billion on biotech and specialty pharma M&A transactions. We estimate that this will only cover a quarter of the revenue gap that is needed just to keep revenue where it is now – not to obtain long-term growth."

Take-aways - Strategies to replace LOE sales include

- **Patent thickets extend LOE**
- **Expansion of indications can extend MOU IP and LOE**
- **New formulations can offer new IP**
- **New internally discovered drugs can offset sales loss**
- **Deals in many forms can offset sales loss**
    - from collaboration revenue
    - to sales from research collaborations many years ahead of the LOE

- to late-stage acquisitions

Different companies have been successful to varying degree in replacing sales lost to LOE, with different mixes of these fundamental strategies.

For those of us in BD, the coming LOE dose mean more deals, but some of the sales will be replaced due to deals already done.