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20
23

Year in Review

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Ophthalmology
Innovation Summit

Timing is everything.

Capital >>> Partnership >>> M&A



| 01

2023 **Biotech Market Snapshot**

Where we are today:



Innovation in biopharma despite macro volatility

Innovation and strategic interest remain strong across therapeutic categories

- Late-stage rare disease remains a focus, with a broader buyer universe than most other therapeutic areas
- Resurgence of interest in large-prevalence diseases and areas such as Autoimmune, Neuroscience, Cardio / Metabolic and Ophthalmology driven by novel science and strong data
- Oncology strategic landscape undergoing fundamental shift with selective rather than broad interest after years of heightened investment and deal activity
- Proof-of-concept across gene directed modalities in both rare and specialty diseases

Large pharma has remained relatively insulated from key macro issues (ie, inflation, rising rates, geopolitical tensions), with generalist investors seeing sector as a defensive play



Acute need for growth industry-wide has catalyzed M&A

Most large-cap pharma have a priority to significantly bolster 2025-2030 topline growth profiles, and are adopting distinct M&A strategies

- Competition for de-risked, blockbuster assets has been and likely to remain high

>\$400bn balance sheet capacity across the industry, though broadly distributed

- Capacity is being put to work quickly in 2023 with M&A activity on pace for record year
- Into September, 16 transactions ~\$1bn+ announced totaling \$93bn in offer value

Specialty pharma players, particularly in Europe (eg, Alfasigma, Chiesi, Ipsen), have been increasingly active in M&A, particularly in late-stage rare disease deals

Where we are today:



Mixed biopharma regulatory backdrop

IRA: Evolving impact on future pricing, development strategy within therapeutic categories, modalities and diversification

- Initial 10 medicines for negotiation released 8/29; drugs span therapeutic categories and classes, though only one oral oncology drug selected (Imbruvica)

FDA: More constructive in some areas and increasingly conservative in others

- Neuro: Viewed as most accommodating FDA team (eg, Leqembi full approval in AD)
- Cardio / Metabolic: Poster child of Commissioner Califf's appeal for more investment into high prevalence diseases that continue to strain domestic healthcare resources
- Oncology: Less flexible (ie, confirmatory trial timelines vis-à-vis accelerated approvals, Project Optimus, non-reliance on China trials)

FTC: scrutiny across industries, beginning to be borne out in biopharma (eg, Amgen / Horizon)



Ongoing biotech volatility

Combination of macro and biotech-specific events underly ongoing biotech volatility

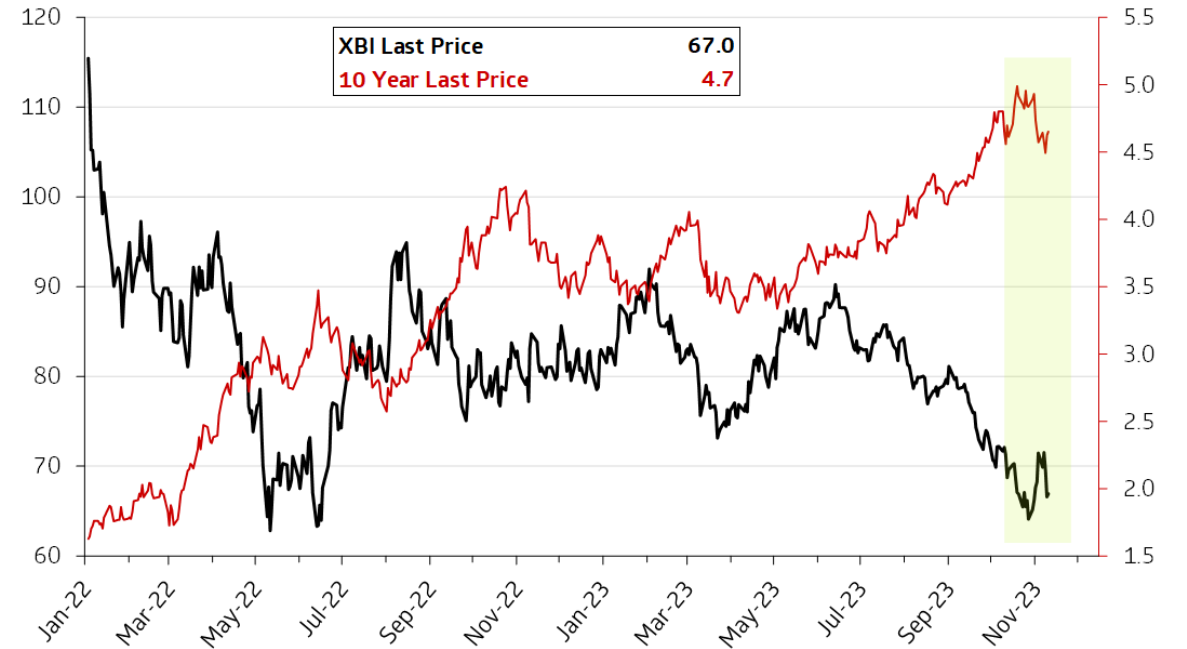
- Macroeconomic: Elevated interest rates, investor rotation out of small / mid-cap biotech and into large-cap healthcare and technology stocks, increased FTC scrutiny on M&A
- Biotech specific: 2022 correction following record levels of IPO activity and private capital raised (only 6 IPOs >\$50mm YTD), increased FDA scrutiny; capital markets and M&A remain challenging for most biotechs but strong for those with compelling data

Larger later-stage companies have materially outperformed smaller, early-stage players; XBI remains depressed

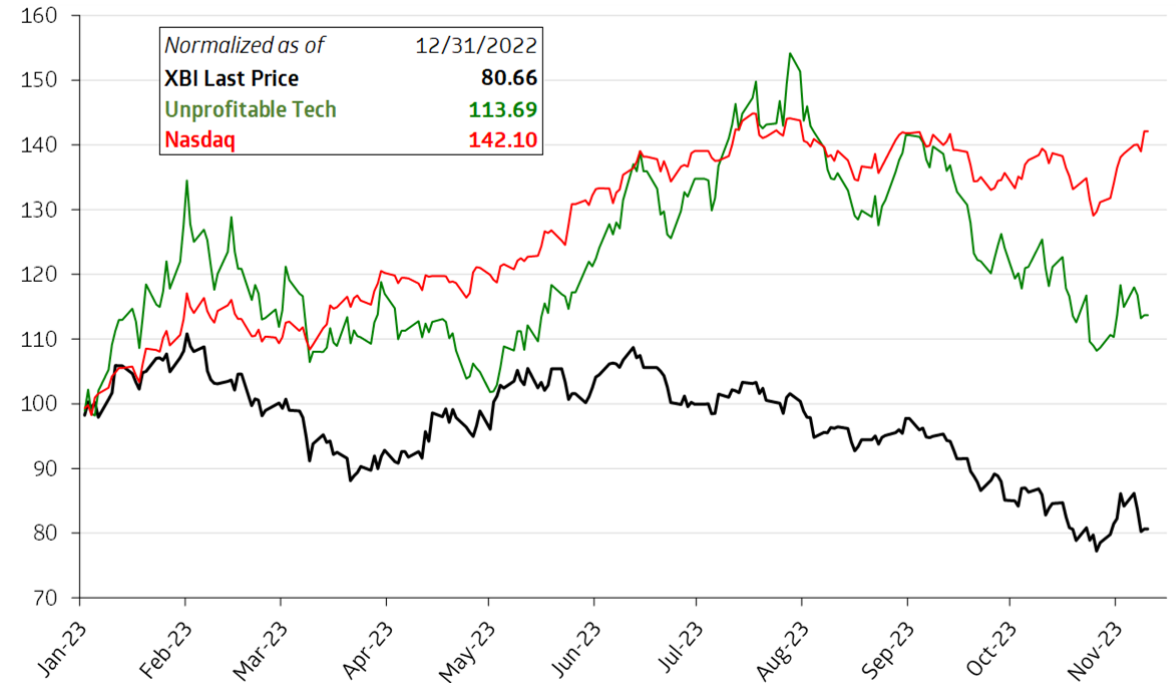
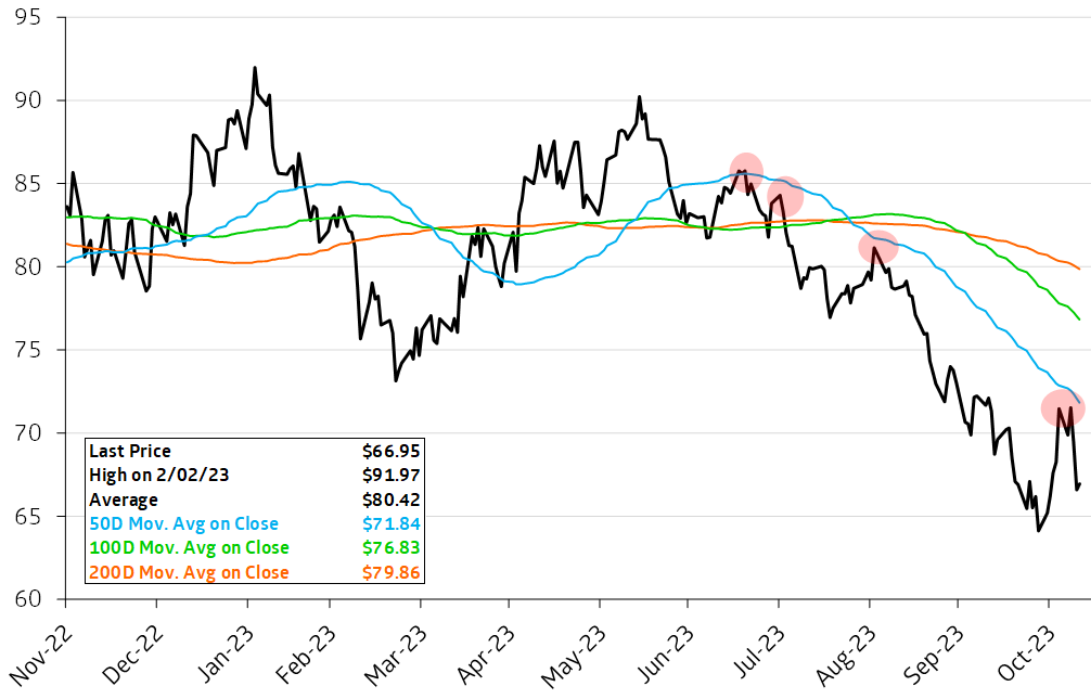
- XBI remains down (57%) from Feb. 2021 peak, vs. S&P up +9% over the same period

Despite large decline in XBI from peaks, still ~70 public biotechs >\$2bn today

Macro-trends: An unprecedented era



Macro-trends: An unprecedented era



Macro-trends: Sector performance and IPO status

13

Total life sciences IPOs

85%

% IPOs priced within range

77%

2023 IPOs trading below offer price

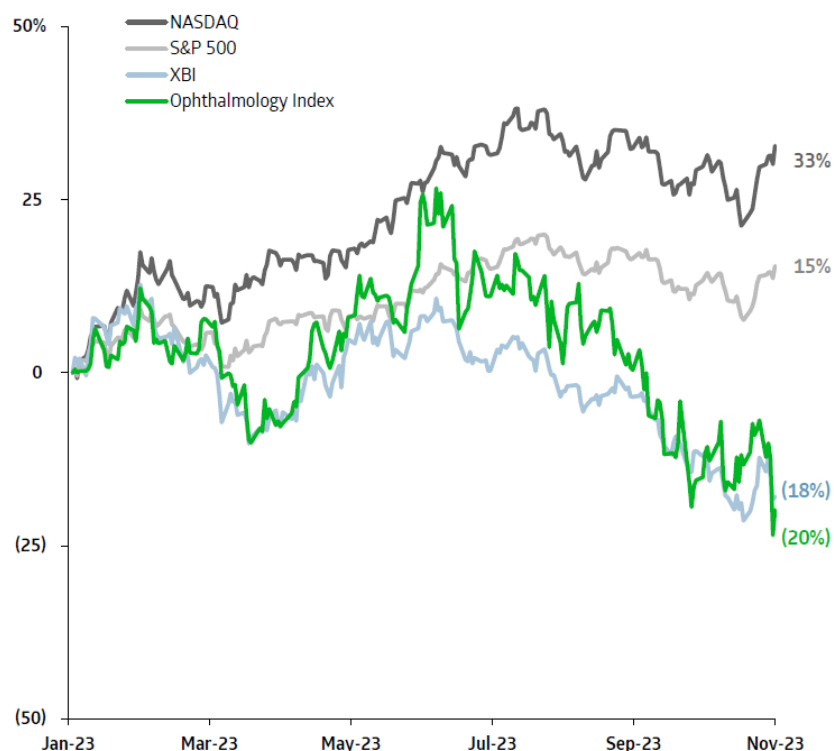
(14.9)%

Median return offer/current

Basket	5-Day	YTD
Alzheimers	(0.5)%	17.4%
Hospitals	(0.7)%	(12.5)%
Obesity	(1.4)%	23.4%
Bi-Multi Spfcs	(2.0)%	(37.0)%
Medtech	(3.2)%	(13.0)%
Spec Pharma	(3.4)%	(10.4)%
Tools Dx	(3.6)%	(19.7)%
PBM/Distys	(3.7)%	(13.2)%
Ophthalmology	(3.8)%	(31.5)%
Vaccine	(5.0)%	(24.4)%
Oncology	(5.6)%	(40.4)%
Precision Oncology	(5.8)%	(46.5)%
AI Based	(6.4)%	(33.0)%
Rare/Genedic Dis	(6.9)%	(30.2)%
Infectious Disease	(7.2)%	(41.4)%
Gene Therapy	(7.3)%	(45.5)%
Cardio	(7.4)%	(25.3)%
Immune Oncology	(7.6)%	(38.7)%
NASH	(8.1)%	(27.7)%
Oncol – Small Mol	(8.3)%	(43.7)%
CNS	(8.8)%	(23.5)%
Protein Degraders	(8.8)%	(56.3)%
Cell Therapy	(9.7)%	(52.1)%
Gene Editing	(10.2)%	(23.5)%
Autoimmune	(10.6)%	(26.4)%
Nephrology	(11.2)%	(82.8)%
ADC/Conjtn	(13.8)%	(57.7)%
Derm	(15.6)%	(35.4)%

Putting ophthalmology in context

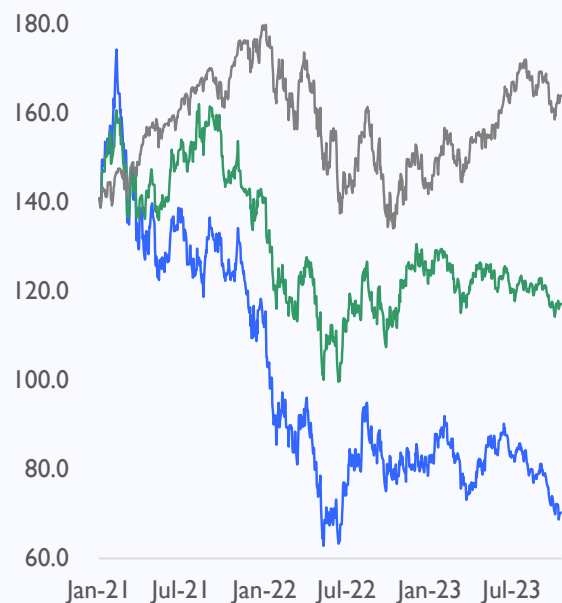
Performance since 2023



Company index	Equity value	Price performance (%) since 2023
NASDAQ	–	33%
S&P 500	–	15
XBI	–	(18)
Ophthalmology trading dashboard		
Apellis	\$5,568	(7%)
IVERIC	–	99(a)
Belite	1071	32
Viridian	722	(52)
REGENXBIO	785	(20)
Tarsus	578	21
Harrow	450	(13)
4D Molecular	465	(46)
EyePoint	226	75
Ocular	167	(25)
Opthea	219	(66)
Lineage Cell	182	(15)
Alimera	170	8
Aldeyra	134	(67)
Kodiak	90	(78)
Outlook	104	(32)
Ocugen	92	(71)
Adverum	95	46
Mean	\$654	(20%)
Median	219	(20)

How XBI trends correlate with financing

Price performance since 2021

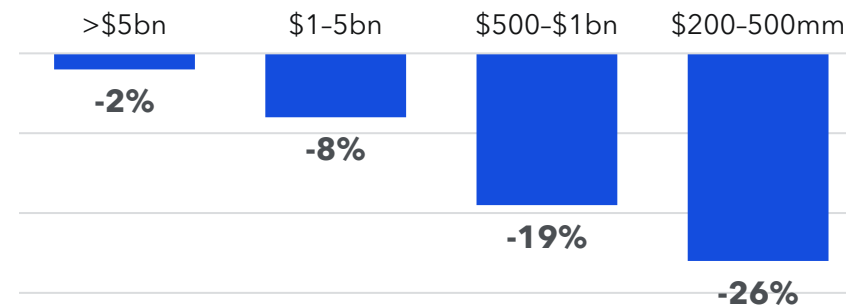


Performance by year

	XBI	NBI	S&P500
2023 YTD	(15%)	(6%)	14%
2022	(28%)	(12%)	(20%)
2021	(20%)	(1%)	27%

2023 price performance by market cap¹

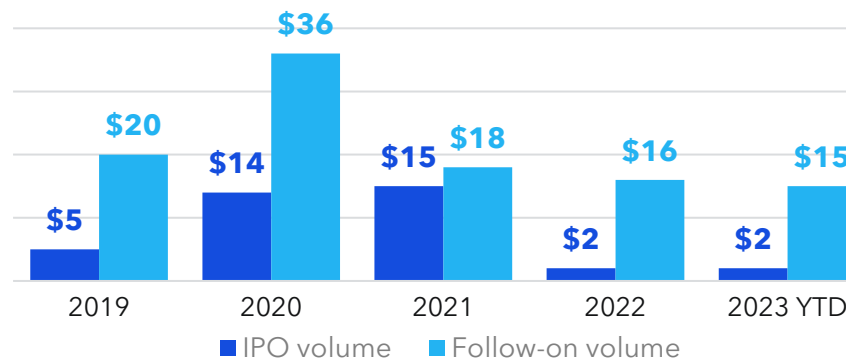
Small cap underperformance has been main driver of XBI declines (equal weighted index)



Financing market overview²

\$ raised (\$bn)

IPO market has remained largely closed during 2023; only 8 IPOs >\$50mm



# of deals	2019	2020	2021	2022	2023 YTD
	41	73	78	11	8
	116	178	114	89	77

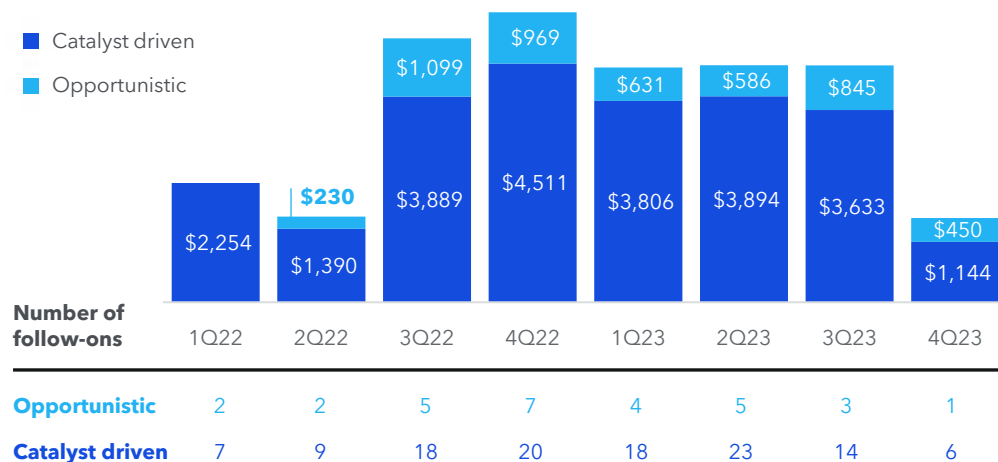
Innovation and selective deployment of capital, despite XBI headwinds

Follow-on market has evolved in 2023, as catalyst-driven financings continue to capture investor attention

However, biotech investors remain extremely selective with IPOs, requiring the right circumstances to facilitate success

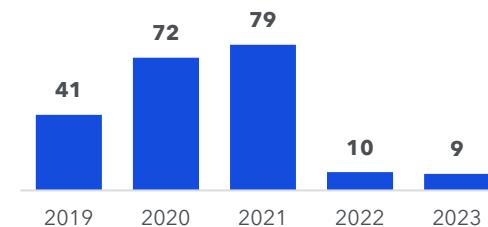
2022-2023 YTD quarterly follow-on deal volume (\$mm)

■ Catalyst driven
■ Opportunistic



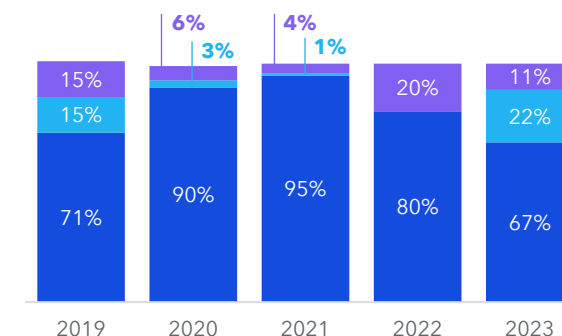
Catalyst-driven financing dynamics demonstrate investor willingness to be patient, but also to fund companies following re-rating events

Annual biotech IPO activity (# of transactions)



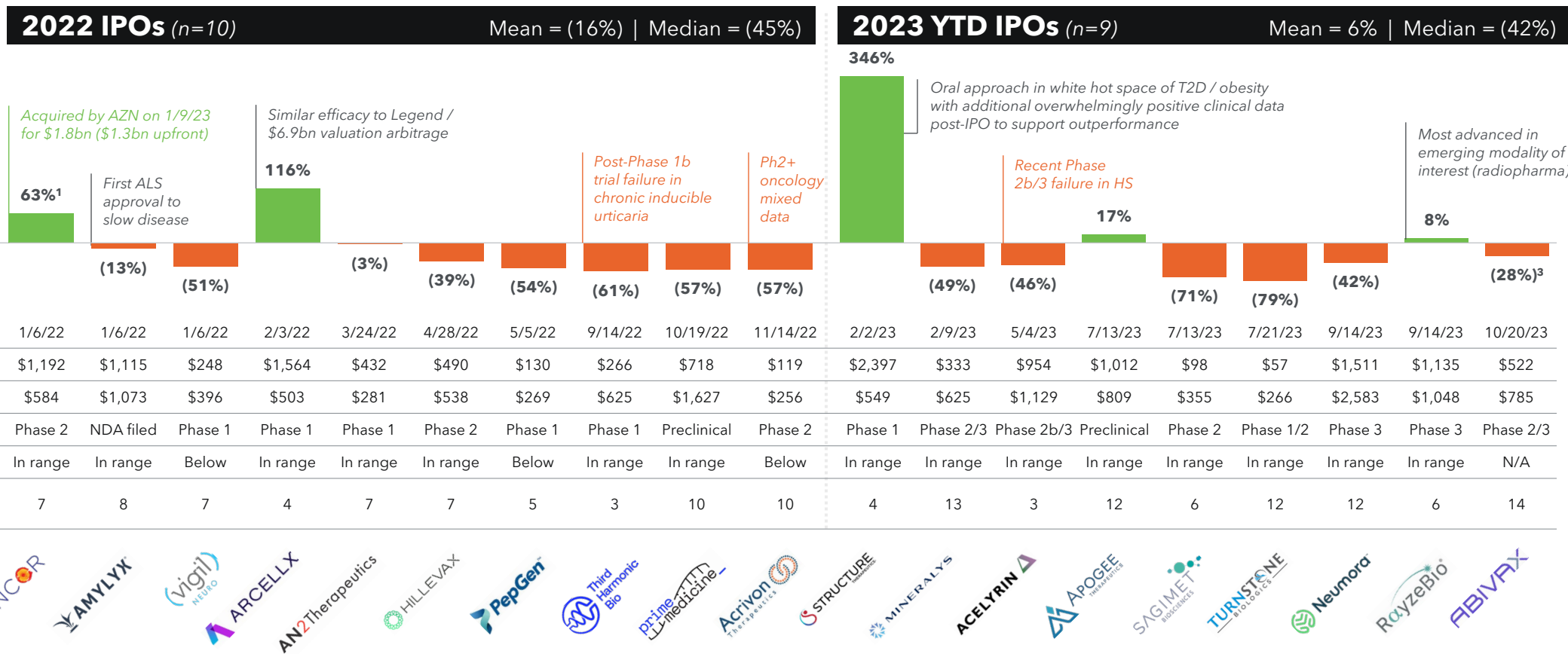
Offer to current performance (% of IPOs)¹

Offer to Current Performance:
■ <0% ■ 0-50% ■ +50%



IPO pressures continue

Offer / current performance of 2022-2023 YTD IPOs



Bank of America. Rx Ophthalmology Market Review, BofA Life Sciences. October 2023. | **Source:** Company filings, press releases and FactSet as of 10/19/23. **(1)** Based on acquisition price by AZN of \$26.00 / share (01/09/23). Only includes upfront payment. **(2)** Market cap at IPO based on common shares outstanding, excluding the impact of greenshoe **(3)** ABVX ordinary shares listed on Euronext Paris. ADS been approved for listing on NASDAQ. Offer to current based on price as of 10/27/23 compared to offering price of 11.60.

Tremendous innovation, especially in ophthalmology

Date	Company	Company Type	Round	China Inv.	Proceeds	Listed Institutional Investors
Jul-23	Tenpoint Therapeutics	Cell Therapy	Series A		\$70	F- Prime; Sofinnova Partners; Britist Patient Capital; Qiming; Eight Roads; UCL Technology Fund
Jun-23	Beacon (fmr AGTC assets)	Gene Therapy	Series A		\$120	Syncona; Oxford Science Enterprises (OSE)
Jun-23	Alkeus	Biotechnology	Series B		\$150	Bain; TCG Crossover; Wellington; Sofinnova
May-23	Ray Therapeutics	Gene Therapy	Series A		\$100	Novo; Deerfield; Norwest; Platanus; MRL Ventures; 4BIO Capital
Apr-23	Therini	Biotechnology*	Series A		\$36	Dementia Discovery Fund; MRL Ventures; Sanofi Ventures; SV Health Investors; Eli Lilly; ADDF; others
Apr-23	Complement	Gene Therapy	Series B		\$79	Gimv; Forbion; BioGeneration; Panakès; Cambridge Innovation Capital (CIC) Hadean Ventures; Seroba Life Sciences
Mar-23	Lenz	Reform	Series B		\$84	Sectoral; Alpha Wave; Point 72; RA Capital; Versant; RTW; others
Feb-23	Eluminex	Biotech	Series B	✓	\$40	Cenova; 3E Bioventures; Oriza; Guangzhou Yuexiu Ind. Inv. Fund Mgmt; Lilly Asia; GL Ventures (Hillhouse); Quan Capital
Dec-22	Perceive Bio	Gene Therapy	Series B		\$78	Braidwell; Catalio; Deerfield; RD Fund; J&J Innovation
Dec-22	Re-Vana	Reform	Series A		\$12	Visionary Ventures; ExSight; InFocus; others
Oct-22	Eudora (Replay Sub)	Gene Therapy	Series A		ND	N/A (Replay Investors: KKR. OMX Ventures, ARTIS, Lansdowne, SALT, DeciBio, Axial)
Oct-22	Ascidian	Gene Therapy	Series A		\$50	Apple Tree Partners
Sep-22	SparingVision	Gene Therapy	Series B		\$78	Jeito; UPMC Enterprises; 4BIO Capital; Bpifrance; RD Fund; Ysios
Jul-22	Nacuity	Biotechnology	Series B		\$17	RD Fund; others
Jun-22	Frontera	Gene Therapy	Series B	✓	\$160	Boyu Capital; Sequoia Capital China; Creacion Ventures OrbiMed
Jun-22	Sling	Biotechnology	Series A		\$35	The Rise Fund (TPG)
May-22	Character Bio	Biotechnology	Series A		\$18	Innovation Endeavors; Section 32; Catalio; LifeForce Capital; Casdin; Clover Health; Industry Ventures; Cantos Ventures
Apr-22	Ashvattha	Biotechnology	Series B	✓	\$69	Huadong Medicine; Natural Capital Management; Tribe Capital; Plum Alley investments
Apr-22	Aurion	Cell Therapy	Other		\$120	Deerfield; Pertichor; Flying L; Falcon Vision; Visionary; Alcon
Feb-22	EyeBio	Aggregator	Series A		\$65	SV Health; Samsara; Jeito; MRL Ventures
Feb-22	SpliceBio	Gene Therapy	Series A		\$57	UCB Ventures; Ysios; NEA; Glide; Novartis Venture Fund ; Asabys
Jan-22	SalioGen	Gene Therapy*	Series A		\$115	GordonMD; EPIQ; Fidelity; T. Rowe; D1 Capital; Symbiosis; CF Foundation; RD Fund
Jan-22	Cloudbreak	Biotechnology	Series C	✓	\$130	CDH Investments; China Grand; Shenzhen GTJA; CCB International; Industrial Securities Capital; others
Dec-21	EyeD Pharma	Reform	Other		\$51	Normainvest; SRIW; SFPI.; Fund+; Qbix II; Noshag; other high net worth individuals
Dec-21	iView Therapeutics	Biotechnology	Series A	✓	\$25	Alpha Bioventure; BioAdvance; Cowin; Haitian International; Jiufeng; Jun Yuan; Naxin; Proxima; others
Dec-21	Aramis Biosciences	Biotechnology	Series A		\$11	Safar Partners; Undisclosed Strategic
Nov-21	Neurophth	Gene Therapy	Series C	✓	\$63	CMG-SDIC Capital; Sequoia Capital China; other Chinese investors
Nov-21	Kedalion	Reform	Series B		ND	Novartis (+option)
Nov-21	OcuTerra (fka SciFlour)	Biotechnology	Series B		\$35	Dreavent; Hambro Perks.
Nov-21	Gyroscope	Gene Therapy	Series C Ext.		\$40	Sanofi
Oct-21	Intergalactic Therapeutics	Gene Therapy*	Series A		\$75	Apple Tree Partners

Tremendous innovation, especially in ophthalmology

Select public and private ophthalmology biotechs

(excluding genetic medicines)

	Company	Equity value	Cash	Stock Price		Revenue			Ophthalmology Asset(s)					
				% of 52 Wk. Hi.	1-Year Perf.	2023E	2028E	Ev/Rev. 2028E	Name	Indication	Mechanism	RoA	Phase	Launch
Marketed / Filed	Apellis	\$5,026	\$899	46%	(27%)	\$353	\$2123	2.2x	Empaveli Syfovre	PNH Geographic atrophy	C3 inhibitor C3 inhibitor	Subcutaneous injection Intravitreal injection	Marketed Marketed	2021 2023
	TARSUS	\$532	\$179	66%	(2%)	\$7	\$514	0.7x	Xdemvy	Demodex blepharitis Meibomian gland disease	GABA A receptor antagonist	Topical eye drop solution	Marketed P1	2023 ---
	OUTLOOK THERAPEUTICS	\$60	\$35	12%	(82%)	\$-	\$554	0.1x	Lytenava (bevacizumab-vikg)	Wet AMD	Anti-VEGF mAb	Intravitreal injection	BLA re-filed	2023
	Ocular Therapeutics	\$225	\$68	37%	(35%)	\$60	\$398	0.6x	Dextenza OTX-TIC OTX-CS1 OTX-DED OTX-TK1	Post-surgical ocular inflammation/pain Allergic conjunctivitis Glaucoma and ocular hypertension Dry eye disease Episodic dry eye disease Wet AMD	GCR agonist PGF2 alpha agonist Tear secretion enhancer Corticosteroid Anti-VEGF TKI	Intracanalicular insert Intracameral implant Intracanalicular insert Intracanalicular insert Intravitreal implant	Marketed Marketed P2 P2 P2 P1 data	2019 2021 2025 2025 2025 2025
	RVL PHARMACEUTICALS	\$21	\$19	8%	(92%)	\$36	\$250	0.2x	Upneeq	Acquired ptosis	α-adrenoceptor agonist	Topical eye drop solution	Marketed	2022
	EYEPOINT PHARMACEUTICALS	\$306	\$143	57%	42%	\$37	\$309	0.5x	Yutiq Dexycu EYP-1901 (voronlanib)	Posterior segment uveitis Post-operative inflammation Wet AMD, NPDR, DME	Corticosteroid Corticosteroid Anti-VEGF TKI	Intravitreal implant Intraocular injection Intravitreal insert	Marketed Marketed P2	2018 2019 2025
Clinical Stage	VIRIDIAN	\$604	\$334	37%	(31%)	\$0	\$855	0.3x	VRDN-001 VRDN-002	Thyroid eye disease Thyroid eye disease	Anti-IGF-IR-mAb Anti-IGF-IR-mAb	Intravenous injection Subcutaneous injection	P3 P2 ready	2025 2027
	KODIAK	\$93	\$385	19%	(76%)	-	\$1138	-0.1x	KSI-301	Retinal vein occlusion Wet AMD Diabetic macular edema Diabetic retinopathy	Anti-VEGF biopolymer conjugate	Intravitreal injection	P3 data P3 data P3 data P3 data	2024 2025 2025 2025
	aldehyra	\$338	\$152	49%	8%	-	-	-	Reproxalap ADX-2191	Dry eye disease Allergic conjunctivitis Primary vitreoretinal lymphoma Proliferative vitreoretinopathy Retinitis pigmentosa	RASP inhibitor DHFR inhibitor	Topical eye drop solution Intravitreal injection	NDA filed P3 CRL P3 P2	2023 2024 --- 2023 ---
	OPTHEA	\$142	\$89	32%	(67%)	-	-	-	OPT-302	Wet AMD DME	VEGF C/D inhibitor	Intravitreal injection	P3 P1/2a data	2025 ---
Private Clinical Stage	Sydnexis								SYD-101	Pediatric progressive myopia	Low-dose atropine formulation	Topical eye drop solution	P3	2025
	ORASIS PHARMACEUTICALS								CSF-1	Presbyopia	Low-dose pilocarpine hydrochloride for pupil modulation	Topical eye drop solution	NDA ready	2023
	AURION BIOTECH								HCEC-1	Corneal edema secondary to endothelial dysfunction	Human cultured corneal endothelial cell (hCEC) therapy	Intravitreal implant	NDA ready (JPN) P2 ready (US)	2023 (JPN) ---
	RE-VANA PHARMACEUTICALS								EyeLief	TBD TBD	Gel-based photocrosslinked implant Gel-based photocrosslinked implant	Intravitreal / intracameral implant Intravitreal / intracameral implant	PC PC	---
	MITOTECH SKQ								Visomitin	Dry eye disease Glaucoma Uveitis Dry AMD LHON	Cardiolipin peroxidation inhibitor	Topical eye drop solution	P3 P2 ready P2 ready P2 ready P2 ready	---
	AZURA								AZR-MD-001	Meibomian gland disease Vision quality associated with CLD	Keratolytic agent	Topical ointment applied to meibomian glands	P3 ready P2	---

Private - Not Applicable

Innovation in ophthalmology, especially pharma

Breaking down the eye care universe

Eye care market⁽¹⁾ benefits from high barriers to entry and secular growth prospects, with ophthalmic drugs comprising 50%+ of total market

Vision care
Combined ~\$16bn in 2021

Ophthalmic drugs
Combined ~\$39bn in 2021

Surgical devices ~\$11bn in 2022	Traditional contact lenses ~\$10bn in 2022	Ocular health / OTC / legacy prescription ~\$6bn / ~15bn in 2022	Innovative Therapeutics ~\$25bn in 2022
<ul style="list-style-type: none"> Market comprised of implantables (intraocular lenses and surgical glaucoma devices), consumables (vitreoretinal and refractive disposable instruments) and equipment (cataract and vitreoretinal consoles and accessories) approx. 30%, 50% and 20% of market size, respectively Growth driven by implantables, w/ greater access to surgery, adoption of new technologies in low income countries and shift to advanced-technology intraocular lenses 	<ul style="list-style-type: none"> Four players owning >95% share Market is characterized by high barriers to entry (specialized manufacturing, stringent regulation), and expanding target market (emerging markets growth) Growth driven by unmet medical and consumer needs, aging population, wealth effect and lifestyle changes (myopia epidemic; digital eye strain) 	<ul style="list-style-type: none"> Similar to contact lenses market, ocular health is relatively concentrated and benefits from substantial barriers to entry Market includes contact lens care solutions, ocular health treatments for dry eye, ocular allergy and eye redness, drugs for glaucoma and retinal disorders, and ocular vitamins Shift from reuseable to daily contact lenses weighs on growth for cleaning solutions, however OTC drops represent a growing market Overall OTC and legacy prescription market is expected to experience a steady growth on the back of rising incidence of eye-related disorders 	<ul style="list-style-type: none"> Innovative therapeutics market is the largest component (compared to OTC / legacy prescription) of the global ophthalmic drugs market Some of the most attractive indications based on 2028E sales potential are wet AMD (~\$9bn), macular edema (~\$6.5bn), dry AMD (~\$2.5bn), glaucoma (~\$2bn) and dry eye (~\$2bn) Mainly comprised of select large players, but independent biotechs with novel therapeutics beginning to commercially compete Number of independents also focused on rare ophthal. / IRDs

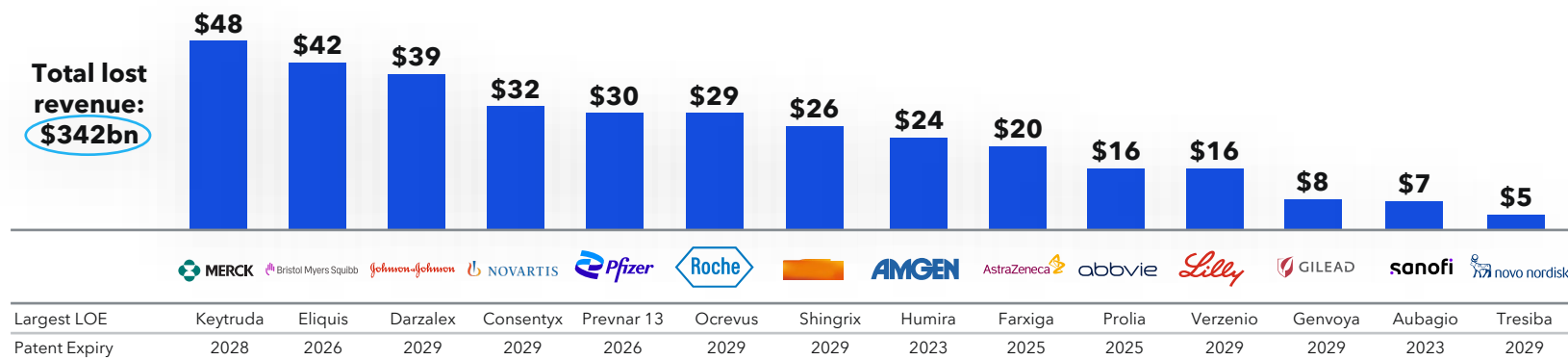
INDEPENDENT COMPANIES — LARGER PLAYERS — LARGE PHARMA



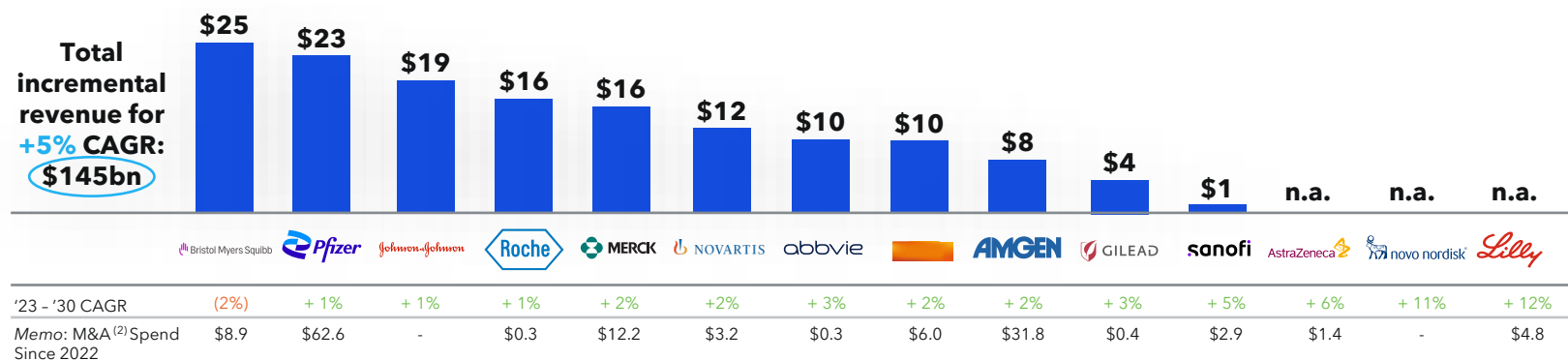
Centerview Partners. Biopharma Market Overview. October 2023. | **Source:** Analyst research, company filings. **(1)** Definition excludes sunglasses, spectacle frame & spectacle lenses.

Large strategics have strong need for acquisition

Revenue at risk from LOEs in 2023-2030 period (\$bn)⁽¹⁾



Incremental 2030 revenue needed to achieve +5% (\$bn)



Leading ophthalmic companies also facing erosion of franchises

The top five players are all facing decline, but a handful of players are looking to disrupt the field

■ 2021 sales ■ 2026E sales (launched) ■ 2026E (not yet approved)
 ► Asset held by emerging biotech/pharma

Top 15 companies ranked by:

2021 sales		
Company	2021 & 2026 net sales	CAGR
REGENERON	\$5,792 \$5,759	(0.1%)
NOVARTIS	\$4,214 \$2,673	(8.7%)
Bayer	\$3,454 \$2,589	(5.6%)
abbvie	\$3,348 \$1,997	(9.8%)
Santen	\$2,161 \$1,716	(4.5%)
AMGEN / HORIZON	\$1,661 \$3,876	18.5%
Roche	\$1,557 \$3,598	18.2%
BAUSCH+LOMB	\$953 \$1,157	4.0%
VIATRIS™	\$489 \$497	0.3%
Alcon ⁽¹⁾	\$335 \$305	(1.8%)
SUN PHARMA	\$130 \$278	16.5%
Rayner	\$111 \$166	8.4%
aerie ⁽¹⁾	\$109 NA	NA
Théa / AKORN	\$57 \$9	(30.5%)
Alimera	\$48 \$105	17.0%

2026 sales		
Company	2021 & 2026 net sales	CAGR
REGENERON	\$5,792 \$5,759	(0.1%)
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Apellis	\$1,538	NM
BAUSCH+LOMB	\$953 \$1,157	4.0%
astellas / IVERIC BIC	\$589	NM
VIATRIS™	\$489 \$497	0.3%
TARSUS	\$390	NM
aldehyra	\$359 Expected CRL?	NM
OUTLOOK THERAPEUTICS	\$356 CRL received ?	NM
VIRIDIAN	\$348	NM

Bank of America. Rx Ophthalmology Market Review, BofA Life Sciences. October 2023.
 Source: EvaluatePharma. Data as of 06/30/23. Note: Certain businesses, such as B&L's, include revenue from selected OTC products and others, like Viatris', include generic sales.
 (1) Alcon revenue projections do not include Aerie revenue (acquired in November 2022).

Approved ophthalmic drugs under pressure

With approved drugs under severe pressure, the focus has shifted to clinical stage / early launch stories

- 2021 sales
- 2026E sales (launched)
- 2026E (not yet approved)
- ▶ Asset held by emerging biotech/pharma

Top 15 products ranked by:

2021 sales		
Product	2021 & 2026 net sales	CAGR
EYLEA (aflibercept) injection For intravitreal injection	\$9,893 \$8,621	(2.7%)
LUCENTIS RANIBIZUMAB	\$3,641 \$1,074	(21.7%)
TEPEZZA toprotumumab-svw	\$1,661 \$3,876	18.5%
Restasis (cyclosporine ophthalmic emulsion) 0.05%	\$1,290 \$102	(39.8%)
LUMIGAN	\$579 \$443	(5.2%)
xidra	\$468 \$523	2.2%
Refresh Lubricant Eye Drops	\$393 \$413	1.0%
Ocuville	\$351 \$414	3.3%
Ozurdex	\$340 \$398	3.2%
Combigan bimatoprost tartrate/tafluprost, ophthalmic solution 0.2/0.03%	\$339 \$94	(22.7%)
Systane LUBRICANT EYE DROPS	\$335 \$305	(1.8%)
Patanol olopatadine hydrochloride ophthalmic solution 0.1%	\$314 \$222	(6.7%)
SIMBRINZA	\$312 \$223	(6.5%)
TRAVATAN	\$292 \$146	(13.0%)
Xalatan latanoprost ophthalmic solution 0.005%	\$249 \$203	(4.0%)

Notable exclusion
oxervale is being sold to a new owner

Notable exclusion
oxervale is being sold to a new owner

2026 sales		
Product	2021 & 2026 net sales	CAGR
EYLEA (aflibercept) injection For intravitreal injection	\$9,893 \$8,621	(2.7%)
TEPEZZA toprotumumab-svw	\$1,661 \$3,876	18.5%
YABYSMO faricimab-svaia injection 6 mg	\$2,726	NM
SYFOVRE (pegcetacoplan injection)	\$1,538	NM
LUCENTIS RANIBIZUMAB	\$3,641 \$1,074	(21.7%)
izervay (avacincaptad pegol ophthalmic solution)	\$589	NM
susvimo ranibizumab injection 0.5mg/0.05mL	\$542	NM
xidra	\$468 \$523	2.2%
LUMIGAN	\$579 \$443	(5.2%)
Ocuville	\$351 \$414	3.3%
Refresh Lubricant Eye Drops	\$393 \$413	1.0%
Ozurdex	\$340 \$398	3.2%
xdemvy	\$390	NM
LYTENAVA	\$356	Expected CRL?
Reproxalap Eye Drop	\$349	CRL received ?

Bank of America. Rx Ophthalmology Market Review, BofA Life Sciences. October 2023.
Source: EvaluatePharma and company filings. Data as of 06/30/23. *Note:* Certain businesses, such as B&L's, include revenue from selected OTC products and others, like Viatrix's, include generic sales.

Large strategics have capacity for acquisition



**Significant
firepower
across industry**



**All players have
ability to increase
activity**

Biopharma M&A activity and spend since 2018⁽¹⁾

Company	Mkt. cap	Gross biopharma M&A spend last 5 years	Deal size (\$bn)				Deal stage			Total	Deals per year	
			>\$20	\$10-20	\$5-10	<\$5	Early	Late	Comc'l			
Bristol Myers Squibb	\$120	\$21 \$111 ⁽²⁾	/	/	-	2	-	2	2	4	0.8	
abbvie	\$263	\$83 ⁽²⁾	/	-	-	-	-	-	/		0.2	
Pfizer	\$185	\$82	/	2	2	/	/	/	4	6	1.2	
AMGEN	\$152	\$48	/	/	-	2	-	/	3	4	0.8	
AstraZeneca	\$213	\$41	/	-	-	/	-	/	/	2	0.4	
MERCK	\$264	\$32	-	2	-	5	2	5	-	7	1.4	
NOVARTIS	\$221	\$27	-	-	2	3	-	4	/	5	1.0	
GILEAD	\$100	\$26	-	/	-	2	/	-	2	3	0.6	
sanofi	\$138	\$18	-	-	-	7	4	-	2	7	1.4	
Lilly	\$577	\$12	-	-	/	4	-	4	/	5	1.0	
Roche	\$229	\$12	-	-	/	/	-	2	-	2	0.4	
novo nordisk	\$75	\$9	-	-	/	2	-	2	/	3	0.6	
novo nordisk	\$456	\$8	-	-	-	4	2	2	-	4	0.8	
Johnson & Johnson	\$376	\$7	-	-	/	-	-	/	-		0.2	
			# of deals	5	7	8	34	10	26	18	54	0.8

Centerview Partners. Biopharma Market Overview. October 2023. |
Source: Public filings, Wall Street research and FactSet. Note:
Dollars in billions.

(1) Reflects upfront deal value; excludes contingent consideration.
(2) Approximately \$90bn of Bristol Myers Squibb M&A spend over
the period comes from acquisition of Celgene in January 2019 and
all of AbbVie's acquisition spend comes from acquisition of
Allergan in May 2020 for \$83bn.

Deals are being done...

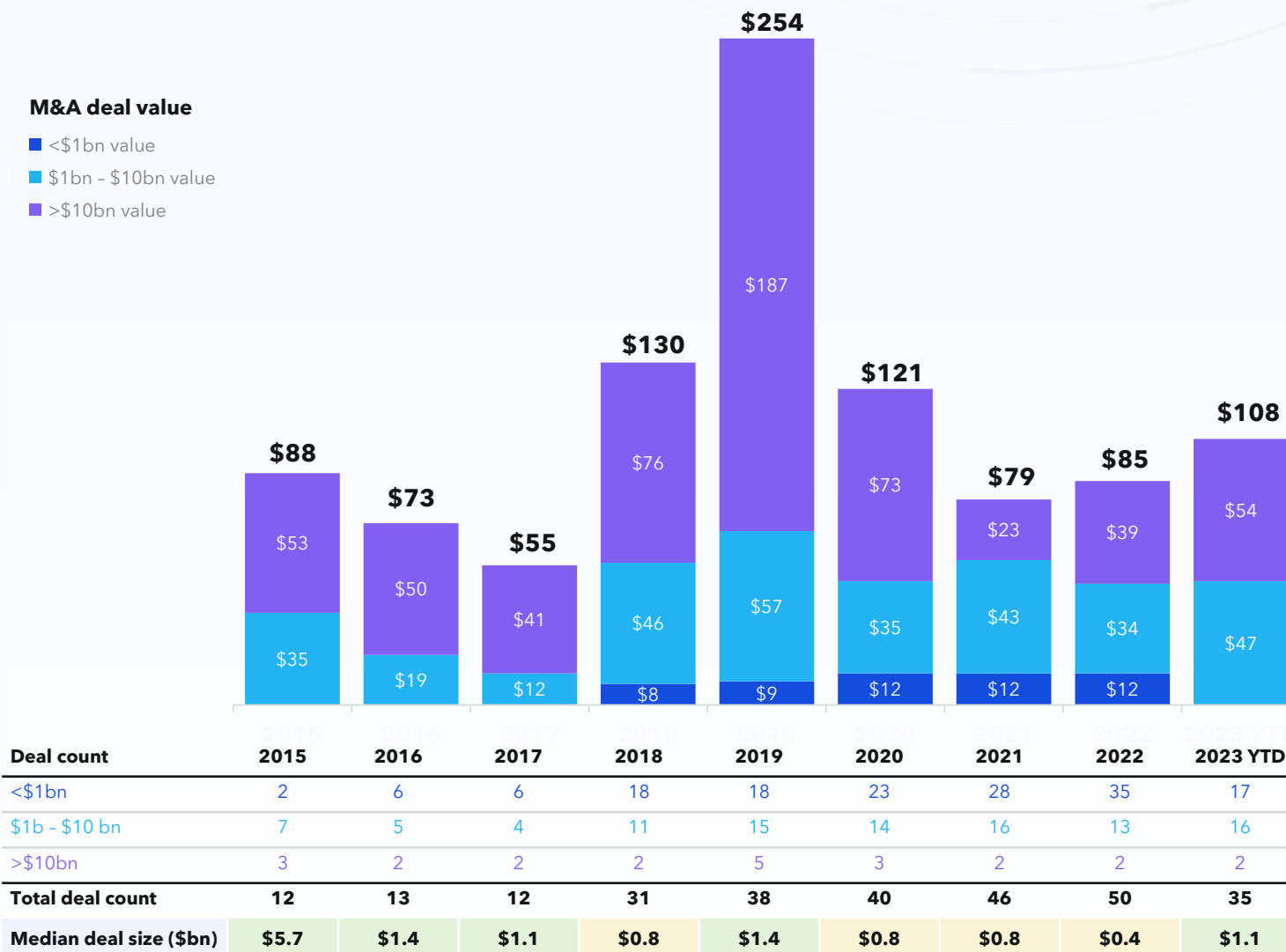
YoY activity

(1/1-10/23, 2022 vs 2023)¹

Deals	Count	Value
Deals with <\$1bn value	(47%)	(34%)
Deals with \$1bn - \$10bn value	60%	89%
>\$10bn value	100%	364%

M&A deal value

- <\$1bn value
- \$1bn - \$10bn value
- >\$10bn value



...but acquisition targets are changing

95% of transactions since 2022

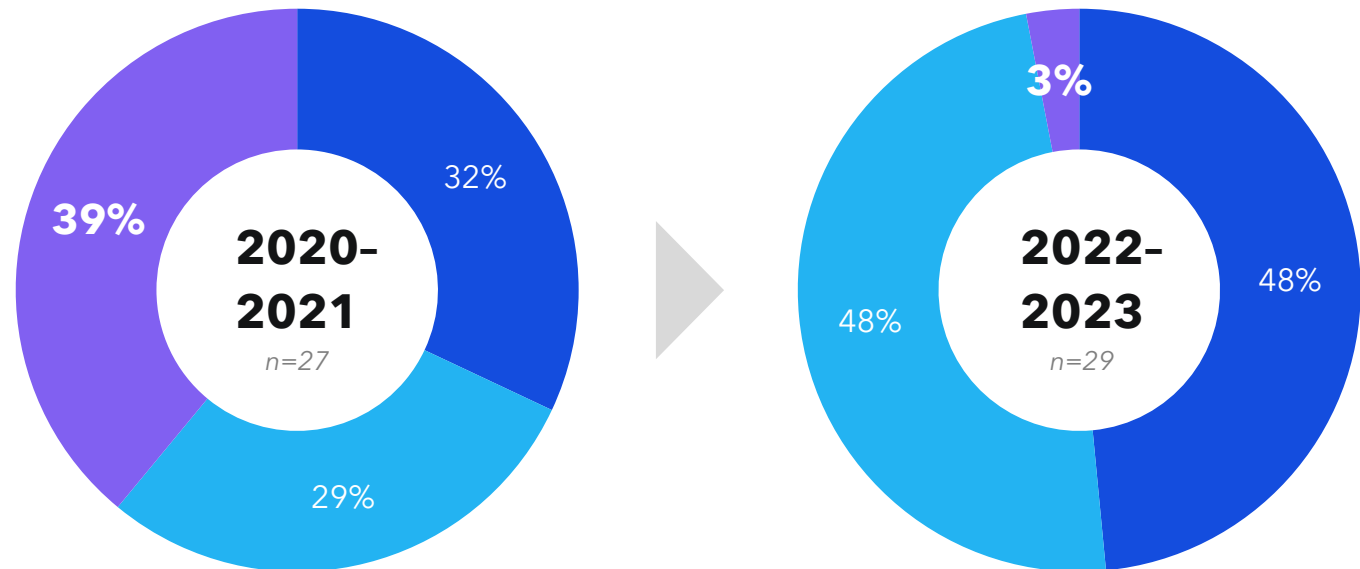
have been for late-stage/marketed assets focused on filling 2025-2030 revenue gaps from impending LOE

Only 1 transaction

has been for early-stage asset in last 2 years **vs 11 deals** for early-stage assets in 2020 to 2021

Deals by stage

(>\$1bn)



■ Commercial ■ Late-stage (filed/P3) ■ Early stage (P1/2)

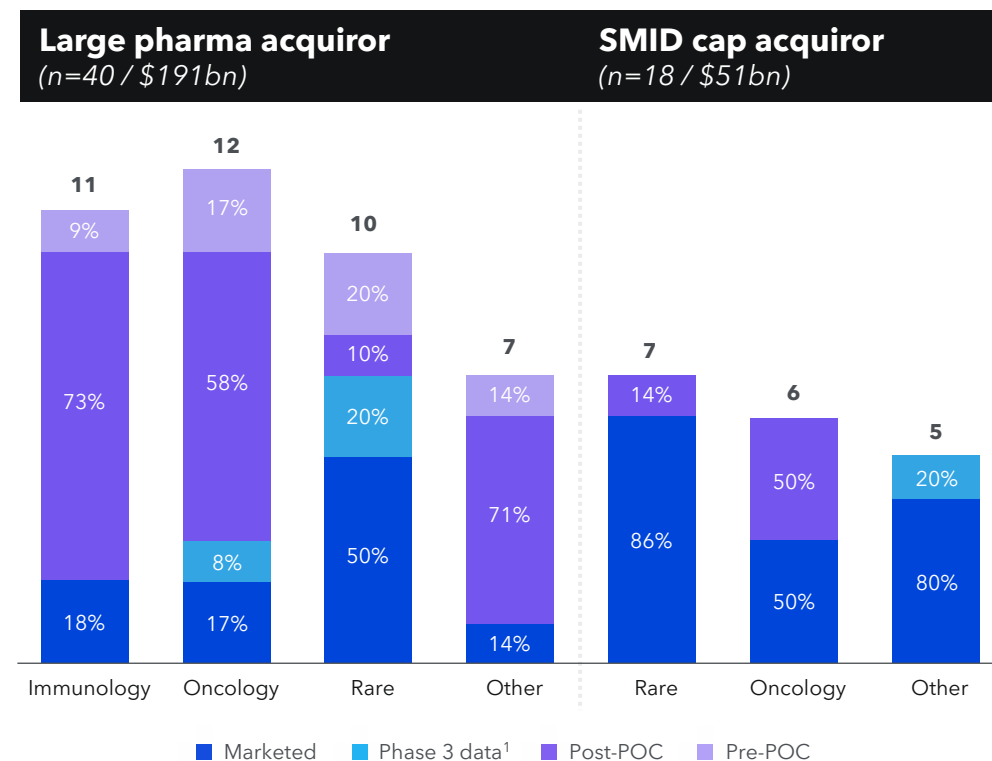
...but acquisition targets are changing

Deal volume by acquiror size (% of deals)

	Large pharma (n=40)	SMID cap (n=18)
Marketed	25%	▶ 72%
Phase 3 data	8%	6%
Post-POC	▶ 53%	22%
Pre-POC	15%	0%

- Large pharma represents >65% of transactions and >75% of total dollar volume
- Large pharma transacts for clinical stage companies with reasonable frequency assuming they are in core areas and have obtained POC (oncology, I&I primarily)
- The SMID cap buyer universe clearly prefers the safety of acquiring commercial stage products, particularly when surpassing >\$1bn upfront

M&A Volume by asset stage (2020 - 2023 YTD)

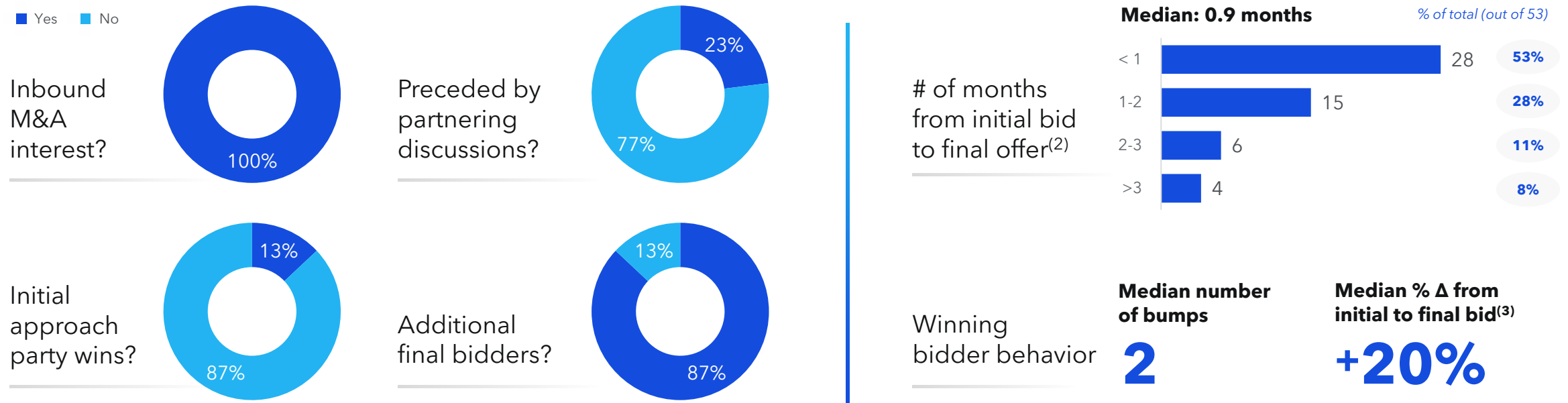


...but acquisition targets are changing

	Early Stage (P1-P2)	Late Stage (P3 - Filed)	Commercial (Marketed)
2023 (16 deals)	<p>6%</p> <p>DICE</p>	<p>44%</p> <p>CINCOR, Prometheus Biosciences, CHINOOK THERAPEUTICS, Bellus HEALTH, IVERIC BIO, VectivBio, POINT BIOPHARMA</p>	<p>50%</p> <p>Intercept pharmaceuticals, proventionbio, AMRYT PHARMA, Albireo, MIRATI THERAPEUTICS, Seagen, CTI, REATA PHARMACEUTICALS</p>
2022 (12 deals)	<p>0</p> <p>None</p>	<p>50%</p> <p>Affinivax, IMAGO BIOSCIENCES, SIERRA ONCOLOGY, forma THERAPEUTICS, nimbus THERAPEUTICS, Turning Point Therapeutics</p>	<p>50%</p> <p>biohaven pharmaceuticals, HORIZON, MYOVANT SCIENCES, ZOGENIX, GBT</p>
2021 (15 deals)	<p>40%</p> <p>AMUNIX, kymab, PANDION THERAPEUTICS, TRILLIUM THERAPEUTICS INC, vividion THERAPEUTICS, TranslateBIO</p>	<p>33%</p> <p>Dicerna, ARENA PHARMACEUTICALS, Constellation PHARMACEUTICALS, ACCELERON, FivePrime</p>	<p>27%</p> <p>GW pharmaceuticals, Kadmon, VIFOR PHARMA, VIELA BIO</p>
2020 (13 deals)	<p>15%</p> <p>AskBio, VELOS BIO</p>	<p>54%</p> <p>Dermira, eidos a bridgebio company, MYOKARDIA, FORTY SEVEN, Momenta, PRINCIPIA BIOPHARMA</p>	<p>31%</p> <p>aimmune THERAPEUTICS, MYR Pharmaceuticals, Immunomedics, PORTOLA</p>

Acquisition is substantially driven by prior partnerships

Biopharma transactions of ~\$1bn - \$50bn since 2019 (n=53)⁽¹⁾



Centerview Partners. Biopharma Market Overview. October 2023. | **Source:** Public filings, Wall street research, FactSet. Includes deals from 2019-2023 YTD. Excl. consumer healthcare deals. Offer value excl. contingent payments. Premium as of unaffected date for rumored transactions. **(1)** Includes deals involving publicly traded acq. targets disclosing background deal process information (eg, 14D9, DEF14A). **(2)** Reflects time starting from beginning of "final process" in which the final winning bidder was involved. **(3)** Based on midpoint of range where applicable.

Acquisition is substantially driven by prior partnerships

Key statistics for >\$1bn last 5 years

0

of deals that began with banker-led process

76%

% of deals preceded by partnership discussions

83%

% of deals where the first bidder wins

35%

% of deals with multiple **first-round** bidders

10

of deals with **2 final-round** bidders¹

1

of deals with **3+ final-round** bidders

1

Biopharma M&A begins organically

- Deals begin with pre-existing relationships, often developed through partnership discussions
- Very rare for companies to receive unsolicited acquisition proposals with no prior interaction
- Banker-led sales processes not effective

2

First bidder almost always wins

- Initial bidder has significant advantage
 - Management / Board alignment secured
 - Many months of work already invested
 - Strong desire to own the asset
- Very difficult for other parties to catch up

3

Rare to have two final bidders

- Deals typically come together very quickly
 - Average 1.1 months from initial bid to final bid
- Rare to have multiple final bidders
 - Value is in the eye of the beholder
 - Requires a differentiated view from the market

Shift in 2023 M&A playbook

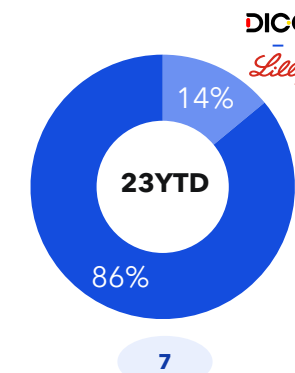
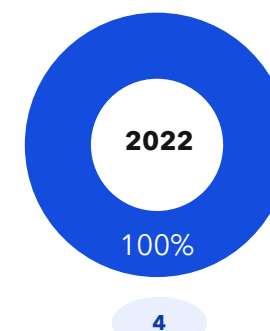
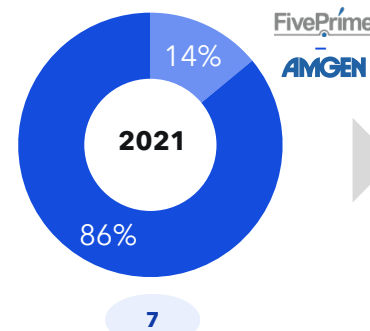
Observations & insights

- **Increased M&A competition** driven by a **scarcity of de-risked, needle-moving assets**
- **First-mover advantage** remains intact for clinical-stage deals, with over 80% of first-bidders winning transactions for clinical-stage targets in 2023 YTD
- **Commercial-stage deals** present a different narrative, with **fewer than half** of first bidders winning transactions in 2023 YTD
- **This bifurcation** speaks to increasing competition for de-risked assets and the trend of transactions having **broader outreach to counterparties**; majority of deals in 2023 YTD had 3+ parties actively involved in the process

% of first clinical bidders winning transactions

- First clinical bidder wins
- Subsequent clinical bidder wins

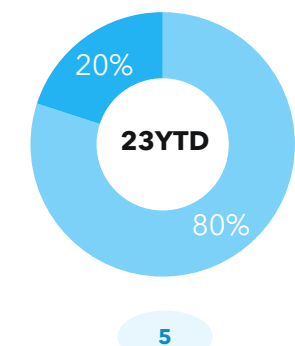
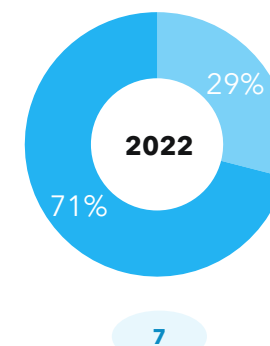
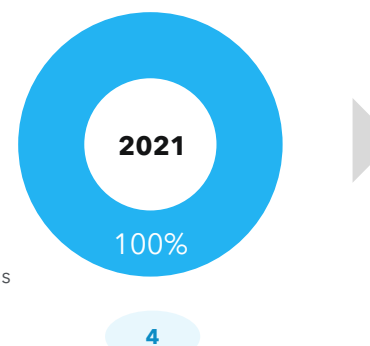
(# of Clinical Stage M&A Deals)



% of first commercial bidders winning transactions

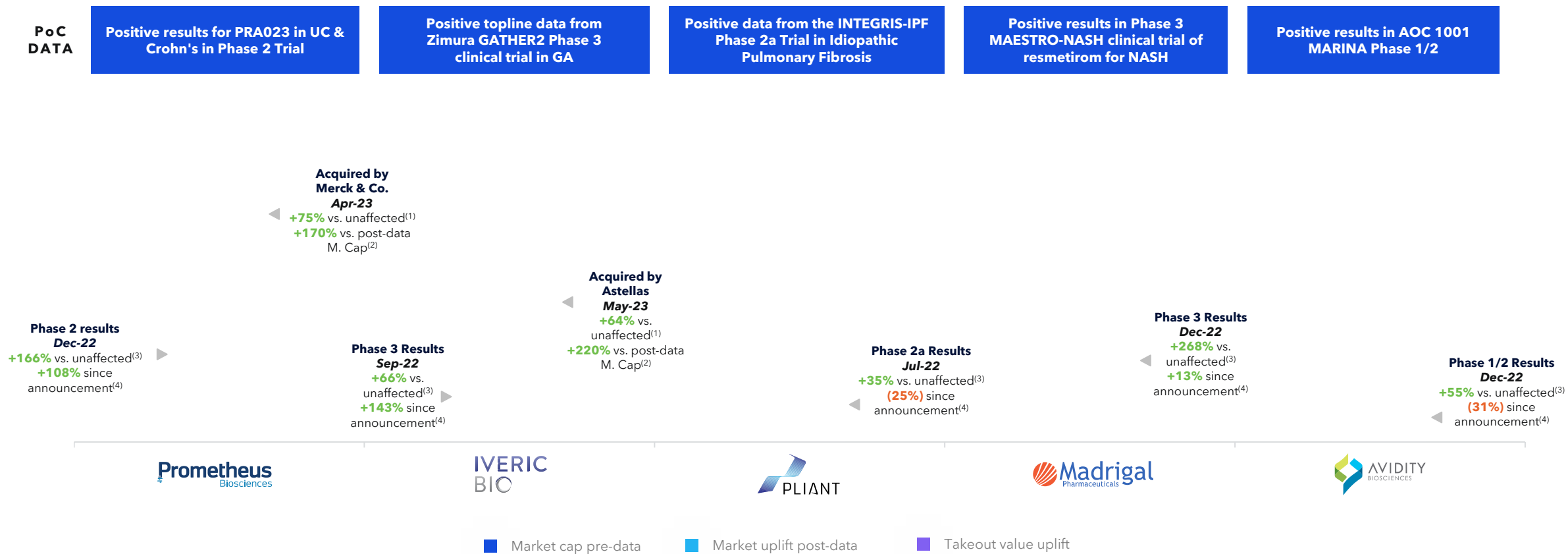
- First commercial bidder wins
- Subsequent commercial bidder wins

(# of Commercial Stage M&A Deals)



Positive data drives probability of success

Uplift in market cap following positive data



Centerview Partners. Biopharma Market Overview. October 2023. | Dollars in millions. **(1)** Premium of takeout price to last unaffected close prior to transaction announcement. **(2)** Takeout premium to closing market cap. post data announcement. **(3)** Premium of closing price post data announcement to last unaffected close prior to data announcement. **(4)** Based on share price change between closing price on date of data announcement and current share price.

But post-commercialization, value goes down

Company	First Product Launch(es)	Category	Approval date	Years on market	Mkt cap. @ appr.	Curr./{exit} mkt cap	Pre-appr. shr px to curr./{exit}	Notes
Independent Companies							Current	
Regeneron	Eylea (wet AMD)	NCE (growing mkt, best in class)	Nov-11	11.9	\$4,611	\$84,153	1,456%	Eylea is one of the best selling products in history; company also continued further successful development and launches
Apellis	Syfovre (geographic atrophy) ²	NCE (new mkt, first in class)	Feb-23	0.7	\$5,777	\$5,597	(8%)	Share price performance post-launch was extremely robust; vasculitis reports caused material decline (situation evolving)
Tarsus	Xdemvy (demodex bleph)	Novel reform (new mkt, first in class)	Jul-23	0.3	\$643	\$449	(43%)	Too early to analyze; no earnings reports provided
Ocular Therapeutix	Dextenza (post cataract)	Reform (Gx/competitive mkt)	Dec-18	4.9	\$274	\$192	(64%)	Slow and steady Dextenza growth; TKI success has been a primary tailwind in recent years
Eyenovia	Mydcombi (mydriasis)	Reform (Gx/competitive mkt)	May-23	0.5	\$175	\$46	(77%)	Difficult market; acquired another cataract asset post-launch
Alimera	Iluvien (DME)	Reform (Gx/competitive mkt)	Sep-14	9.1	\$212	\$28	(96%)	No pipeline; launch underperformed; added Yutiq in 2023
Acquired companies (below approval share price)							@ Exit	
Ista {acq. by B&L}	Xibrom (post cataract)	Reform (competitive mkt)	Mar-05	6.0	\$253	{\$485}	(8%)	Franchise sustained by concentration changes
Oyster Point {acq. by Viatrix}	Tryvaya (dry eye)	Novel reform (comp. mkt, first in class)	Oct-21	1.1	\$354	{\$415}	(19%)	Launch underperformed; limited pipeline)
Inspire {acq. by Merck}	AzaSite (allergic conj.)	Reform (competitive mkt)	Apr-07	4.8	\$312	{\$425}	(32%)	Launch underperformed; had multiple pipeline failures
Aerie {acq. by Alcon}	Rhopressa (IOP lowering) Rocklatan (IOP lowering)	NCE (Gx/competitive mkt)	Dec-17	4.7	\$2,140	{\$770}	(74%)	Rocklatan added Mar-19; launches underperformed; ophth pipeline yielded no material successes
Sold commercial assets (while below approval share price)							@ Sale	
Omeros {assets to Rayner}	Omidria (cataract adjunct)	Reform (Gx/competitive mkt)	May-14	7.5	\$396	{\$458}	(37%)	Sold Omidria to fund development outside of ophthalmology
EyePoint {assets to HROW/ALIM}	Dexycu (post cataract) Yutiq (uveitis)	Reform (Gx/competitive mkt)	Feb-18	5.3	\$47	{\$210}	(41%)	Dexycu licensed to Harrow and Yutiq (which was approved in Oct-18) was sold to Alimera; pivoted to TKI development
Kala {assets to Alcon}	Inveltys (dry eye) Eysuvis (dry eye flares)	Reform (Gx/competitive mkt)	Aug-18	3.8	\$332	{\$44}	(96%)	Pivoted to cornea development after acquiring Combangio
Acquired company (above approval share price)							@ Exit	
Spark {acquired by Roche}	Luxturna (RPE65)	GTx (new mkt)	Dec-17	1.2	\$1,811	{\$4,800}	134%	Acquired for pipeline/platform outside of ophth; launch has since underperformed (no additional INDs in the eye)

Bank of America. Rx Ophthalmology Market Review, BofA Life Sciences. October 2023. | **Source:** Company filings, press releases and FactSet. Data as of 10/27/23. **(1)** Two other notable successful launches are not possible to benchmark in a like manner: (A) Horizon, as they had multiple products and billions of sales at time of Tepezza launch and (B) Dompe, as they are a private despite Oxervate success. **(2)** Excludes prior launch of Apellis' PNH asset, which only drove minor share price momentum.

But post-commercialization, value goes down

To date pure-play, small-cap ophthalmology launches have not met expectations...

in fact, companies that have launched a drug and are trading above/near their approval share price have largely had material pipeline momentum driving additional value

	Company	First Asset Launched	Category	Approval Month	Mkt Cap @ Appr.	Year on Mkt	Current (or Exit) Mkt Cap	Approval to Curr./Exit Share Price	Additional Drivers?	
									Other Launches?	Pipeline Value
Exits	Ista {acquired}	Xibrom ⁽¹⁾	Reform	Mar-05	\$249	{6.7}	{\$485}	(6%)	✗ Concentration changes	✗
	Inspire {acquired}	AzaSite	Reform	Apr-07	\$312	{3.6}	{\$425}	(32%)	✗	✗ Pipeline failure
	Omeros {licenced asset}	Omidria	Reform	Jun-14	\$401	{6.7}	{\$458}	(38%)	✗	🔍 Mixed; not in ophth
	EyePoint {pivot to retina}	Dexycu	Reform	Feb-18	\$47	3.1	\$414	(17%)	✔ Yutiq (pivoted to retina)	✔ TKI
	Ocular Therapeutix	Dextenza ⁽²⁾	Reform	Dec-18	\$235	2.8	\$372	(15%)	✔ Label expansion	✔ TKI, glaucoma, dry eye (~)
	Oyster Point	Tyrvaya	Reform (2 nd order)	Oct-21	\$361	Early 0.4	\$298	(19%)	✗	✗ Early stage
	Aerie	Rhopressa		Dec-17	\$2,138	3.9	\$439	(84%)	✔ Rocklatan	🔍 Mixed; not yet material
	Kala	Inveltys	Reform	Aug-18	\$308	3.2	\$95	(90%)	✔ Eysuvis	✗
	Alimera	Iluvien	Reform	Sep-14	\$229	7.1	\$38	(93%)	✗	✗
	Spark {acquired}	Luxturna	GTx	Dec-17	\$1,811	{0.9}	{\$4,805}	134%	✗	✔ Not in ophth

Source: FactSet, company websites and press releases. Data as of 01/01/22. {} Denotes amount at exit. (1) Excludes ISTA's prior launches of Istalol and Vitrase and bases the performance based on the data of Xibrom's launch. Also excludes concentration changes to Xibrom to Bromday and Prolensa. (2) Excludes Ocular's earlier launch of Resure.

Looking ahead: 2024 and beyond

1

Biopharma market will rebound

- Record innovation in new modalities continues, including new antibody constructs, recombinant proteins, cell therapies, gene therapies and RNA
- Once-dormant areas of medicine are experiencing newfound attention and positive data (obesity, diabetes, Alzheimer's, immunology, inflammatory diseases)
- Inflation is easing and biotech markets will benefit as rates stabilize

2


Majority of deals in 2024 will be for late-stage / commercial assets

- Expect majority of deals in 2024 to be for late-stage / commercial assets as pharma continues to plug revenue gaps created by impending LOEs
- Bristol, Pfizer, and Merck have largest end-of-decade growth needs and are likely acquirors of commercial-stage assets in near term

3

Starting in 2025, M&A will shift toward earlier-stage assets again

- Expect increasing share of deals in 2025+ to be for early-stage assets as pharma looks for new technologies that will fuel growth for next decade
 - Gene therapy, cell therapy, gene editing, RNA, undruggable targets
- Lilly, Novo and AstraZeneca are the most likely acquirors of early-stage assets in near-term given already strong growth profiles in 2025 to 2030 period



| 02

Zooming in on **Ophthalmology**

State of the overall ophthalmology market

2023 notable transactions



- Astellas agreed to acquire Iveric Bio, including lead program avacincaptad pegol (IZERVAY), for \$40 per share in cash for a total equity value of \$5.9B
- Goal PDUFA date set for IZERVAY of August 19, 2023



- Novartis announced divestment of 'front of eye' ophthalmology assets to Bausch + Lomb in transaction valued up to \$2.5B, consisting of \$1.8B in upfront cash plus milestones
- Divestment included Xiidra, marketed therapy for dry eye disease

1-Day stock price reactions to ophthalmology data have been mixed

Company	Phase	Date	1-Day	Company	Phase	Date	1-Day	Company	Phase	Date	1-Day
VIRIDIAN	Phase I/II	1/8/23	+20%	ANNEXON biosciences	Phase II	5/24/23	-59%	4DMT	Phase I/II	7/29/23	0%
Ocuphire PHARMA	Phase II	1/25/23	-20%	Ocular Therapeutics	Phase I	6/10/23	-13%	Oculis	Phase III	8/8/23	+2%
CLEARSIDE BIOMEDICAL	Phase I/IIa	2/2/23	-3%	VIRIDIAN	Phase I/II	7/10/23	-16%	EYEPOINT PHARMACEUTICALS	Phase II	9/11/23	+16%
Ocular Therapeutics	Phase I	2/11/23	+35%	REGENXBIO	Phase II	7/11/23	0%	ocugen	Phase I/II	9/13/23	+4%
ocugen	Phase I/II	4/14/23	-6%	4DMT	Phase II	7/17/23	-2%	ADVERUM	Phase II	9/26/23	-3%
4DMT	Phase I	4/27/23	-20%	KODIAK	Phase III	7/24/23	-46%	LINEAGE CELL THERAPEUTICS	Phase I/IIa	10/5/23	+10%
Oculis	Phase III	5/22/23	+5%	EYEPOINT PHARMACEUTICALS	Phase II	7/27/23	+3%	KODIAK	Phase III	11/2/23	+37%

Despite a difficult market backdrop, several drug approvals have bolstered sentiment

November 6, 2023
Kodiak resurrects failed eye drug after Phase III data rejuvenates approval prospects



September 8, 2023
Otsuka, Shape Ink potential \$1.5B deal to develop eye AAV gene therapies



August 18, 2023
Regeneron expands Eylea's label with high-dose approval in AMD, RVO and DR



August 4, 2023
FDA approves IZERVAY™, a new treatment for GA



February 17, 2023
FDA approves SYFOVRE™ as the first and only treatment for geographic atrophy, a leading cause of blindness



January 8, 2023
Hottest IGF-1R (available) leaps getting hotter; 3mg/kg data paves path for SQ



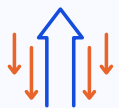
State of the overall ophthalmology market



Potential Tailwinds

Late-stage assets only

- GA launches
- Demodex blepharitis
- MGD in dry eye
- New rare diseases
- XR glaucoma
- Refractive errors



Potential Headwinds

- Biosimilar VEGFs (muted thus far)
- GA safety signals (ongoing situation)
- Poor launches can transition from tailwind to anchors



Ophthalmology themes in 2023

APPROVAL

All eyes on GA (sales, ACP, safety)

FDA Approves SYFOVRE™ (pegcetacoplan injection) as the First and Only Treatment for Geographic Atrophy (GA), a Leading Cause of Blindness



February 17, 2023

Bloomberg

US Biotech Firm Apellis Is Said to Attract Takeover Interest

- Larger drugmakers are eyeing \$7.6 billion company; sources
- Apellis shares rise as much as 12% in Monday premarket trading

Strategic universe continues to shift

01.06.2023
Viartis Closes Acquisitions of Oyster Point Pharma and Famy Life Sciences, Establishing New Eye Care Division



10 years after selling B+L, controversial dealmaker Brent Saunders is back as CEO

Bloomberg

Novartis Starts Sale of Some Ophthalmology Assets

- Pharma firm is seeking buyers for front-of-eye portfolio
- Assets include Xiidra, which had \$487 million in 2022 sales

Can Anti-VEGF field be disrupted?



Eye disease: Roche chasing third indication for Vabysmo as it releases positive trial data



UNITY Shares Nearly Halved after Lead Asset Fails to Match Regeneron's Eylea

Ocular Therapeutix™ Announces Interim 10-month Data from the Ongoing U.S. Phase 1 Clinical Trial Evaluating OTX-TKI for the Treatment of Wet AMD

EyePoint Pharmaceuticals Completes Enrollment in Oversubscribed Phase 2 DAVIO 2 Clinical Trial of EYP-1901 for Maintenance Treatment of Wet AMD



EYLEA HD (AFLIBERCEPT) INJECTION 8 MG APPROVED BY FDA

FDA Denies Outlook's Wet AMD Bid, Issues Complete Response Letter

IRDs have been hard, hope remains

March 31, 2023

Today we announce our decision to wind down Vedere Bio II.

Nanoscope Therapeutics announces positive topline results from Phase 2b RESTORE trial of MCO-010 for treatment of retinitis pigmentosa

Mar 31, 2023

SprayingVision appoints Joseph C. Papa as Chairman

Former Bluebird and Lumb Chairman and CEO joins as non-executive independent Chairman as SprayingVision enters the clinic with first gene-agnostic AAV program SPVND05

Alkermes Announces \$150 Million Series B Financing, Supporting Rapid Registration Path for giledeuretinol (ALK-001) in the Treatment of Stargardt Disease

Ray Therapeutics Closes Oversubscribed \$100M Series A Financing to Advance Optogenetic Gene Therapies for Blinding Diseases

Beacon Therapeutics launches with \$96 million (\$120 million) to develop a new generation of gene therapies for retinal diseases resulting in blindness

APPROVAL

Apellis Pharmaceuticals Reports First Quarter 2023 Financial Results

May 4, 2023

~\$18mm in SYFOVRE sales in ~5 weeks

ASRS Research and Safety in Therapeutics (ReST) Committee Update on Adverse Event Reports Associated with Syfovre

Committee Urges Members to be Vigilant in Detecting and Reporting Adverse Events

Apellis Pharmaceuticals Reports Second Quarter 2023 Financial Results

July 31, 2023

~\$67mm in SYFOVRE sales; +safety update

Iveric Bio Receives U.S. FDA Approval for IZERVAY™ (avacincaptad pegol intravitreal solution), a New Treatment for Geographic Atrophy



Novartis stops work on gene therapy acquired in Gyroscope deal

Iveric Bio Announces Positive 24-Month Topline Results from Phase 3 Study of IZERVAY™ (avacincaptad pegol intravitreal solution) for Geographic Atrophy

Presented at AAO

B+L acquires XIIDRA (+ other assets)

\$1.75 bn



B+L acquires Blink eye drops

\$100 mm



Harrow (2 deals)

\$8 mm



\$8 mm



Visiox acquires Omlonti

\$6 mm



Otsuka enters field with ShapeTx partnership



Note: Not comprehensive for events in GA field

Note: Not comprehensive for all transactions in field

Rx ophthalmology landscape

MAJOR COMMERCIAL PLAYERS



PIPELINE INTEREST



OTHER PLAYERS



	Abbvie	Roche	Alcon	Aerie	SUN OPTHALMICS	IVERIC BIO	VIATRIX	OYSTER POINT	B+L	Théa	J&J	MERCK	Boehringer Ingelheim	NOVARTIS	AMGEN	HORIZON	REGENERON	BAYER	GLAUKOS	Santen	Dompé	
Market cap (\$ billions)	\$245bn	\$215bn	\$35bn	\$32bn	\$23bn	\$11bn	\$6bn	Private	\$351bn	\$261bn	Private	\$211bn	\$140bn	\$84bn	\$42bn	\$3bn	\$3bn	Private				
Cash / net cash (debt)	\$8.8 / (\$52.2)	\$8.2 / (\$19.5)	\$0.6 / (\$4.3)	\$1.8 / \$1.0	\$3.8 / \$1.4	\$0.7 / (\$18.1)	\$0.4 / (\$2.2)	Private	\$23.5 / (\$6.4)	\$6.4 / (\$30.5)	Private	\$12.7 / (\$12.5)	\$34.2 / (\$27.3)	\$8.9 / \$6.2	\$4.7 / (\$44.5)	\$0.3 / (\$0.1)	\$0.3 / \$0.1	Private				
Ophth. focus / importance																						
Anti-VEGF	Regenxbio						Sold biosim to Biocon	Returned biosim to Xbrane			Exonate (status TBD)						Beovu (not promoted)	Biosim	US only	Ex-US only	Preclinical	Japan (Eylea)
wAMD (ex-VEGF only)		+Ang2																				
DR & DME (ex-VEGF only)	Steroid									Ripple		Terminated (KalVista)										Preclinical
Dry AMD / GA			Factor B; OpRegen							Preclinical	Hemera	NGM (option)					Gyroscope					
Uveitis																						
Glaucoma						Preclinical											SOLD			+Device		SOLD
Dry eye / MGD	Gx entry										MGD device											
Refractive errors							Presbyopia	Myopia														Myopia (ex-US)
Conjunctivitis / infl. / bleph.																						SOLD
Post-operative pain / infl.																						SOLD
Corneal disorders				Aurion investment		Preclinical																
Non-GTx orphan																						
Other							RM & NVD	Pain														
GTx / cell (orphan indic.)	Exited	US (Luxturna)					Preclinical			Preclinical							Ex-US (Luxturna)		Preclinical	Preclinical		Ex-US (iCyte)
GTx / cell (broad indic.)	RegenxBio	Ionis; Lineage								Preclinical	Hemera						Gyroscope		Preclinical	Preclinical		Ex-US (iCyte)

- Marketed product in category
- Pipeline product in category
- Recent failure / Gx entry / asset on hold
- Other (modest product, partner, etc.)

ORPHAN EXPOSURE



PIPELINE EXPOSURE



BIOSIMILARS *Not comprehensive*



HISTORICAL OR LOOSE EXPOSURE



Rx ophthalmology landscape: retina

	PRIMARYLY RETINA														BIOSIMILAR/ OTHER		OTHER RETINA	
	IVERIC BIO	Apellis	Belite BIO	VIRIDIAN	Oculus	aura	EYEPOINT PHARMACEUTICALS	Ocular THERAPEUTICS	Alimera	OPTHEA	KODIAK	Ocuphire	CLEARSIDE TECHNOLOGICAL	UNITY BIOTECHNOLOGY	Coherus BIOSCIENCES	OUTLOOK THERAPEUTICS	REZOLUTE	AKARI THERAPEUTICS
Market cap (\$ millions)	\$5.9bn (acquired)	\$5,597mm	\$1,014mm	\$541mm	\$347mm	\$277mm	\$208mm	\$192mm	\$175mm	\$135mm	\$74mm	\$58mm	\$43mm	\$27mm	\$292mm	\$130mm	\$36mm	\$18mm
Cash / net cash (debt)	N/A	\$617 / \$173	\$87 / \$87	\$334 / \$327	\$125 / \$125	\$162 / \$142	\$218 / \$211	\$67 / \$2	\$27 / (\$40)	\$89 / \$89	\$379 / \$194	\$40 / \$40	\$35 / (\$4)	\$69 / \$23	\$145 / (\$334)	\$34 / (\$1)	\$102 / \$99	\$7 / \$7
Ophth. focus / importance	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Anti-VEGF											Terminated		Internal + RGNX / ABBV			CRL (TBD)		
wAMD (ex-VEGF only)	Preclinical	Preclinical																
DR & DME (ex-VEGF only)					Steroid									Preclinical	Mixed data			
Dry AMD / GA								Preclinical			Preclinical							Preclinical
Uveitis							Alimera (Partner)						B&L (Partner)					
Glaucoma					Preclinical													
Dry eye / MGD																		
Refractive errors													Partner (Viatris)					
Conjunctivitis / infl. / bleph.																		On hold
Post-operative pain / infl.							Harrow (Partner)											
Corneal disorders																		
Non-GTx orphan	Stargardt		Stargardt	TED		Cancer									Aura Bio			
Other											Preclinical							
GTx / cell (orphan indic.)														Preclinical				
GTx / cell (broad indic.)		Preclinical													RGNX / ABBV			

- Marketed product in category
- Pipeline product in category
- Recent failure / Gx entry / asset on hold
- Other (modest product, partner, etc.)

SELECTED PRIVATE COMPANIES Ophth. focus



SELECTED PUBLIC COMPANIES

Ophth. assets but not core focus



Rx ophthalmology landscape: anterior seg

	PRIMARYLY FRONT OF THE EYE										CORNEA	OTHER		
	aerie	OYSTER POINT	HARROW	Tarsus	eyenovic	OKYO PHARMA	PALATIN	nicox	RVL	KALA BIO	aldehyra	Rayner		
Market cap (\$ millions)	\$770mm (acquired)	\$329mm (acquired)	\$481mm	\$449mm	\$46mm	\$45mm	\$28mm	\$17mm	\$1mm	\$52mm	\$86mm	Private		
Cash / net cash (debt)	N/A	N/A	\$30 / (\$148)	\$178 / \$153	\$17 / \$1	\$4 / \$2	\$11 / \$10	\$20 / (\$4)	\$19 / (\$39)	\$59 / \$26	\$152 / \$136	Private		
Ophth. focus / importance	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Anti-VEGF	Preclinical													
wAMD (ex-VEGF only)	Pipeline product in category													
DR & DME (ex-VEGF only)	Pipeline product in category													
Dry AMD / GA	Pipeline product in category													
Uveitis	Pipeline product in category													
Glaucoma	Pipeline product in category													
Dry eye / MGD	Pipeline product in category													
Refractive errors	Pipeline product in category													
Conjunctivitis / infl. / bleph.	Pipeline product in category													
Post-operative pain / infl.	Preclinical													
Corneal disorders	Pipeline product in category													
Non-GTx orphan	Preclinical													
Other	Anesthesia, Mydriasis													
GTx / cell (orphan indic.)	Preclinical													
GTx / cell (broad indic.)	Preclinical													

■ Marketed product in category
 ■ Pipeline product in category
 ■ Recent failure / Gx entry / asset on hold
 ■ Other (modest product, partner, etc.)

PRIVATE COMPANIES

Dry eye disease, MGD



Glaucoma



Presbyopia



Myopia



Neuroprotection



Corneal transplant



Rare cornea



Corneal edema



Other



Commercial presence of existing franchises

	MAJOR COMMERCIAL PLAYERS					PRIMARILY ANTI-VEGF			GA LAUNCHES		NARROW FOCUS		OTHER/EMERGING COMMERCIAL					
	abbvie	Alcon	SUN OPTHALMICS	B+L	Théa	Roche	REGENERON	BAYER	astellas IVERIC BIC	Apellis	NOVARTIS	Santen	VIATRIS OYSTER POINT [®]	HARROW [®]	TARSUS	Ocular Therapeutix	Alimera	
	Market cap (\$B / \$M)	\$258bn	\$36bn	\$33bn	\$6bn	Private	\$219bn	\$88bn	\$43bn	\$23bn	\$5bn	\$217bn	\$3bn	\$11bn	\$506mm	\$428mm	\$187mm	\$169mm
	Cash / net cash (debt)	\$8.8 / (\$52.2)	\$0.6 / (\$4.3)	\$1.8 / (\$1.0)	\$0.4 / (\$2.2)	Private	\$8.2 / (\$19.5)	\$8.9 / \$6.2	\$4.7 / (\$44.5)	\$3.8 / \$1.4	\$0.6 / \$0.2	\$10.9 / (\$16.8)	\$0.3 / \$0.1	\$0.7 / (\$18.1)	\$30 / (\$148)	\$178 / \$153	\$67 / \$2	\$27 / (\$40)
UNITED STATES	Retinal Specialist	Device										Beovu						
	General Ophth.											SOLD	SOLD					
	Optometrist			?								SOLD	SOLD					
	Surgical	Device																
	IRD/Rare																	
EUROPE	Retina	Device										Lucentis (+Tail)						
	Front / other	Device										Tail						
	IRD / rare																	
M&A / LICENSE	Recent NDA- / commercial-stage M&A or licenses of assets	aerie	KALA BIO ASSETS		OAKORN ASSETS				IVERIC BIC		xiidra	eyevence	OYSTER POINT [®]	DEXYCU NOVARTIS ASSETS OMLONTI [®] vêvy [®]				YUTIQ

■ Denotes substantial / primary marketing presence (Rx only)

■ Denotes minor marketing presence (Rx only)

SELECTED OTHER US COMPANIES WITH APPROVED / COMMERCIAL ASSETS / EXPOSURE

BioTissue, eyenovio, FERA, Halozyme, Mallinckrodt, mObius, ORASIS, Padagis, Rayner, RVL, VISI-X

BROAD RETINA ASSETS WITH PIVOTAL DATA ⊗ None

RARE DISEASE FOCUS

AMGEN, Dompé, RECORDATI RARE DISEASES, HORIZON

EUROPEAN ONLY

ADVANZ PHARMA, Chiesi, NORDIC PHARMA, VISUfarma

DEVICE WITH Rx PIPELINE

GLAUKOS, J&J

RARE RETINA ASSETS WITH PIVOTAL DATA

Alkeus, neur@tech

SELECTED APPROVED / FILED / BLA PREP BIOSIMILARS

Biocon, Biogen, CELLTRION, Coherus, STADA, teva, OUTLOOK THERAPEUTICS

SELECTED FRONT OF THE EYE ASSETS WITH PIVOTAL DATA

aldehyra, TearClear, Vyluma

Excludes several companies with one of two Ph3 complete

Bank of America. Rx Ophthalmology Market Review, BofA Life Sciences. October 2023. | Source: EvaluatePharma, Biomedtracker, ClinicalTrials.gov, company materials and FactSet as of 10/27/23. Note: Reflects major pipeline products in clinical development and marketed products from the United States and Europe, not necessarily inclusive of all companies with commercial/clinical assets.

Ophthalmic gene therapy landscape

	MAJOR CONSOLIDATORS					OTHERS		PRIMARILY AAV (ANTI-VEGF)				PRIMARILY AAV (IRDs)			RNA-BASED		EDITING		CELL TX
	J&J janssen	Roche	BAYER	astellas IVERIC BiC	Otsuka	NOVARTIS	Biogen	abbvie	REGENXBIO	4DMT	ADVERUM	MEIRAGTx	GenSight	agtc beacon therapeutics	generation bio	PYC Therapeutics	prime L-medicine	LINEAGE Cell Therapeutics	
Market cap (\$B / \$M)	\$368bn	\$219bn	\$43bn	\$23bn	\$19bn	\$217bn	\$37bn	\$258bn	\$710mm	\$426mm	\$977mm	\$223mm	\$33mm	\$24mm (acquired)	\$74mm	\$137mm	\$695mm	\$210mm	
Cash / net cash (debt)	\$28.5 / (\$17.1)	\$8.2 / (\$19.5)	\$4.7 / (\$44.5)	\$3.8 / \$1.4	\$3.3 / \$2.1	\$10.9 / (\$16.8)	\$6.1 / (\$0.5)	\$8.8 / (\$52.2)	\$320 / \$229	\$310 / \$295	\$141 / \$50	\$93 / \$2	\$1 / (\$16)	N/A	\$314 / \$234	\$10 / \$10	\$208 / \$182	\$46 / \$43	
Ophth. focus / importance																			
LCA (multiple genes)		Luxturna (US)				Luxturna (ex-US)								On hold (RPE65)					
Stargardt		Preclinical																	Preclinical
Retinitis Pigm. (multiple genes)						RLBP1							Optogen.			PRPF31			Preclinical
XLRP	RPGR (MeiraGTx)						Failed Ph3 (RPGR)			RPGR (fmr Roche)		RPGR (J&J)		RPGR; RS1					
XLRS																			
Choroideremia		Terminated					Failed Ph3 (REP-1)			REP-1 (fmr Roche)									
Achromatopsia	'B3 / 'A3 (MeiraGTx)											'B3 / 'A3 (J&J)		'B3 / 'A3					
LHON																			
Other IRD / not disclosed			Preclinical	Preclinical	Preclinical		Preclinical			Preclinical	Preclinical	Preclinical				Preclinical (OPA1)	Preclinical	Preclinical	Preclinical
Wet AMD / DME								REGENXBIO (partner)	Abbvie (partner)					Preclinical	Preclinical	Preclinical			
Dry AMD / GA	Hemera acq. (AAV)	Ionis collab. (RNA)	Preclinical			Gyroscope acq. (AAV)				Preclinical (Aevitas)			Preclinical	Preclinical					Roche collab.
Glaucoma				Preclinical															
Technology	AAV	AAV; Cell Tx	CellTx	AAV; Cell Tx	AAV	AAV	AAV	AAV	AAV	AAV	AAV	AAV	AAV; Optogen.	AAV; Optogen.	ceDNA	RNA	Prime Editing	iPSC	
Partners (ophth. specific)	MeiraGTx	Lineage; Avista	Opis	Multiple	Shape	Dyno; Intellia	ViGeneron	REGENXBIO	Abbvie	Roche (former)	Regeneron (former)	J&J		Biogen (former)					Roche
GeneticMed Acquisitions	Hemera	Spark	BlueRock	Ocata; Quethera	-	Vedere; DTx	Nightstar												

- Marketed product in category
- Pipeline product in category
- Recent failure / Gx entry / asset on hold
- Other (modest product, partner, etc.)

OTHER PUBLIC & PRIVATE COMPANIES *Not comprehensive*

Bank of America. Rx Ophthalmology Market Review, BofA Life Sciences. October 2023. | **Source:** EvaluatePharma, Biomedtracker, ClinicalTrials.gov, company materials and FactSet as of 10/27/23. *Note 1:* Excludes ReNeuron, OxfordBiomedica, Healios, SanBio, Aivita, Iveric, Clearside, DTx Pharma, Variant, ViGeneron and others. *Note 2:* Reflects major pipeline products in clinical development and marketed products from the United States and Europe, not necessarily inclusive of all companies with commercial/clinical assets.

Wet AMD landscape

Leading companies & selected emerging players (not comprehensive)

	Preclin	Pre-POC	Post POC	NDA	Market
Anti-VEGF only biologic (including XR)	 		 	 	 <i>Bayer (ex-US, JPN)</i> <i>Novartis (Lucentis, ex-US)</i>
Anti-VEGF + other MOA	 				
Tyrosine kinase inhibitors		 			
Gene therapies	 				
Orals/topicals/other		 			
Other therapies		 			
Biosimilars		<i>Excludes multiple biosimilar assets</i> 			

The anti-VEGF therapies in wet AMD are akin to the statins in CV – **anti-VEGF biologics reign supreme** and the debate is now around delivery, duration or additive mechanisms in smaller sub-categories

Key notes for the field

- Large and growing population
- Anti-VEGF still has non-responders and wearing off
- Dosing frequency can still be improved
- How will long-acting anti-VEGFs fit into paradigm?
- Impact of CRL for high-dose Eylea
- What is the right trial design for approval, uptake and favorable reimbursement for new entrants?
- Will other mechanisms have any viable success?
- Pricing/reimbursement landscape in competitive brand and biosimilarized market (however, biosimilars have yet to make much of an impact)
- No margin around safety

Asset profile goals / field progress

- Improve dosing frequency of anti-VEGF therapy
 - 1st wave is long-duration and VEGF+ biologics
 - 2nd wave is extended release TKIs
 - 3rd wave is GeneticMed or systemic therapies
- Improve wearing off effect
- Address non-responders

Diabetic eye disease landscape

Leading companies & selected emerging players (not comprehensive)

	Preclin	Pre-POC	Post POC	NDA	Market
XR anti-VEGF only (selected)			<p>SCS still unknown</p>		
Steroids					
Anti-VEGF + other MOA					
Novel MOA IVT					
Orals/systemic					
Topicals/other					

The category continues to be driven by anti-VEGF therapies, however there remain substantial unmet medical needs in addressing non-responders, durability and early treatment of disease

Key notes for the field

- Large and growing population of diabetics
- Anti-VEGF therapy has non-responders and wears off
- Steroid side effects limit broad utilization despite anti-inflammatory and anti-VEGF sparing capability
- No early treatment options with favorable dosing
- Well-validated endpoints; openness for new ones...
- What new mechanism will be successful?
- What are the right, "winning" endpoints?
- Will HD Eylea penetrate further into DR?
- Pricing/reimbursement landscape in anti-VEGF remains a high bar in severe patients
- Tough population to treat (multiple comorbidities)

Asset profile goals / field progress

- Improving the duration of anti-VEGF activity
 - Nearer term: XR IVT biologics and IVT TKIs
 - Long term: topicals / gene therapies / other
- New mechanisms with combo/monotherapy impact
- Non-invasive and/or safe long-acting therapies that slow/halt/reverse DRSS progression may provide the next class of mega-blockbusters

Geographic atrophy landscape

Leading companies & selected emerging players (not comprehensive)

	Preclin	Pre-POC	Post POC	NDA	Market
IVT complement					
Gene therapies				<p>Scare... but rare</p>	
Cell therapies					<p>With the approval and recent launch of Izervay, the focus shifts to real-world physician acceptance, utilization and safety (as well as upcoming data and impact on potential label amendments)</p>
Systemic therapies					<p>If Izervay safety is clean through early use (vasculitis seems lower vs. Syfovre so far), Astellas has an opportunity to build a preferred first-line complement asset</p>
Other mechanisms					<p>Regardless of Syfovre/Izervay, the field remains rather open for next-generation assets</p>

GA is a dominant and polarizing Wall Street theme for ophthalmology...Apellis was executing a top-tier launch until vasculitis emerged; meanwhile Iveric was acquired for \$5.9bn and ACP was approved

Key notes for the field

- Large patient populations (advanced, intermediate)
- Progressive and blinding disease = reimbursement
- Lots of room for new and improved therapies
- Vasculitis cases - manageable or Beovu 2.0?
- European stance on slope and other endpoints
- Long-term motivation of patients to show up will take time to digest in real world setting
- Will new mechanisms show promise?
- Lesion slope analysis is approvable but is it the true goal? Visual benefit in trials has not been undeniable
- Progressive disease that is difficult to halt or improve

Asset profile goals / field progress

- Near-term focus on safety given vasculitis cases
- Lesion slope remains approvable (in US) with the expectation of visual benefit over longer period
- Faster acting therapies (ie, slow BCVA decline faster)
- Longer-duration therapies
- Potential restorative therapies

Glaucoma landscape

Leading companies & selected emerging players (not comprehensive)

	Preclin	Pre-POC	Post POC	NDA	Market
Excludes assets that are a tail brand or have gone generic eg, Abbvie (Lumigan, etc.), Novartis (Travatan), Alcon (Simbrinza), Thea (Zioptan)					
New topicals			<p>Ph3 #2 ongoing</p>	<p>Aug 4, 2023 CRL ?</p>	
Long-acting approaches				<p>TRANSFORMING VISION Dec 22, 2023</p>	
Neuroprotection					
Other approaches					

In a highly genericized market, the bar is high and debate around additional mmHg lowering remains - **but millions of patients** could clearly benefit from a safe, long-acting therapy and neuroprotection

Key notes for the field

- Massive patient population, continues to grow
- Real-world compliance remains extremely poor
- Community likely to jump at new options
- No neuroprotective agents
- How much additional mmHg lowering is meaningful
- Safety profile of XR alternatives yet to be overcome
- Long-term impact of devices (MIGS, SLT, etc.)
- Pricing/reimbursement in highly genericized market
- Drop compliance is high the clinical setting, making any differentiation much harder to prove

Asset profile goals / field progress

- Enhanced compliance via safe, extended release
- Product requires re-dosable capability
- Safety profile needs to be very clean
- Does not need to be a new mechanism
- Neuroprotection
- Preservative-free options

DED/MGD landscape

Leading companies & selected emerging players (not comprehensive)

	Preclin	Pre-POC	Post POC	NDA	Market
Anti-inflammatory & flare products <i>Multiple companies excluded in this anti-inflammatory category (full competitive detail can be provided)</i>		IOLYX THERAPEUTICS Aramis Biosciences <i>Recent Ph2 data</i> Oculis surface <i>Ph2 data</i> BRM 全福生物科技 Stuart Therapeutics OKYO PHARMA	PALATIN <i>Ph3 ongoing</i> ALLYSTA <i>Ph3 ongoing</i> VIATRIS <i>Ph3 ready</i>	aldehyra <i>Nov 23, 2023</i> <i>Acquired for \$8mm></i>	abbvie Restasis B+L xiidra SUN PHARMA Cequa Alcon EYSUVIS HARROW veyve <i>Restasis Gx (Viatris, Apotex, +)</i>
Meibomian gland dysfunction (dry eye)		TARSUS Cloudbreak	AZORA <i>Recent Ph2 data</i>		B+L Miebó
Tear stimulant			Alcon aerie <i>Ph3 ongoing</i>		VIATRIS tyrVaya OYSTER
Tear enhancement	MCAL Therapeutics	TEARSOLUTIONS LUBRIS BIOPHARMA			
Other delivery		Ocular Therapeutics GLAUKOS			

The category has meaningful unmet needs, but assets face a challenging commercial environment; several upcoming approvals and launches will be an important barometer

Key notes for the field

- Large patient populations
- Opportunities for entrants to differentiate
- Response rates
- Speed of onset
- Instillation discomfort
- Impact of meibomian gland dysfunction entrants
- Abundance of anti-inflammatories “stuck” in clinic
- Variable disease with difficult endpoints to meet
- High safety and tolerability bar
- Abundance of OTC options
- Restasis rebating may have scorched earth impact

Asset profile goals / field progress

- Improve:
 - Product requires re-dosable capability
 - Safety profile needs to be very clean
 - Does not need to be a new mechanism
- Desire for new mechanisms / immunomodulatory capability
- Ability to target wider population of MGD

IRD and rare disease landscape

Leading companies & selected emerging players (excluding preclin./early clin.)

	Pre-POC (excludes most co's)	Post POC	NDA	Market
IRDs (AAV)	 FDA desires new pivotal 	 	 Europe only (delays)	 Novartis (ex-US)
IRDs (RNA, DNA, Cell Tx)				
IRDs (SmMol, Biologic)		 Pivotal data (STG)		
Thyroid eye disease	 			
Neurotrophic keratitis / PCED				
Other non-IRD orphan		 Pivotal data (MacTel)	 Jun 21, 2023	

Luxturna sales and clinical outcomes have soured the outlook on gene therapies; meanwhile Tepezza and Oxervate have seen great success and other non-GeneticMed assets look poised to follow

Key notes for the field

- High unmet medical needs, virtually no treatments
- Favorable pricing can be achieved
- Improving prevalence of genetic testing / awareness
- Endpoints are not always validated / reliable
- Will AAVs get enough transduction to matter?
- Natural history data can be unreliable
- Outside of Stargardt there are few large, single-mutation IRDs (RP has several large mutations)
- Few other non-IRD orphan conditions in general
- Pricing / reimbursement can be difficult without clean win (particularly with single administration therapies)










Asset profile goals / field progress

Highly variable profile depending on disease

- Preservation of vision (multiple metrics used in clinical studies to determine impact on vision and/or quality of life)
- Convenient, safe and reliable administration
- Restorative therapies are the end goal

Presbyopia landscape

Leading companies & selected emerging players (not comprehensive)

	Preclin	Pre-POC	Post POC	NDA	Market
Pilocarpine drops				 Oct 22, 2023	 
Aceclidine					
Pilocarpine + delivery		 Cream	 Status TBD		
Other APIs (Carbachol, Phentolamine)		  Inactive			
Other		 	 		

“Wait, what” happened with the launch?...Vuity’s reception from patients and its sales left a lot to be desired...can new (admittedly much better) products prove out the multi-billion dollar market thesis?

Key notes for the field








- **Massive** addressable patient population
- Cash pay market (no payor negotiations)
- Aging population with societal desire to look younger (note the size of the Botox market, Lasik demand)
- “True” level of demand unclear until real world use
- Impact more temporary vs. Botox / Lasik / etc.
- Ability to change the course of Vuity perception
- Promotion sensitive field (requires DTC)
- Non-reimbursable (wallet tied to performance)
- Lifestyle product (vs. chronic use)
- Limited to no margin around safety

Asset profile goals / field progress

- Improve responder rate overall
- Improve duration of effect
- Reduce risk of severe AEs (retinal detachment)
- Improve tolerability
- Improve ability to treat older patients

Myopia landscape

Leading companies & selected emerging players (not comprehensive)

	Preclin	Pre-POC	POC / In Ph3	Ph3 Data	NDA	Market
Atropine			 Data 2024  	 NDA Prep (0.2% formulation did not hit responder analysis)		
Copper						
Other mechanisms		Limited new targets of interest...				
Compounding						 Multiple Others

The patient impact of reducing axial expansion is massive... however, compounded therapy is available, so the bar for atropine brands is expected to be high

Key notes for the field























- Large patient population
- Strong reimbursement (children, high impact)
- Some motivated parents already paying out of pocket
- Patient compliance
- Existing compounded atropine players
- Ability to build market
- Likely requires substantial marketing push
- Lack of NCE therapies
- Three year endpoint (also provides barrier)
- No margin for error on safety and tolerability

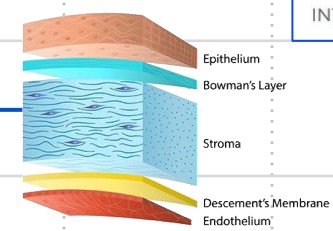
Asset profile goals / field progress

- Need to improve myopic progression
- Need to have a safe therapy
- A new mechanism with high-dose atropine efficacy but without the atropine AEs is the "holy grail" profile

Cornea landscape

Leading companies & selected emerging players (not comprehensive)

	Preclin	Pre-POC	POC / In Ph3	Ph3 Data	NDA	Market
NGF <i>Note that several of these assets are also included within rare diseases</i>						 
Other		      				
Amniotic tissue products (not inclusive of clinical assets or comprehensive for all commercial assets, such as Corza's AmbioDisk)						     
Epithelial disorders⁽¹⁾ (NK, Fuch's, Sjögren's, Microbial/Viral Keratitis, Trauma, PCED)						
Endothelial disorders⁽²⁾ (Fuch's, Corneal Edema, High Risk Cataract, PBK, MIGS, other dystrophies)						
Transplant alternatives (Cell Tx, Drug)		   				
Corneal edema						Donor transplants



The corneal disease field is still emerging with companies seeking to define indications in the epithelial side and seek to disrupt the donor transplant paradigm on the endothelial side

Key notes for the field

- Oxervate demonstrated the need state for corneal diseases based on success in neurotrophic keratitis
- Multiple additional indications remain unaddressed
- Clear opportunity to disrupt donor transplant market
- Relatively clear endpoints across diseases (total resolution based on staining, three-line benefit, etc.)
- Narrow audience of surgeons / prescribers
- When will the larger strategics prioritize the cornea?
- How does pricing evolve across bigger markets?
- The high-value indications are associated with major damage - true disease modification is required

Asset profile goals / field progress

- Epithelial**
- Address wider range of PECDs
 - Improve dosing regimen for patients
- Endothelial**
- Eliminate the need for donor transplants
 - Improve vision in earlier disease state (or risk state)

2022 & 2023 ophthalmology events

Company	Asset	Indication(s)	Catalyst	Date	Market Cap		Stock Price Reaction		
					Pre Ann.	1D +/-	1-day	7-day	30-day
Selected positive catalysts/events with positive stock price response									
Iveric	Avincaptad pegol	GA	Ph3 GATHER2 data	Sep-22	\$1115	\$739	66%	93%	122%
EyePoint	-N/A-	-N/A-	Open market buyer; high volume	Apr-23	\$195	\$114	58%	10%	14%
Ocular	OTX-TKI	wAMD	Ph2 data (10-month)	Feb-23	\$298	\$105	35%	62%	32%
Harrow	Iheezo	Ocular surface analgesia	FDA approval	Sep-22	\$206	\$57	28%	68%	58%
Iveric	Avincaptad pegol	GA	Breakthrough Designation	Nov-22	\$2081	\$532	26%	26%	29%
EyePoint	Vorolanib	wAMD	{Update} 12mo Ph1 data	Jul-22	\$277	\$60	22%	32%	36%
Ocuphire	Nyxol	RM, NVD, presbyopia	Viartis collaboration	Nov-22	\$43	\$9	20%	30%	49%
Glaukos	iDose	Glaucoma	Ph3 data	Sep-22	\$2289	\$424	19%	17%	18%
Apellis	--company--	GA	Takeover rumor	Apr-23	\$7550	\$1227	16%	19%	26%
Harrow	Novartis assets	Multiple	Acquisition of Novartis assets	Dec-22	\$304	\$46	15%	11%	29%
Aldeyra	Reproxalap	Dry eye	Chamber crossover data	Jul-22	\$261	\$39	15%	7%	73%
Kodiak	KSI-301	RVO	Ph3 data in RVO	Aug-22	\$506	\$71	14%	25%	(3%)
Iveric	--competitor--	GA	APLS approval	Feb-23	\$2681	\$261	10%	5%	18%
Iveric	--company--	GA	APLS takeover rumor	Apr-23	\$3336	\$296	9%	11%	55%
4DMT	4D-150	wAMD	Ph1 data	Nov-22	\$405	\$32	8%	76%	98%
Apellis	Syfovre	GA	Approval	Feb-23	\$5777	\$398	7%	29%	21%
Ocular	OCS-01	DME	Ph3 #1 data (PE hit)	May-23	\$395	\$21	5%	(1%)	3%
Aldeyra	Reproxalap	Dry eye	Ph2 chamber data vs. Xiidra	Jan-22	\$227	\$2	1%	(4%)	(9%)
Coherus	Cimerli	Lucentis biosimilar	FDA approval	Aug-22	\$776	\$3	0%	10%	11%

Denotes high impact event (field and/or competitors)

Denotes >\$1bn daily gain / or loss

Company	Asset	Indication(s)	Catalyst	Date	Market Cap		Stock Price Reaction		
					Pre Ann.	1D +/-	1-day	7-day	30-day
Selected positive (or mixed) catalysts/events with negative stock price response									
Tarsus	Xdemvy (fka TP-03)	Demodex blepharitis	Approval	Jul-23	\$643	(\$160)	(25%)	(8%)	(28%)
Tarsus	TP-03	Demodex blepharitis	Ph3 data (trial #2; PE hit)	May-22	\$379	(\$11)	(24%)	(39%)	(25%)
4DMT	4D-150	wAMD	Ph1 data (additional cohorts)	Apr-23	\$684	(\$135)	(20%)	(8%)	(14%)
Aura Bio	AU-011	Choroidal melanoma	{Update} Ph1/2 SCS data	Oct-22	\$530	(\$103)	(19%)	(24%)	(31%)
Ocular	OTX-TKI	wAMD	Ph2 data (6-month)	Sep-22	\$406	(\$75)	(18%)	(23%)	(30%)
Ocuphire	Nyxol	Reversal of mydriasis	Ph3 data (MIRA-3; hit PE)	Mar-22	\$81	(\$13)	(16%)	(24%)	(45%)
Unity	UBX1325	DME	{Update} 24wk Ph2 data	Nov-22	\$39	(\$6)	(15%)	(11%)	(2%)
REGENXBIO	RGX-314 (SCS)	DR	{Update} Interim Ph2 data (new CH)	Nov-22	\$1048	(\$137)	(13%)	(16%)	0%
Ocular	OTX-TKI	wAMD	Ph2 data (12-month) + vlogger video	Jun-23	\$576	(\$72)	(13%)	(35%)	(35%)
Nicox	NCX 470	Glaucoma	Ph3 data (missed superiority)	Oct-22	\$85	(\$9)	(11%)	(14%)	(32%)
Editas	EDIT-101	LCA10	Ph1/2 data	Nov-22	\$842	(\$85)	(10%)	(15%)	(16%)
Outlook	Lytenava	Avastin biosimilar	BLA re-acceptance	Oct-22	\$299	(\$28)	(9%)	(19%)	(20%)
Clearside	CLS-AX	wAMD	Ph1/2a data	Nov-22	\$54	(\$7)	(9%)	(1%)	(16%)
Kala	Eysuvis/Inveltys	Dry eye flares/post-op	Sale of assets to Alcon	May-22	\$47	(\$3)	(6%)	(46%)	(43%)
Eyenovia	MicroLine	Presbyopia	Ph3 data (limited disclosure)	Oct-22	\$82	(\$4)	(5%)	(3%)	(27%)
EyePoint	Yutiq	Uvietis	Asset sale to Alimera	May-23	\$220	(\$10)	(4%)	(2%)	2%
Ocuphire	Nyxol	NVD	Ph3 data (LYNX-1; hit PE)	May-22	\$40	(\$2)	(4%)	(3%)	(8%)
Oxurion	THR-149	DME	Ph2 data (Part A)	Feb-22	\$82	(\$3)	(3%)	(5%)	(31%)
Aldeyra	Reproxalap	Dry eye	Ph3 TRANQUILITY-2 data	Jun-22	\$210	(\$6)	(3%)	(4%)	21%
Adverum	ADVM-002 (ixo-vec)	wAMD	{Update} OPTIC 2yr data	Nov-22	\$81	(\$2)	(2%)	(11%)	(19%)
Aldeyra	ADX-2191	PVR	Ph3 data (Part 1)	Oct-22	\$325	(\$6)	(2%)	(6%)	(4%)

Selected negative catalysts/events with negative stock price response

Outlook	Lytenava	Avastin biosimilar	CRL	Aug-23	\$637	(\$297)	(81%)	(84%)	(85%)
Kodiak	KSI-301	wAMD	Ph3 data (PE miss)	Feb-22	\$2604	(\$2094)	(80%)	(82%)	(84%)
ProQR	Sepofarsen	LCA 10	Ph2/3 data (PE miss)	Feb-22	\$402	(\$303)	(75%)	(79%)	(83%)
NGM Bio	NGM621	GA	Ph2 data (PE miss)	Oct-22	\$928	(\$654)	(70%)	(60%)	(52%)
Aldeyra	Reproxalap	Dry eye	8-K referencing CRL risk	Oct-23	\$318	(\$211)	(66%)	NA	NA
Annexon	ANX007	GA	Ph2 data (PE miss; post-hoc info)	May-23	\$274	(\$163)	(59%)	(42%)	(33%)
Unity	UBX1325	DME	Ph2 data (PE miss, non-inferiority)	Mar-23	\$60	(\$32)	(53%)	(61%)	(51%)
Kodiak	KSI-301	wAMD	Ph3 data (PE miss) #2; term. Program	Jul-23	\$382	(\$175)	(46%)	(61%)	(68%)
Apellis	Syfovre	GA	Vasculitis reports	Jul-23	\$9841	(\$3731)	(38%)	(59%)	(61%)
Outlook	Lytenava	Avastin biosimilar	BLA delay (FDA data request)	May-22	\$382	(\$122)	(32%)	(44%)	(38%)
Aldeyra	ADX-2191	Lymphoma	CRL	Jun-23	\$623	(\$171)	(27%)	(30%)	(25%)
Ocuphire	APX3330	NPDR	Ph2 data (PE miss; new endpoints)	Jan-23	\$78	(\$16)	(20%)	(6%)	(8%)
Apellis	Syfovre	GA	Safety update at ASRS + earnings	Jul-23	\$3770	(\$738)	(20%)	(23%)	27%

2023 ophthalmology market performance

Ranked by 2023YTD change in share price

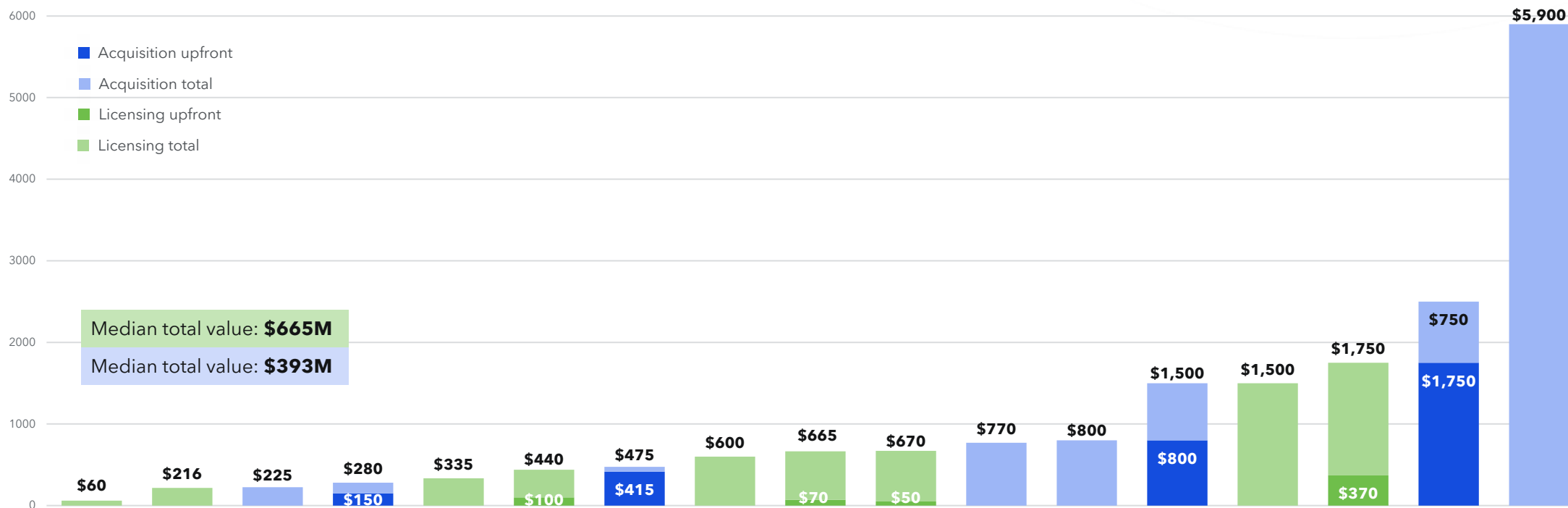
Company	Key Notes	Market Cap ⁽¹⁾			Annual Price Change	
		YE22	Current	YTD Δ	2022	2023YTD
Iveric	Acquired	\$2871	\$5900	\$3029	28%	87%
EyePoint	Sold Yutiq; Ph2 progressing	\$119	\$208	\$89	(71%)	72%
Adverum	Ph2 progressing	\$58	\$96	\$38	(67%)	55%
Belite	Ph3 ongoing	\$751	\$1014	\$264	402%	24%
Alimera	Acquired EyePoint's Yutiq	\$19	\$28	\$9	(47%)	24%
Ocular	Positive data; Ph3 planning	\$226	\$192	(\$24)	(60%)	1%
Lineage	Initiated Ph2 with Roche	\$199	\$198	(\$1)	(52%)	(3%)
Tarsus	Approval; pending launch	\$391	\$449	\$58	(35%)	(3%)
Harrow	Active M&A; earnings performance	\$405	\$481	\$77	71%	(3%)
Oculis	Ph3 data (PE hit)	\$166	\$347	\$182	4%	(3%)
Apellis	Approval; subsequent safety	\$5718	\$5597	(\$121)	9%	(6%)
Ocuphire	Ph2 data; EoP2 4Q23	\$73	\$58	(\$15)	(5%)	(19%)
Eyenovia	Approval; data updates; acquisition	\$60	\$46	(\$14)	(59%)	(20%)
Aura	Initiating Ph3	\$378	\$277	(\$101)	(38%)	(22%)
PYC	IND acceptance	\$149	\$140	(\$9)	(52%)	(23%)
Unity	Ph2 data (mixed reception)	\$39	\$27	(\$12)	(81%)	(27%)
MeiraGTx	J&J data updates (none negative)	\$316	\$220	(\$96)	(73%)	(31%)
Clearside	Limited material newsflow	\$67	\$43	(\$24)	(59%)	(35%)
REGENXBIO	In Ph3 with SRi; Ph2 SCS pending	\$982	\$632	(\$350)	(31%)	(43%)
Outlook	CRL; next steps TBD	\$246	\$130	(\$116)	(21%)	(44%)
4DMT	Ph1/2 data	\$719	\$440	(\$279)	1%	(52%)
Annexon	Ph2 data (mixed reception)	\$246	\$111	(\$136)	(55%)	(56%)
Viridian	Mixed clinical data	\$1176	\$541	(\$635)	48%	(57%)
Akari	Preclinical progress	\$35	\$18	(\$17)	(69%)	(64%)
Opthea	Ph3 ongoing	\$290	\$135	(\$155)	(29%)	(69%)
Nicox	Missed Ph3 PE vs. latanoprost	\$60	\$17	(\$43)	(59%)	(69%)
Aldeyra	Data; CRL (lymphoma); CRL? (dry eye)	\$408	\$86	(\$321)	74%	(75%)
Kodiak	Ph3 data and termination	\$375	\$74	(\$300)	(92%)	(80%)
Kala	Ph2/3 ongoing	\$58	\$17	(\$41)	(37%)	(82%)
NGM	Ph2 data (mixed reception)	\$410	\$63	(\$347)	(72%)	(83%)

Ranked by 2023YTD change in market cap⁽¹⁾

Company	Key Notes	Market Cap ⁽¹⁾			Annual Price Change	
		YE22	Current	YTD Δ	2022	2023YTD
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Eyenovia	Approval; data updates; acquisition	\$60	\$46	(\$14)	(59%)	(20%)
Ocuphire	Ph2 data; EoP2 4Q23	\$73	\$58	(\$15)	(5%)	(19%)
Akari	Preclinical progress	\$35	\$18	(\$17)	(69%)	(64%)
Clearside	Limited material newsflow	\$67	\$43	(\$24)	(59%)	(35%)
Ocular	Positive data; Ph3 planning	\$216	\$192	(\$24)	(60%)	1%
Kala	Ph2/3 ongoing	\$58	\$17	(\$41)	(37%)	(82%)
Nicox	Missed Ph3 PE vs. latanoprost	\$60	\$17	(\$43)	(59%)	(69%)
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Bank of America. Rx Ophthalmology Market Review, BofA Life Sciences. October 2023. | **Source:** Company filings and press releases. Data as of 10/27/23. *Note:* Not comprehensive of all companies, excludes several companies based on size (Palatin, GenSight, etc.) or exposure to ophthalmology (RVL, Editas, etc.). **(1)** Market cap increases also related to share issuances and option exercises, hence some companies may have negative share price performance but an increase in market cap.

2023 ophthalmology-focused transactions




























Target / Licensor	Acquiror / Licensee	Date	Phase	Indication
Kala Bio	Alcon	May-22	Marketed	DED
Splice	Spark	Oct-23	Discovery	IRD
Eyevance	Santen	Sep-20	Marketed	Ophthalmic products
Vedere	Novartis	Sep-20	Preclinical	IRD / GA
Novartis	Alcon	Apr-21	Marketed	IOP in glaucoma
MeiraGTx	Janssen	Jan-19	Phase I/II	ACHM / XLRP
Oyster Point	Viatriis	Jan-23	Marketed	DED
Intellia	Sparkling Vision	Oct-21	Discovery	Ocular diseases
Capsida	AbbVie	Feb-23	Discovery	Ocular diseases
Lineage	Roche	Dec-21	Phase I/IIa	Dry AMD with GA
Aerie	Alcon	Nov-22	Marketed	IOP in glaucoma
Nightstar	Biogen	Jun-19	Phase III	CHM
Gyroscope	Novartis	Feb-22	Phase II	GA
Shape	Otsuka	Sep-23	Discovery	Ocular diseases
REGENXBIO	AbbVie	Sep-21	Pivotal ongoing	wAMD/DR
Novartis	Bausch + Lomb	Sep-23	Marketed	DED
Iveric	Astellas	Jul-23	NDA submitted	GA

2023 ophthalmology transactions

Ophthalmology strategic BD activity: limited M&A activity of scale since 2015

Preliminary working draft; subject to material revision

Date announced	Target	Acquiror	Offer value (\$mm)	Add'l conting. consid.	Phase of lead asset
Jun-23	 <i>(Novartis)⁽¹⁾</i>	BAUSCH + LOMB	\$1,750	\$750	Mkt
Apr-23			5,930	–	Filed
Nov-22	Famy Life Sciences		281	–	P3 Rdy
Nov-22			329	62	Mkt
Aug-22		Alcon	771	–	Mkt
Dec-21			800	700	P1/2
Sep-21			~100	–	PC
Oct-20			150	130	PC
Oct-20		FS Dev't Corp.⁽²⁾	216	–	P2a
Aug-19		GLAUKOS	488	–	Mkt
May-19	 <i>(Takeda)</i>		3,400	1,900	Mkt
Mar-19			877	–	P3
May-17			145	–	P2 data
Nov-15			379	–	P2
Aug-15			300	–	P3






















Only deals >\$1bn upfront

2023 ophthalmology transactions

Ophthalmology strategic BD activity: limited M&A activity of scale since 2015

Preliminary working draft; subject to material revision

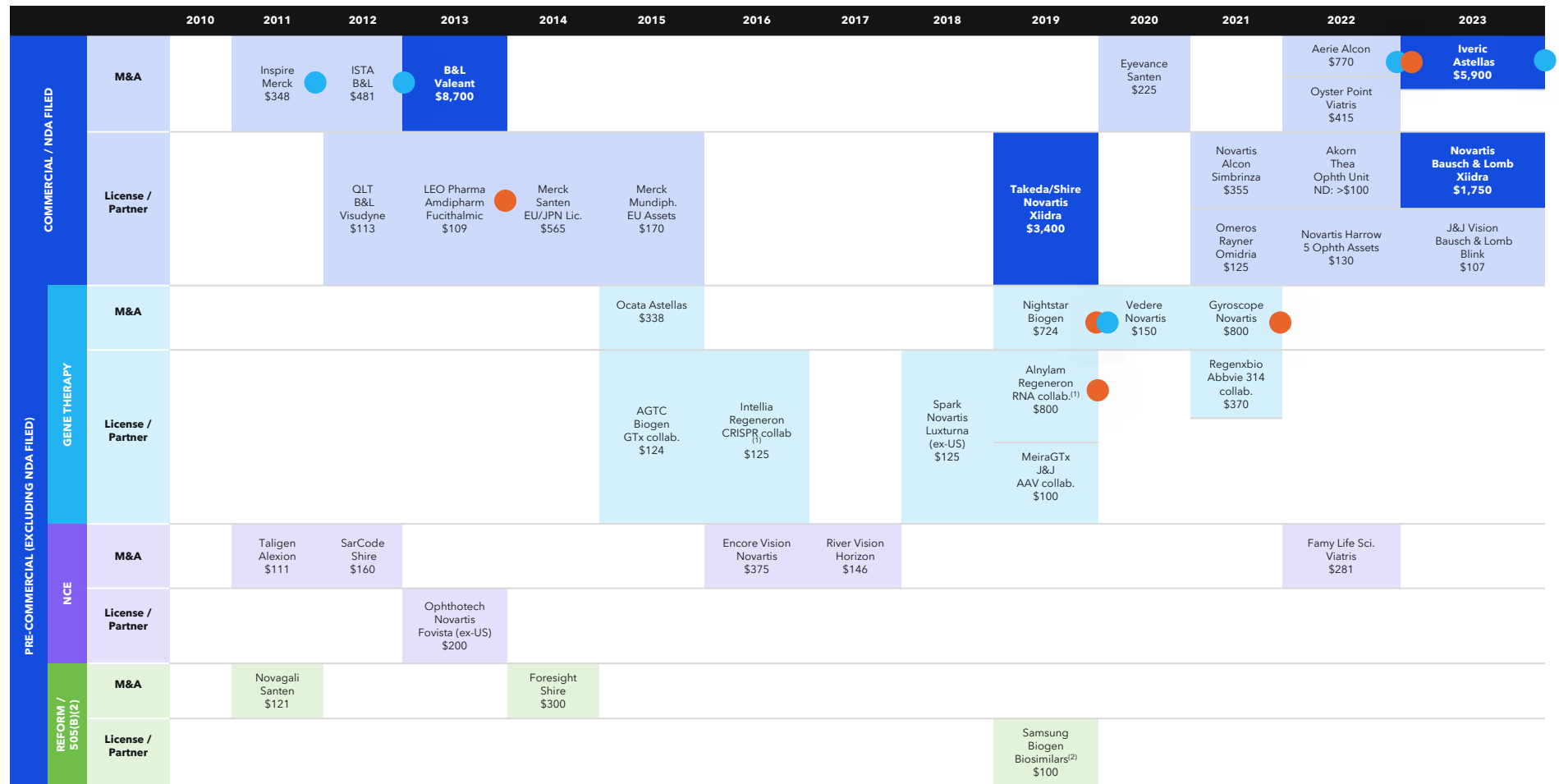
Only deals
>\$1bn
upfront

Date announced	Target	Acquiror	Offer value (\$mm)	Add'l conting. consid.	Phase of lead asset
Jun-23	 (Novartis) ⁽¹⁾	BAUSCH + LOMB	\$1,750	\$750	Mkt
Nov-22	Famy Life Sciences	 VIATRIS™	281	–	P3 Rdy
Nov-22	 OYSTER POINT®	 VIATRIS™	329	62	Mkt
Aug-22	 aerie™	Alcon	771	–	Mkt
Dec-21	GYROSCOPE	 NOVARTIS	800	700	P1/2
Sep-21	 ARCTOS medical	 NOVARTIS	~100	–	PC
Oct-20	 vedere	 NOVARTIS	150	130	PC
Oct-20	 gemini	FS Dev't Corp. ⁽²⁾	216	–	P2a
Aug-19	 avedro	GLAUKOS	488	–	Mkt
May-19	 (Takeda)	 NOVARTIS	3,400	1,900	Mkt
Mar-19	 nightstar THERAPEUTICS	 Biogen.	877	–	P3
May-17	 RIVER VISION	 HORIZON	145	–	P2 data
Nov-15	 OCATA THERAPEUTICS™	 astellas	379	–	P2
Aug-15	FORESIGHT	 Shire	300	–	P3

Ophthalmology transactions

Transactions >\$100mm upfront since 2010, delineated by technology approach & stage

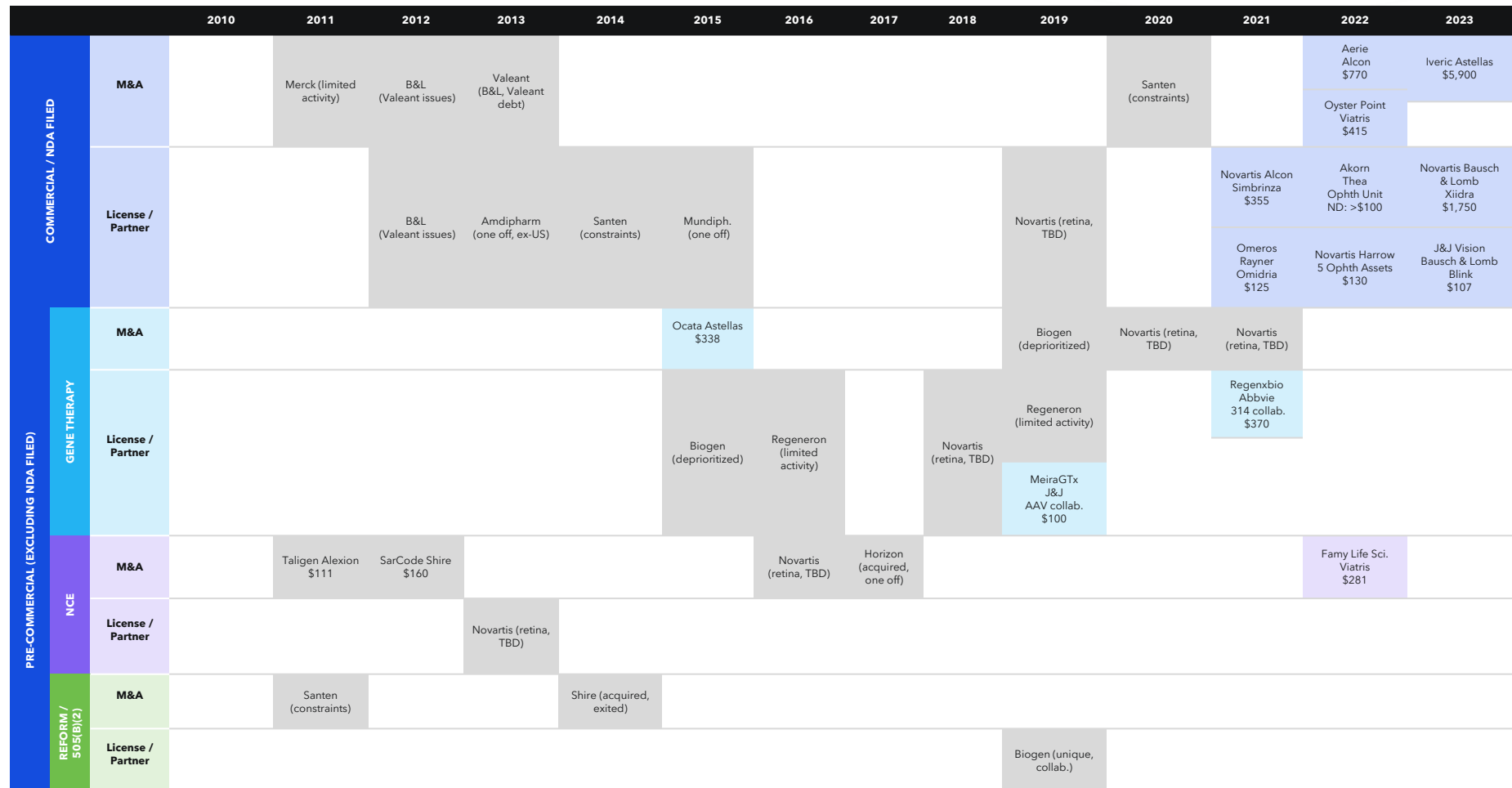
- >\$1bn Upfront
- >\$500mm Upfront
- Public M&A
- Commercial (All Tech)
- Gene Therapy
- NCE
- 505(b)(2)



Bank of America. Rx Ophthalmology Market Review, BofA Life Sciences. October 2023. | **Source:** Company filings and press releases. Data as of 10/27/23. **Note:** Excludes Spark/Roche given the focus primarily on hemophilia. Also excludes Horizon/Amgen given diversified business and fact that Tepezza was not considered purely ophthalmology by Amgen. Value of contingent consideration not shown. (1) Focus included multiple other therapeutic areas. (2) Biogen had an existing collaboration with Samsung Bioepis that may have distorted value given that other biosimilar transactions were in the single to low double digits upfront.

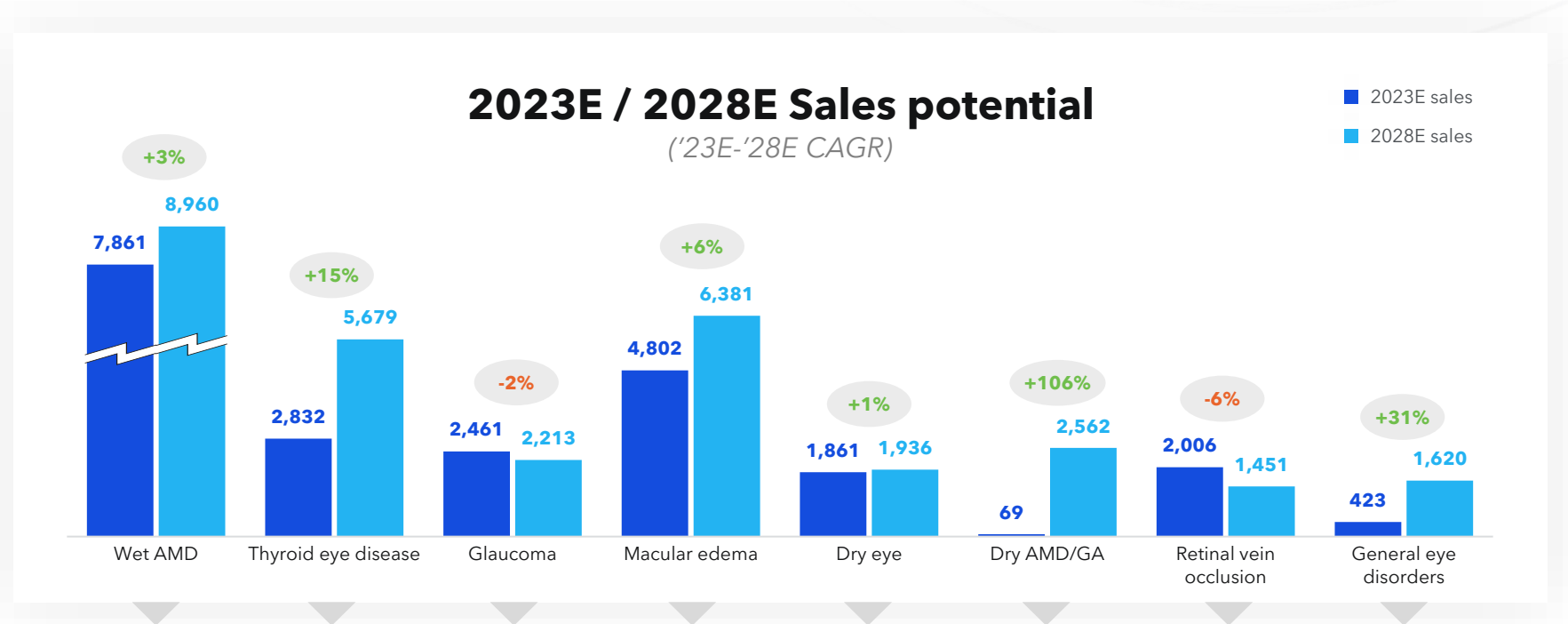
Movement of strategics that will shape ophthalmology

Removing companies that are capital constrained or have shifted their direction (see ■), it is clear that the field needs a new set of serial acquirors with the hope Alcon, B&L and others expand



Looking ahead

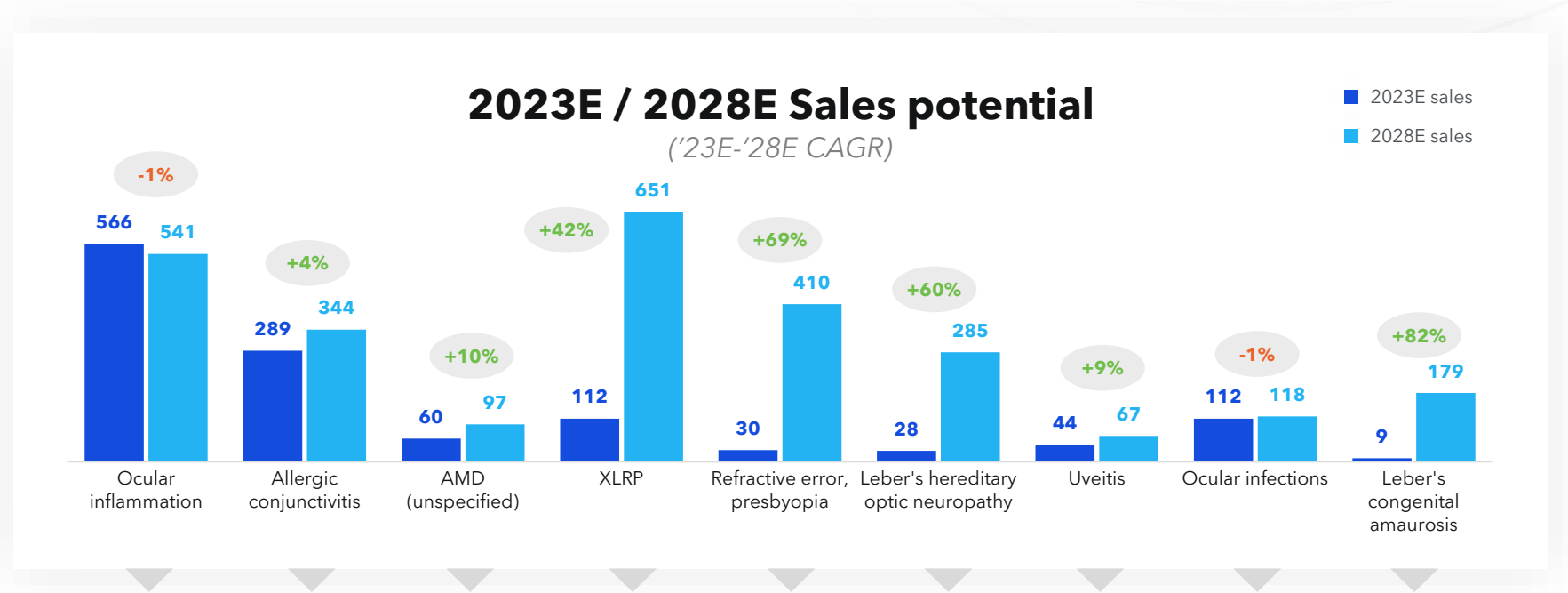
Ophthalmology indications with attractive 2028E sales potential pursued by unencumbered biotech companies



Centerview Partners. Biopharma Market Overview. October 2023. | Source: EvaluatePharma as of October 2023, Indications classified per EvaluatePharma. Indications organized by 2026E sales. (1) Reflects companies with ~+\$50m in sales in 2028E

Looking ahead

Ophthalmology indications with attractive 2028E sales potential pursued by unencumbered biotech companies (continued)



FDA: Regulatory backdrop



FDA is more constructive in some areas and increasingly conservative in others

- **Neuro:** Viewed as most accommodating FDA team (eg, Leqembi full approval in AD)
- **Cardio / Metabolic:** Poster child of Commissioner Califf's appeal for more investment into high prevalence diseases that continue to strain domestic healthcare resources
- **Oncology:** Less flexible (ie, confirmatory trial timelines vis-à-vis accelerated approvals, Project Optimus, non-reliance on China trails)



Dr. Wiley A. Chambers

Supervisory Medical Officer Division of Transplant and Ophthalmology Products (DTOP)

2023 ophthalmology regulatory update

FDA approvals in 2023



XDEMZY

Demodex Blepharitis



IZERVAY

Geographic Atrophy

REGENERON

EYLEA

Wet AMD, DME & DR



MIEBO

Dry eye disease



&



RYZUMVI

Pharmacologically induced mydriasis

Apellis

Syfovre

Geographic Atrophy



MydCombi

Pupil dilation

**HEIDELBERG
ENGINEERING**

ANTERION

Anterior segment

Genentech

Vabysmo

Macular Edema

NOVALIQ

Transforming Ocular Therapeutics

VEVYE

Dry eye disease



VUITY

Presbyopia

FDA 510(k) Clearance in 2023

NORLASE

ECHO Green Pattern Laser

Pattern laser treatment



ALTRIS IMS

Image & data management



iTrack Advance

Schlemm's Canal

J&J

VISION

ELITA Femtosecond Laser

LASIK flaps

Noteworthy FDA denial

Outlook Therapeutics® Provides Regulatory Update on FDA Review of ONS-5010 / LYTENAVA™ (bevacizumab-vikg) for the Treatment of Wet AMD

August 30, 2023

FDA issues Complete Response Letter (CRL) for ONS-5010 BLA based on CMC and need for further confirmatory clinical evidence

Outlook Therapeutics working with FDA to address the Agency's issues

Company to host conference call and webcast, today, August 30 at 8:30 AM ET

ISELIN, N.J., Aug. 30, 2023 (GLOBE NEWSWIRE) -- [Outlook Therapeutics, Inc.](#) (Nasdaq: OTLK), a biopharmaceutical company working to achieve FDA approval for the first ophthalmic formulation of bevacizumab for the treatment of retinal diseases, today announced the U.S. Food and Drug Administration (FDA) has issued a CRL to the Company's BLA for ONS-5010, an investigational ophthalmic formulation of bevacizumab under development to treat wet AMD. While the FDA acknowledged the NORSE TWO pivotal trial met its safety and efficacy endpoints, the Agency concluded it could not approve the BLA during this review cycle due to several CMC issues, open observations from pre-approval manufacturing inspections, and a lack of substantial evidence.

"We continue to believe in the public health need to provide the retina community with an FDA-approved bevacizumab treatment option for wet AMD. We will request a formal meeting as soon as possible with the FDA to further understand the BLA deficiencies and how best to resolve them. Following this meeting with the FDA, the Company will be able to discuss next steps and the expected timing for resolution," said Russell Trenary, President and CEO of Outlook Therapeutics.

Julia A. Haller, MD, Ophthalmologist-in-Chief at Wills Eye Hospital and an Outlook Therapeutics Board member, commented, "The retina community needs an FDA-approved ophthalmic bevacizumab to deliver an alternative targeted on-label treatment for patients with wet AMD."

Investor Conference Call and Webcast

Outlook Therapeutics management will host a corporate update conference call and webcast today, August 30, 2023 at 8:30 AM ET.

Interested participants and investors may access the conference call by dialing (877) 407-8291 (domestic) or (201) 689-8345 (international). The [live webcast](#) will be accessible on the [Events](#) page of the [Investors](#) section of the Outlook Therapeutics website, [outlooktherapeutics.com](#), and will be archived there for 90 days.

About ONS-5010 / LYTENAVA™ (bevacizumab-vikg)

ONS-5010 is an investigational ophthalmic formulation of bevacizumab under development as an intravitreal injection for the treatment of wet AMD and other retinal diseases. Because no FDA-approved ophthalmic formulations of bevacizumab are available currently, clinicians wishing to treat retinal patients with bevacizumab have had to use unapproved repackaged IV bevacizumab provided by compounding pharmacies—products that have known risks of contamination and inconsistent potency and availability. If approved, ONS-5010 would provide an FDA-approved option for physicians that currently have no choice but to prescribe unapproved repackaged oncologic IV bevacizumab from compounding pharmacies for the treatment of wet AMD.

Bevacizumab-vikg is a recombinant humanized monoclonal antibody (mAb) that selectively binds with high affinity to all isoforms of human vascular endothelial growth factor (VEGF) and neutralizes VEGF's biologic activity through a steric blocking of the binding of VEGF to its receptors Flt-1 (VEGFR-1) and KDR (VEGFR-2) on the surface of endothelial cells. Following intravitreal injection, the binding of bevacizumab-vikg to VEGF prevents the interaction of VEGF with its receptors on the surface of endothelial cells, reducing endothelial cell proliferation, vascular leakage, and new blood vessel formation in the retina.

Outlook Therapeutics® Provides Update on Type A Meetings with FDA

November 2, 2023

ISELIN, N.J., Nov. 02, 2023 (GLOBE NEWSWIRE) -- [Outlook Therapeutics, Inc.](#) (Nasdaq: OTLK), a biopharmaceutical company working to achieve FDA approval for the first ophthalmic formulation of bevacizumab for the treatment of retinal diseases, today announced that it has completed the requested Type A Meetings with the U.S. Food and Drug Administration (FDA) to discuss the Complete Response Letter (CRL) dated August 29, 2023 regarding the Biologics License Application (BLA) for ONS-5010, an investigational ophthalmic formulation of bevacizumab under development to treat wet AMD.

The FDA informed Outlook Therapeutics that an additional adequate and well-controlled clinical trial would be required for the approval of ONS-5010 for the treatment of wet AMD. During the meetings, Outlook Therapeutics reached an agreement in principle with the FDA on a clinical trial design that would most likely allow for the resubmission of the ONS-5010 BLA as early as the end of calendar year 2024, and subsequent approval around mid-2025, pending final agreement on a clinical trial protocol with the FDA and successful completion of the required additional clinical trial. The FDA and Outlook Therapeutics also agreed on the approaches needed to resolve the CMC comments in the CRL and Outlook Therapeutics believes these efforts should be sufficient to support approval.

"We are confident that we can meet the additional requirements that the FDA is requiring for approval of ONS-5010. The retina community of patients, physicians and payers are all in need of an FDA-approved bevacizumab that meets ophthalmic standards for the treatment of wet AMD, and we remain focused on achieving this critical treatment option," said Russell Trenary, President and CEO of Outlook Therapeutics.

About Outlook Therapeutics, Inc.

Outlook Therapeutics is a biopharmaceutical company working to achieve FDA approval for the launch of ONS-5010/ LYTENAVA™ (bevacizumab-vikg) as the first FDA-approved ophthalmic formulation of bevacizumab for use in retinal indications, including wet AMD, DME and BRVO. The FDA accepted Outlook Therapeutics' BLA submission for ONS-5010 to treat wet AMD with an initial PDUFA goal date of August 29, 2023; FDA did not approve the BLA during this review cycle and the Company is working with the FDA to address the issues that have been raised so that the BLA may be re-submitted. If ONS-5010 ophthalmic bevacizumab is approved, Outlook Therapeutics expects to commercialize it as the first and only FDA-approved ophthalmic formulation of bevacizumab for use in treating retinal diseases in the United States, United Kingdom, Europe, Japan, and other markets. As part of the Company's multi-year commercial planning process, Outlook Therapeutics and Cencora, formerly AmerisourceBergen, entered into a strategic commercialization agreement to expand the Company's reach for connecting to retina specialists and their patients. Cencora will provide third-party logistics (3PL) services and distribution, as well as pharmacovigilance services and other services in the United States. For more information, please visit [www.outlooktherapeutics.com](#).

Changing mentality at FTC



For Release

Biopharmaceutical Giant Amgen to Settle FTC and State Challenges to its Horizon Therapeutics Acquisition

Amgen will be prohibited from leveraging its drug portfolio to disadvantage rivals and will be required to seek prior approval before acquiring related products

September 1, 2023



Tags: [Competition](#) | [Bureau of Competition](#) | [Merger](#) | [Horizontal](#) | [Pharmaceuticals](#)

The Federal Trade Commission reached a proposed consent order with Amgen Inc. to address the potential competitive harm that would result from Amgen's \$27.8 billion acquisition of Horizon Therapeutics plc. As part of a nationwide settlement of their challenge to the acquisition, the FTC and attorneys general from six states – California, Illinois, Minnesota, New York, Washington, and Wisconsin – also will dismiss the related federal court preliminary injunction action.

"Consolidation in the pharmaceutical industry has given companies the power and incentive to engage in exclusionary rebating practices, which can lead to sky-rocketing prices on essential medications," said Henry Liu, Director of the FTC's Bureau of Competition. "Today's proposed resolution sends a clear signal that the FTC and its state partners will scrutinize pharmaceutical mergers that enable such practices, and defend patients and competition in this vital marketplace."

Under the [proposed order](#), Amgen is prohibited from bundling an Amgen product with either Tepezza or Krystexxa, Horizon's medications used to treat thyroid eye disease (TED) and chronic refractory gout (CRG), respectively. In addition, Amgen may not condition any product rebate or contract terms related to an Amgen product on the sale or positioning either one of these drugs.

AMGEN COMPLETES ACQUISITION OF HORIZON THERAPEUTICS PLC

Advances Amgen's Mission to Serve Patients With First-in-Class Rare Disease Medicines

THOUSAND OAKS, Calif., Oct. 6, 2023 /PRNewswire/ -- Amgen (NASDAQ: AMGN) today announced that it has completed its acquisition of Horizon Therapeutics plc for \$116.50 per share in cash, representing a transaction with an equity value of approximately \$27.8 billion.

"Today marks an exciting milestone as we welcome Horizon employees to Amgen and begin working together to serve even more patients at the world suffering from serious illnesses," said Robert A. Bradway, chairman and chief executive officer. "We have strong momentum in our core business and the addition of Horizon will further position Amgen as a leader across a broader range of diseases."

The compelling strategic and financial rationale for the acquisition includes:

- Alignment with Amgen's core strategy of delivering innovative medicines that make a significant difference for patients suffering from serious diseases.
- Strengthening of Amgen's leading inflammation portfolio by adding first-in-class, early-in-lifecycle medicines such as TEPEZZA® (teprotumumab-trbw), KRYSTEXXA® (pegloticase) and

FT.C.'s Court Loss Raises Fresh Questions About Its Chair's Strategy

Lina Khan has said a fear of defeat should not deter the agency from suing big tech companies. But after Microsoft won a ruling this week, her critics say that strategy is flawed.

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For too long, Ms. Khan said at the time, the agency had been a weak cop and needed to challenge behemoths like Microsoft, Amazon, Meta and Google in the courts to stem their growing power. Even if the F.T.C. lost the cases, she later added, they [would be a partial victory](#) because the agency would signal that antitrust laws needed to be updated for the modern internet era.

years ago on a promise to bring bold action against the biggest tech companies.

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But on Tuesday, Ms. Khan suffered the biggest blow yet to her hallmark agenda. A federal judge rejected the F.T.C.'s attempt to [stop Microsoft's \\$70 billion acquisition](#) of the video game maker Activision Blizzard from closing, saying the agency failed to prove the deal would reduce competition and harm consumers. On Wednesday, the F.T.C. filed a notice that it would appeal the judge's decision.

That followed a loss in February, when a [judge rejected](#) an F.T.C. lawsuit seeking to block Meta from buying the virtual reality start-up Within.



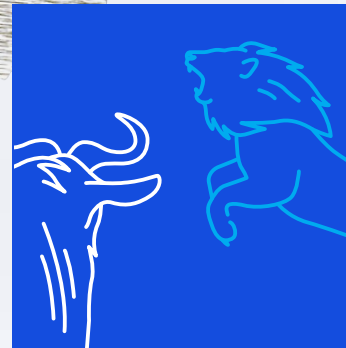
**Now, more than ever,
timing is everything.**



Capital



Partnership



M&A

- Proof of concept
- Approval
- Commercialization



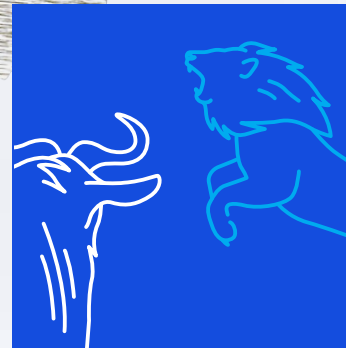
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Capital



Partnership



M&A

- Proof of concept
- Approval
- Commercialization

2023 Year in Review

Thank you

PRAVIN DUGEL, MD

**Ophthalmology
Innovation Summit**