First-In-Class, Best-In-Class – a quick pulse check

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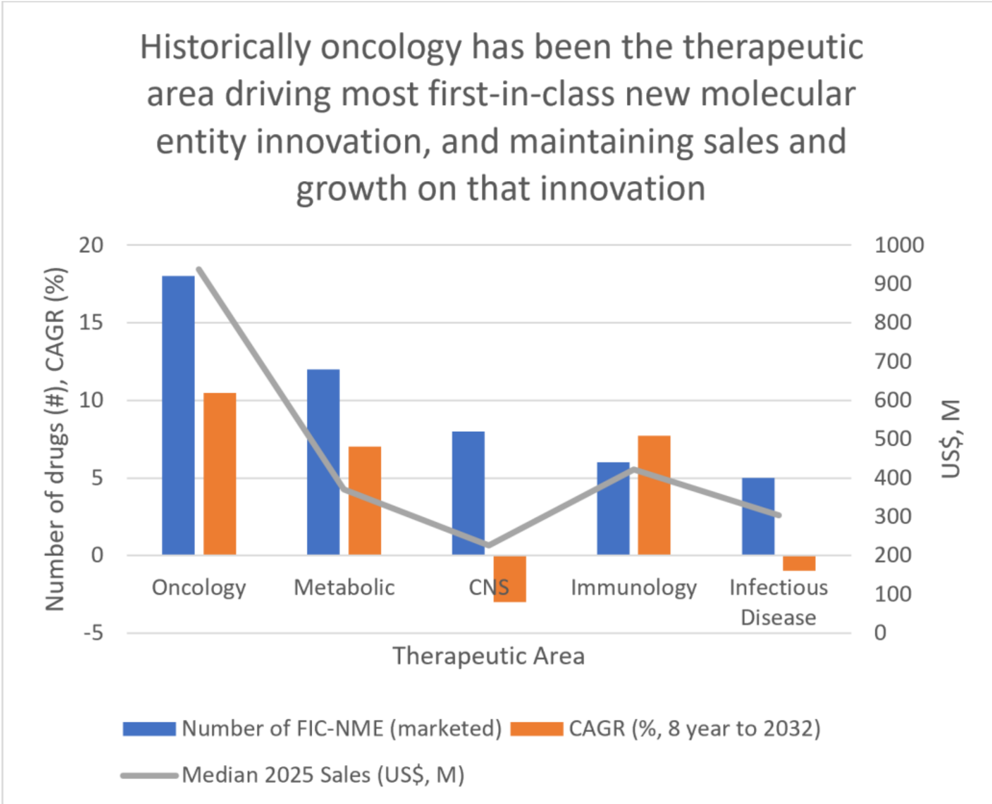
On reading the news of Merck & Co's approval for Lipfendra, a best-in-class (BIC) oral PCSK9 inhibitor marketed for Heterozygous Familial Hypercholesterolemia (heFH), I wanted to take a quick pulse check on first-in-class (FIC) historically, FIC/BIC comparators in the PCSK9 inhibitor group specifically, and contemporary M&A deals across BIC, FIC and FIC/BIC.



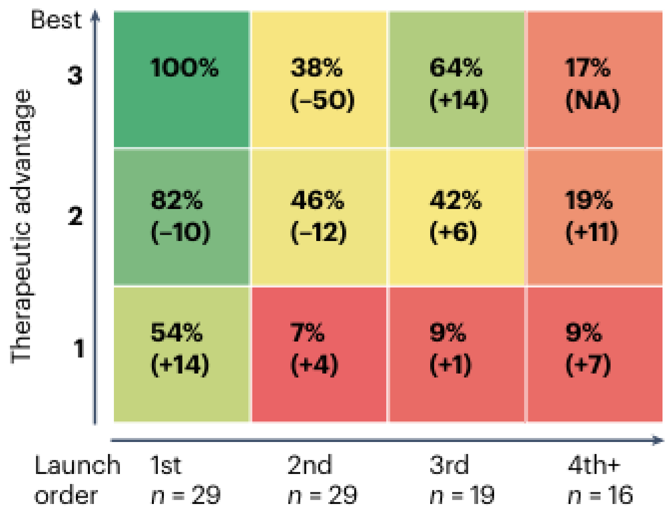
GlobalData: from 252 FIC New Molecular Entity (NME) marketed drugs, 72 of which have 2025 sales and forecast sales to 2032 a cohort of 49 drugs across 4 therapeutic areas where more than 4 FIC-NME are approved.

From 23 additional drugs across 10 therapeutic areas, respiratory and cardiovascular have also supported strong commercial FIC-NME innovation, including Alirocumab in cardiovascular, the FIC-NME PCSK9 inhibitor for heFH.

Therapeutic Area	Number of FIC-NME (marketed)	CAGR (%, 8 year to 2032)	Median 2025 Sales (US$, M)
Genetic	3	-4.26	203.08
Genitourinary	3	12.45	947.19
Hematology	3	46.26	54.00
Musculoskeletal	2	5.24	1837.89
Non-malignant	2	16.24	489.09
Hormonal	2	11.76	222.26
Dermatology	2	19.13	263.94
GI	2	6.91	605.12
Respiratory	2	36.07	1054.50
Cardiovascular	2	17.72	1255.50

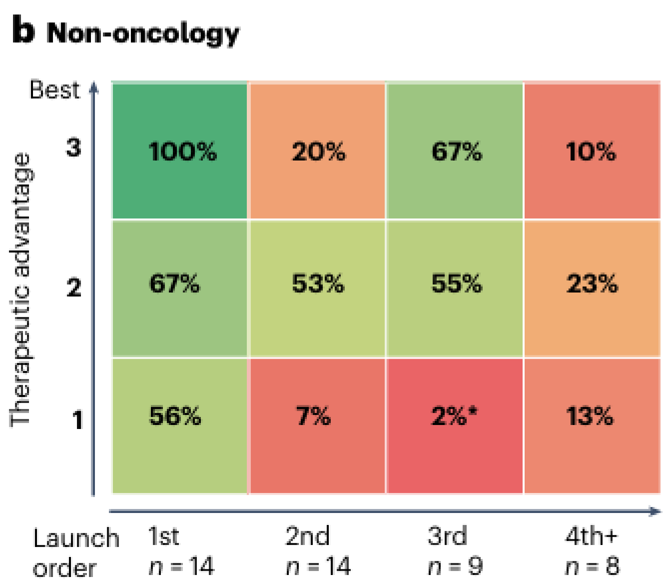
The Boston Consulting Group (BCG) conducted an elegant series of analyses in 2013 and 2023 which examined launch order versus therapeutic advantage to heat map commercial value.

2023 analysis: Trends in the value captured as a function of launch order and therapeutic advantage. Value is expressed in terms of the average percentage of the present value of global sales, normalized to the average for products that were first-to-launch and best-in-class (top left). The change from the 2013 analysis in percentage points is indicated in parentheses below each value. NA, not available. (Figure 1 from the 2023 paper)

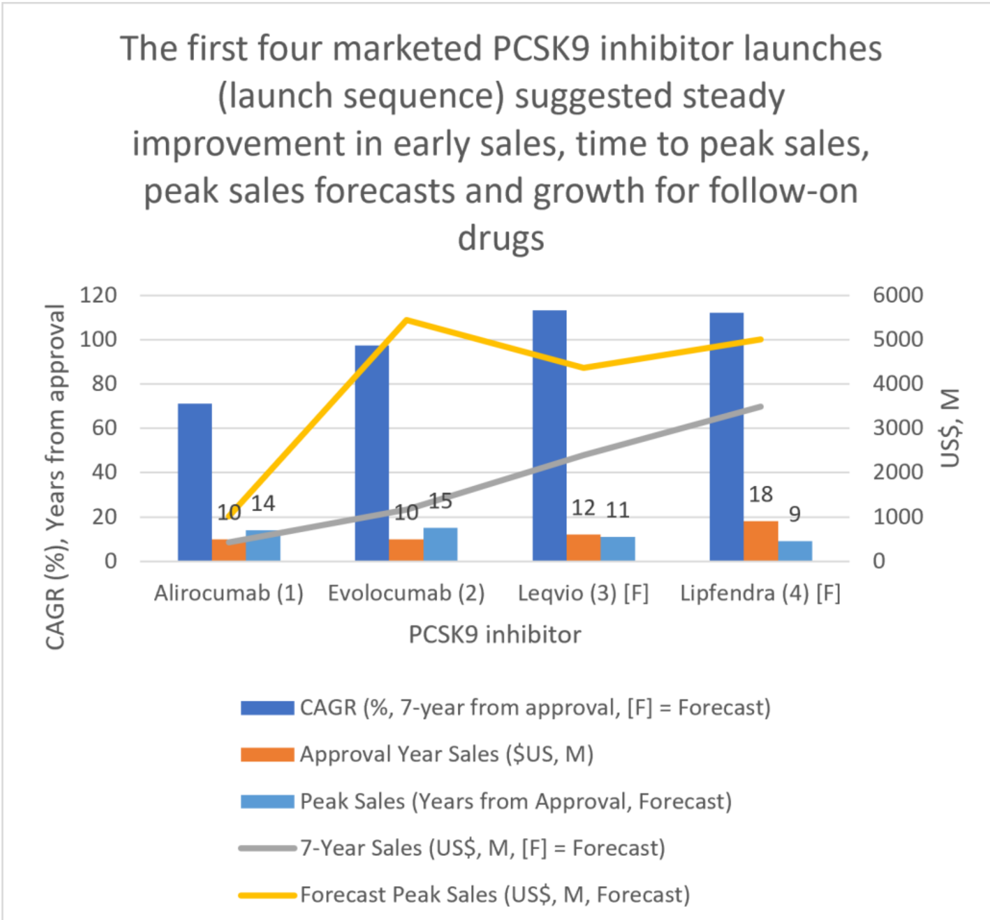


This analysis suggested that BIC 2nd and 3rd launches would in general do worse commercially than a 1st to launch even where therapeutic advantage was relatively diminished in the 1st to launch.

While this analysis covered a range of classes of drugs including oncology a similar trend was observed for non-oncology drugs (Figure 2 from the paper).



While not a strict apples-for-apples technical comparison, the historical thesis did not appear to hold for the PCSK9 inhibitor class.



In looking at potential BIC 2nd, 3rd and 4th launches in the PCSK9 inhibitor class some of the fundamental tenants of the BIC versus FIC approach seemed to hold true:

- Alirocumab (mAb) – FIC, novel biology validated, biologics and data exclusivity attained;
- Evolocumab (mAb) – BIC, efficacy improvement and better safety profile, in-home dosing every 2 to 4 weeks;

- Leqvio (siRNA) – BIC, new modality, durable efficacy improvement based on cardiovascular outcomes, reduced dosing frequency to 4-times per year in healthcare setting;
- Lipfendra (Macrocyclic Peptide) – BIC, improved efficacy, once-daily oral dosing formulation, expansion of patient access.

So, given this clear trend, I wanted to take a look at a contemporary cross section of FIC, BIC and FIC/BIC deals in the context of a another very nice BCG analysis that showed trends for pursuit of (a) novel modalities and (b) large population indications for the top 20 biopharma (Exhibit 2 of paper), both of which can, but not necessarily, signal shifts from FIC to BIC approaches.

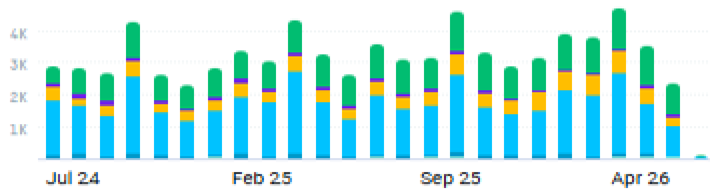
A vibe check on AlphaSense indicated a lower volume of discussion related to First-In-Class compared to Best-In-Class, but the 90-day trends were very similar and negative as expected given the clear cyclical nature of the trends.

AlphaSense – FIC

Document Trend •••

79,321
TOTAL

-25.7%
90D CHANGE



Date Range

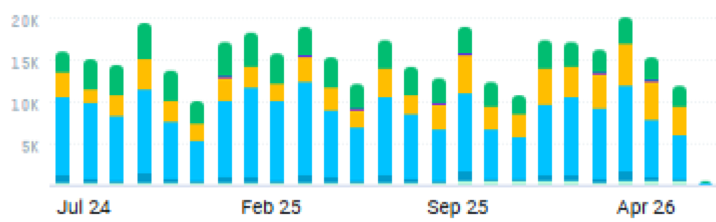
Expert Calls	496
Transcripts	2,327
Company Docs	39,995
Research	10,372
Patents	2,403
News	23,728

AlphaSense - BIC

Document Trend •••

372,048
TOTAL

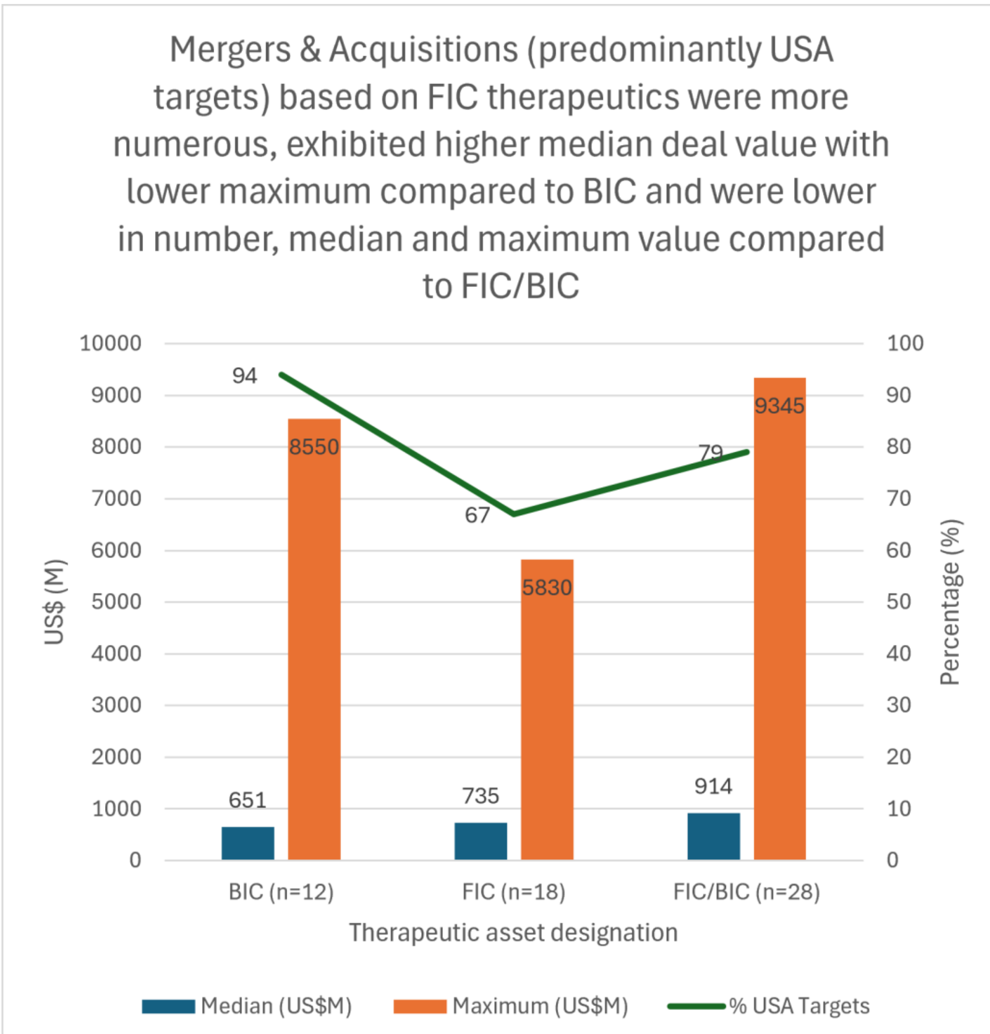
-29.9%
90D CHANGE



Date Range

Expert Calls	7,487
Transcripts	13,815
Company Docs	195,979
Research	74,432
Patents	1,436
News	78,899

The numbers of deals available for analysis are too small for breakdown by modality, numbers of assets, indication, stage of development and deal type as is the Pullan normal. However, the high-level picture is still instructive…



AlphaSense: from 188 Mergers and Acquisitions in the first 6-months of 2026, 58 of which were based on therapeutic assets that could be discerned as FIC, BIC or a combination of FIC/BIC.

BIC – Premium deal ~US$8.5B, GSK/Nuvalent: ROS1 and ALK inhibitors for non-small cell lung cancer that address efficacy and tolerability gaps in current standard of care.

FIC – Premium deal ~US$5.8B, Biogen/Apellis: C3 inhibitors for paroxysmal nocturnal hemoglobinuria (renal) and geographic atrophy (ophthalmology).

FIC/BIC – Premium deal ~US$9.3B, Novartis/Avidity: delpacibart-oligonucleotide conjugates for Myotonic Dystrophy Type 1, Fascioscapulohumeral Muscular Dystrophy, Duchenne Muscular Dystrophy (Exon 44) and AOC 1045 for Duchenne Muscular Dystrophy (Exon 45).

Take aways from this quick pulse check:

FIC innovation is still valuable: FIC gets market share with exclusivity/regulatory benefits in most cases that can be used to create strong competitive commercial positioning even in the face of inevitable competition. Deep knowledge of target biology, modality strengths and weaknesses and regulatory/clinical/commercial pathways are supported by investors and buyers. The Bayer AG and Perfuse Therapeutics, and Neurocrine Bioscience and Soleno Therapeutics M&A deals at more than $2B each are notable.

But BIC is not far behind and may drive higher premiums where significant differentiation in efficacy/safety can be obtained, particularly where biology has been de-risked and the market may be large and/or less competitive and/or supportive of higher payer budgets. Differentiation in the GLP-1 space is instructive here (weightloss efficacy, side-effect/lean muscle mass profile for adherence/maintenance, oral dosing).

And, companies that can drive **simultaneous FIC and BIC programs**, or couple assets with platforms to drive new markets, expand patient access and indications and optimize target validation and modality selection/performance may be able to drive significant revenue and value compared to FIC or BIC alone. The SL Science Holdings M&A deal with a SPAC and the Eli Lilly M&A deal with Centessa Pharmaceuticals Plc for more than $5B, and the Novartis/Avidity premium deal in the musculoskeletal space (mentioned previously) are good examples of this approach.
