

General Market Overview

PUBLIC MARKETS

While the third quarter of 2018 took biotech valuations almost up on par with the 2015 highs, the worries of a possible correction proved to be right as we entered Q4. What at the time seemed to be another bull year for biotech turned negative already in October due to worries about slowing economic growth and uncertainty about the US-China trade war. Increased market volatility was expected and even though life science generally resists economic downturns relatively well, high risk sectors usually struggle in a volatile market. Q4 turned out to be one of the worst quarters for public biotechs in this century with all market cap tiers tracked by BioCentury falling and ending the year in red numbers. The median share price decline was about 20% for companies with market caps above USD 500 million, and as high as 29% for the small caps below. Seven out of ten listed companies tracked by BioCentury closed the full year losing value.

As we head into 2019, it is with analyst expectations of a volatile year, but with some optimism of increased M&A activity, which could attract investors back to the sector.

<i>Index</i>		<i>Q4 2018</i>		<i>2018</i>
NYSE Arca Biotech	↓	-22%	→	0%
NASDAQ	↓	-18%	↘	-4%
S&P 500	↓	-14%	↘	-6%
NASDAQ Biotech	↓	-21%	↓	-9%
BC 100	↓	-24%	↓	-12%

The biotech sector took a hard beating in the volatile markets resulting from general market fears. The sector bottomed out around christmas, but recovered some of the loss in the final week of the year.

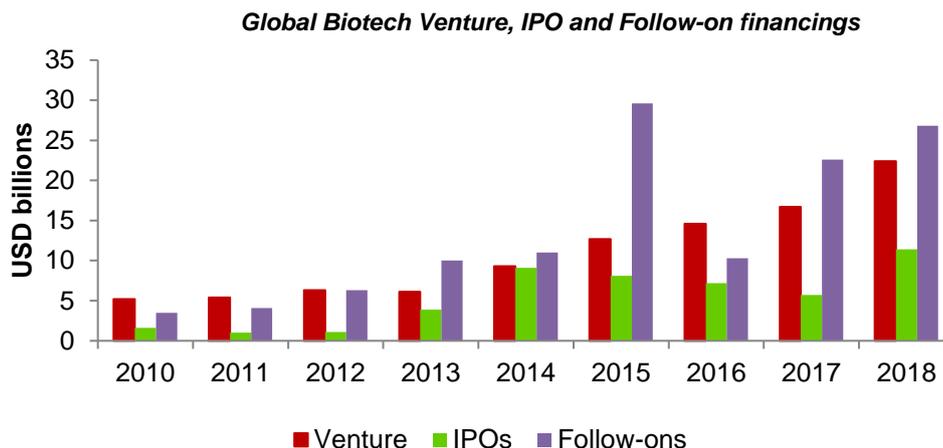
Index performance. Source: BioCentury Financial Center

Most public companies in HealthCap's portfolios were affected by the general market downturn. HealthCap V company MIPS resisted the downturn, trading flat in Q4 to end the full year up 112%. HealthCap VI company Oncopeptides, despite losing 18% in the final quarter, ended the year 64% up after presenting strong clinical progress as well as initiating preparations for commercialization of lead product Ygalo.

FINANCINGS

The biotech sector financings reached record levels in 2018 and the availability of capital for high-quality companies is better than ever. Venture investments surpassed USD 20 billion worldwide, some USD 6 billion more than in 2017, and almost 50 venture rounds were larger than USD 100 million (twice as many as in 2017). Many of these large financings included crossover investors and many companies have subsequently gone public.

IPO financing numbers also reached record levels as more than USD 11 billion was raised by 101 companies - an average of well above USD 100 million in gross listing proceeds. A recent Silicon Valley Bank report concludes that pre-money valuations also reached a five-year high.



Biotech financings 2010-2018. Source: BioCentury Financial Center

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The USD 27 billion raised in public follow-on financings was second only to the record year of 2015, both venture and IPO financings posted record numbers in 2018.

In October, public HealthCap VII company **Victore Pharma** raised EUR 8 million in an oversubscribed rights issue and another EUR 16 million in a directed share issue in late November.

HealthCap VII also made its eleventh investment in Q4, as Belgian radiopharmaceuticals company **Camel-IDS** closed a EUR 37 million financing.

In December, Swedish HealthCap VII company **Aprea** closed a EUR 50 million financing. Funds will be used to initiate a phase III study with lead compound APR-246 to treat myelodysplastic syndromes (MDS).

The partial US government shutdown, beginning on December 22, delayed the SEC from reviewing and approving registration documentation, resulting in a paused US IPO and follow-on financing window. The only sector IPO in early 2019 is so far a minor Chinese IPO and follow-on financings were delayed until the second half of January, reaching only half the number of closed financings compared to the same time of the year in 2018.

However, two public HealthCap VI companies have started 2019 by closing significant follow-on financing rounds. **Oncopeptides** raised EUR 53 million in a directed share issue with the aim to expand ongoing clinical development and to enforce the company's commercial function to prepare for market launch. A few days later, **Nordic Nanovector** closed a EUR 22 million private placement, with proceeds planned to be used to strengthen the company's clinical and commercial activities.

M&A

The total number of announced M&A deals in 2018 was similar to the year before, and lower than in 2015 and 2016. However, the total announced deal value was significantly higher in 2018 compared to 2017 as the average deal value tripled up to more than USD 3 billion. The most notable deal of the year in the biopharma sector was Takeda's acquisition of Ireland based rare diseases specialist Shire worth some USD 62 billion.

Announced M&A by year announced



M&A. Source: BioCentury Financial Center as of Jan 22, 2019

In HealthCap's portfolio, HealthCap VII start-up company **INIM Pharma** was acquired for shares by **Vicore Pharma** in a deal worth approximately EUR 8 million, closed in July.

M&A wise, 2019 is off to a good start with **Bristol-Myers Squibb** announcing a merger agreement to acquire **Celgene** in a cash and stock transactions at a value of approximately USD 74 billion and a 54% share price premium. The deal value makes it the largest pure-biotech takeout by a pharma company ever, with a deal value almost USD 30 billion higher than the 2009 acquisition of the remaining Genetech shares by Roche. Only a few days later, **Lilly** announced its USD 8 billion offer to acquire all outstanding shares of **Loxo Oncology** at a premium of 68%, a deal many analysts see as a potential spark for the sector as it is a clear acquisition of innovation and premiums at such levels give strong support for innovative companies.

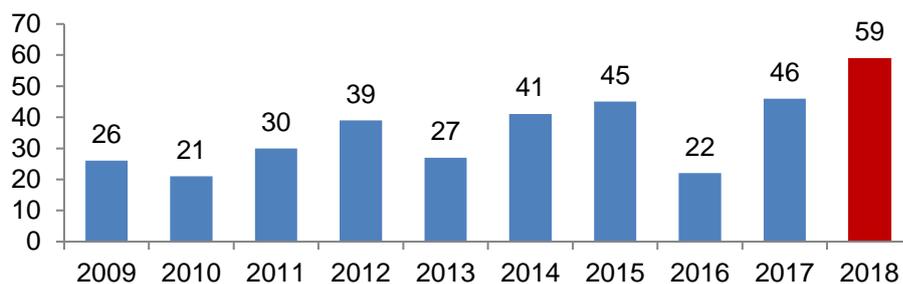
DRUG APPROVALS

In 2018, the FDA approved 59 new drugs, the highest number ever and well above the average of approximately 33 yearly approvals over the last 25-year period.

The number of drugs approved with orphan drug designation almost doubled from the previous year, from 18 to 34, reaching as high as 58% of all approved drugs and new records were also reached for the number of drugs approved to treat both cancer and rare genetic diseases.

As many as 19 drugs approved in 2018 were identified as first-in-class, drugs with mechanisms of actions different from those of existing therapies. There is a sustained high level of innovation, with drugs becoming more specific and efficient and a continued trend can be observed where about two thirds of drugs approved have had its development origin in smaller biopharma companies. What could mark a new trend is that as many as 50% of all new drugs approved in 2018 were also owned by smaller, innovative biopharma companies, according to HBM analysis. Smaller companies (outside top 30 in terms of sales) are playing an increasing role not only as originators, but also as developers and owners of drugs all the way to approval, possibly as a result of a favorable financing market during several years.

Number of approved novel drugs by FDA



FDA approved Novel Drugs 2008-2018. Source:FDA

Heading into 2019, the partial US government shutdown has prevented the FDA from accepting most new drug applications and the administrative backlog could mean that it will take a few months for the FDA employees to catch up. The first new drug approved in 2019 was approved on February 1.