Timmerman Report

Feeding Frenzy: The Ecosystem is Growing Stronger

By Clay Thorp & Ben Scruggs / November 19, 2019

Clay Thorp

Off the coast of South Africa, sardines swim in schools to protect themselves from predators.

Eventually, a single sardine wanders off. It gets snatched and devoured by an alert sea lion.

Over time, a growing set of predators – dolphins, tuna, and copper sharks – see the same opportunity as the sea lion.

A feeding frenzy ensues.

Ben Scruggs

Together, the predators are able to disrupt the school of sardines. All are able to eat despite the seeming increased competition for food.

Eventually, the commotion attracts the attention of a giant Bryde's whale. It moves in slowly, then lunges, taking down everything left with a single gulp.

This type of feeding frenzy is not altogether different from what is emerging in biotech.

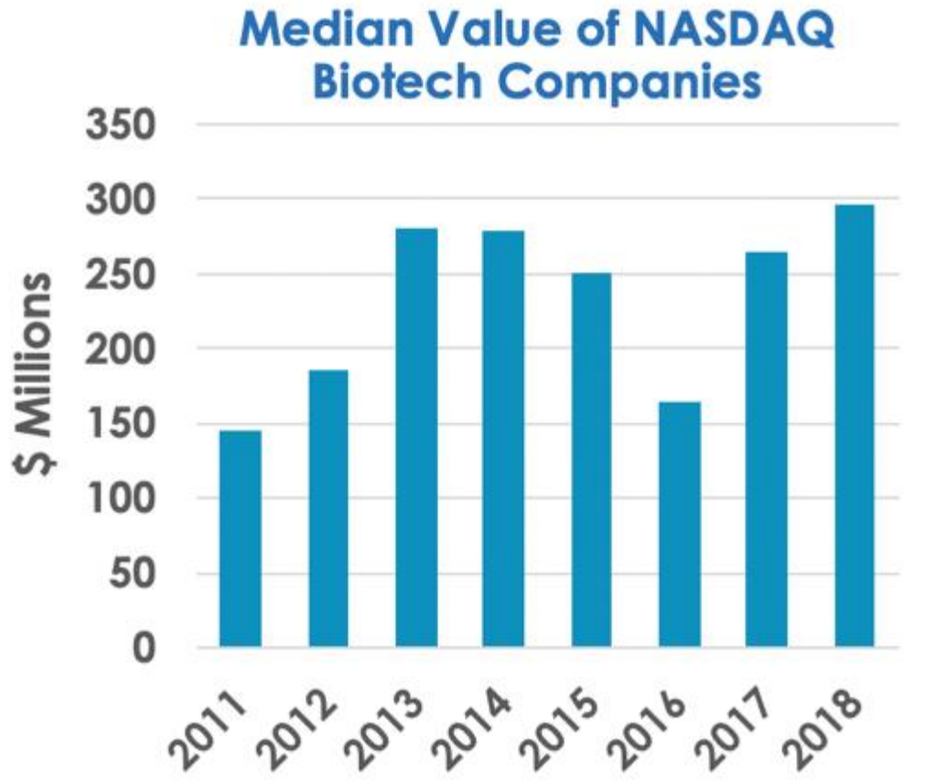
Early stage startups have long been the sardines of the biotech food chain, supplying a source of disruptive technology with the promise of providing better therapies for patients. At the other end of the food chain, the Bryde's whale in our analogy, Big Pharma has a voracious appetite for external innovation because of patent expirations on its franchise products and internal R&D that isn't able to come up with new blockbusters to keep the profits growing.

Small, early-stage biotechs may catch the eye of Big Pharma through novel approaches to address commercially interesting targets, but often, these assets and platforms lack clinical validation and simply appear as a part of the indistinguishable school of startups swimming in a massive ocean.

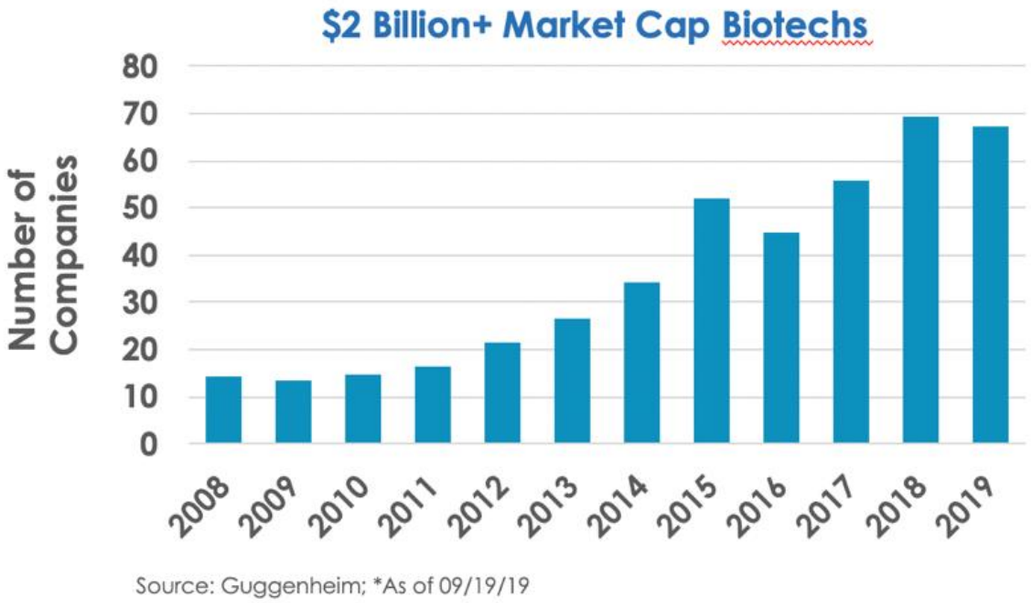
But, to follow the analogy, this is where the food chain is changing.The gap between startups and big pharma is now being filled by a growing class of sea lions, sharks, and tuna, the small-to-medium sized biotechnology companies. We're seeing new types of predators emerge in the middle of the biotech food chain.

Growing companies, growing market caps

Overall, the median market cap of a NASDAQ biotech company is now roughly double what it was in 2011 (~$300 million in 2018 vs ~$150 million in 2011, Figure 1). While we have seen market cycles influencing the overall sector during this time, the total number of biotechs with a market cap greater than $2 billion has been steadily on the rise (Figure 2).

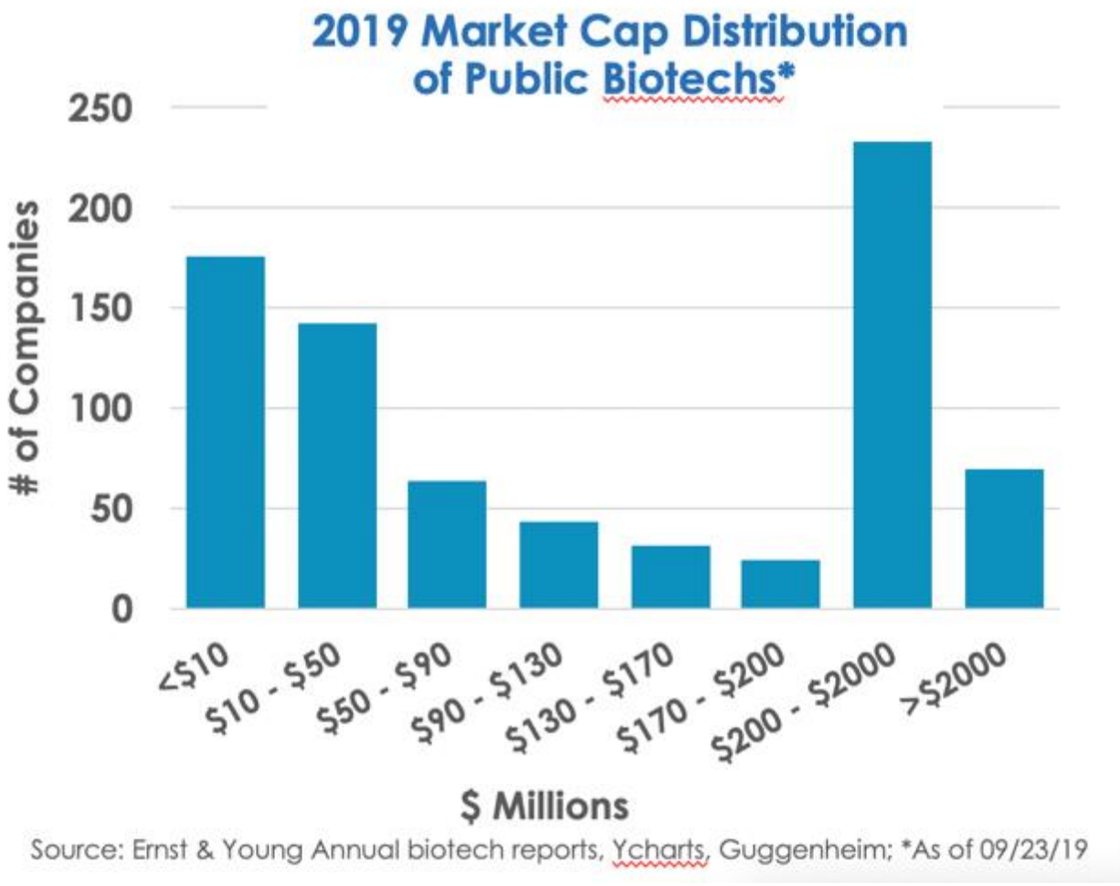


Source: BMO Capital Markets, market caps at 12/31 of the year



Source: Guggenheim; *As of 09/19/19

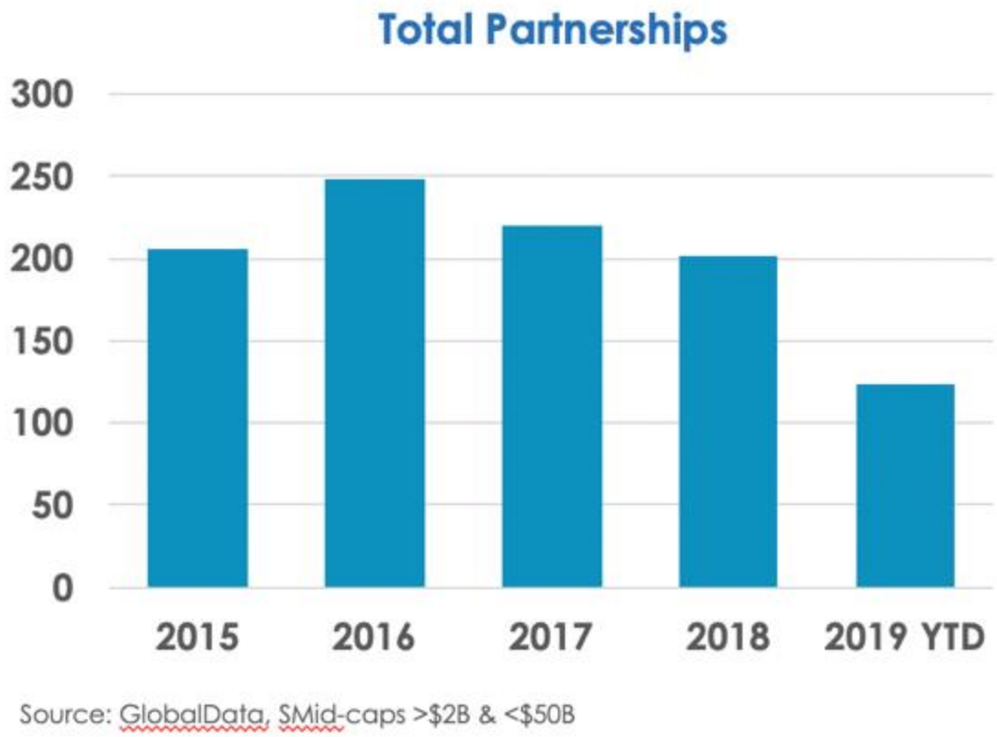
Just a decade ago, many of these companies did not even exist (Allakos, Allogene, Biohaven, Moderna). Many of these companies have only gone public in the past couple years, gaining the kind of stock necessary to play at high levels of M&A. This growing class of SMid caps is shifting the overall distribution of public biotech companies away from the heavy weighting of micro and small cap companies (Figure 3), positioning SMid caps with an increasingly important role in the overall biotech ecosystem.



SMid Caps - Emerging Engines of Growth

Typically, SMid caps are built upon a single R&D competency such as a platform technology like siRNA or an area of therapeutic excellence like neurodegeneration. As these companies grow, they must face the decision of whether to expand into new therapeutic areas and/or gain exposure to new modalities or be acquired by a bigger company.

Now armed with meaningful balance sheets and share currency, many SMid caps are actively and aggressively looking to grow their own pipelines through partnerships and acquisitions. Over 200 SMid cap partnerships have been established each year since 2015, with 2019 on a similar pace (Figure 4). Thanks to the favorable cost of capital for these companies and a high-risk appetite, SMid caps can aggressively pursue their own external sources of innovation.



It is a stretch to consider Vertex Pharmaceuticals ($54 billion market cap) a SMid cap company any longer. But the company's recent activity typifies the idea of leveraging partnerships as a means to diversify the pipeline. The name Vertex has long been associated with cystic fibrosis, and the recent approval of Trikafta will only help maintain strength in this market.

However, Vertex has publicly announced additional areas of interest including alpha-1 antitrypsin deficiency, sickle cell disease, beta thalassemia, pain, and APOL1-mediated kidney disease. Just in the past year, Vertex has actively bolstered its toolbox by establishing or renewing collaborations or partnerships with Arbor Biotechnologies, Kymera Therapeutics, CRISPR Therapeutics, Moderna, and Ribometrix. Additionally, Vertex agreed to acquire Exonics Therapeutics in June 2019 and Semma Therapeutics in September 2019.

Together, these companies provide access to a wide variety of new therapeutic areas and new drug modalities including gene editing, protein degradation, mRNA therapeutics, and RNA targeting small molecules. Without these agreements, it would take a tremendous amount of capital to build in-house expertise across all of these areas.

We are directly seeing the impact of SMid caps on companies in the Hatteras portfolio. The Vertex agreements with Kymera and Ribometrix provide meaningful validation and non-dilutive R&D dollars, allowing these early-stage platform companies to further build their teams without having to spend time fundraising.

Just last week, two Hatteras portfolio sardines, StrideBio and Rodin Therapeutics, entered deals with biotech copper sharks, Sarepta and Alkermes, respectively. In Sarepta's deal with StrideBio, a Hatteras portfolio company developing a next generation of AAV capsids, the company bolsters its gene therapy platforms by accessing new capsids with potentially better tissue tropism and antibody evasion properties. In its deal to acquire Rodin Therapeutics, Alkermes further expands its reach in the CNS space through Rodin's first-in-class therapeutics for addressing synaptic dysfunction

Something New? - Yes and No

So, what does all this mean? Is the emergence of the SMid cap buyer something new? Yes and no.

Historically, there are good examples of SMid cap companies growing innovation and ultimate revenues through partnering and acquisition. Look no further than Allergan and Celgene.

The Celgene example is particularly instructive. The company has leveraged a combination of internal and external programs to grow from SMid cap status to the biotech juggernaut we now know. Today, roughly 50% of the Celgene pipeline is externally sourced and 20+ INDs have been filed/approved through the company's partnering strategy. Acquisitions over the past decade include Receptos, Quanticel Pharmaceuticals, Engmab, Delinia, Impact Biomedicines, and Juno Therapeutics, among others. Additionally, the company manages 50+ collaborations to keep fueling the pipeline. With all this activity, perhaps we should not be surprised that Celgene was able to attract the attention of the Bryde's whale. Indeed, Bristol-Myers Squibb's agreement to acquire Celgene for $74 billion demonstrates that Big Pharma can feed on SMid caps even as they continue to grow.

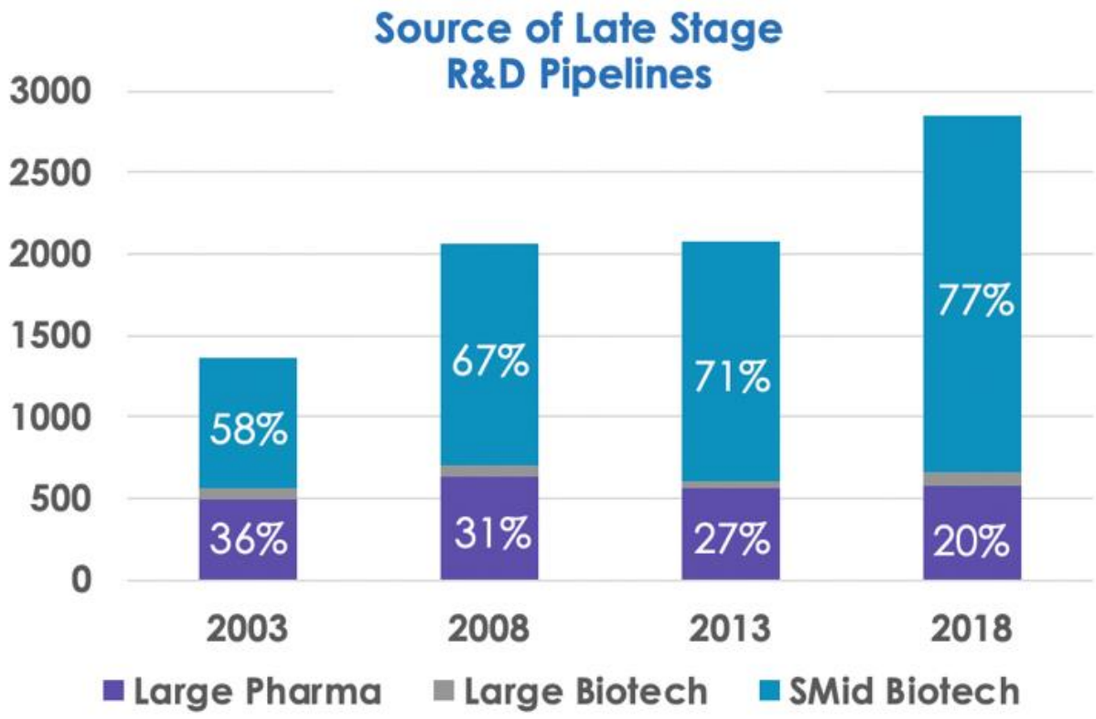
Historically speaking, however, we would argue that Celgene and Allergan are more the exception than the rule, as most of the remaining SMid Cap class over the last decade have developed its pipeline internally, or remained stagnant. The past few years of activity may portend something different.

We've already mentioned Vertex, which has leveraged its CF internal development success to access new technologies and companies with over a dozen deals in the past 12 months. Other companies such as Jazz, Sarepta, CRISPR, PTC, and now Alkermes show similar patterns with multiple deals each. Even SMid cap European companies such as Lundbeck and UCB are now getting into the game with acquisitions of Alder BioPharmaceuticals and Ra Pharmaceuticals, respectively. If this can become a consistent trend, it will be a sign of ecosystem maturity, providing a breadth of risk-taking appetite, thereby generating more consistent liquidity for those of us who feed the next generation of promising sardines.

Maturing Ecosystem – Keeping the Whales Honest

With the growth of hungry, nimble SMid caps now in food chain, Big Pharma is being forced to be an honest bidder for M&A and partnership targets. Big Pharma will be forced to either bid earlier for the young companies or pay-up to acquire the SMid Cap ones. Low-ball offers, which might have been good enough in quieter times, won't cut it in this environment.

Pharma knows where the food supply comes from. Over 75% of late stage R&D pipelines originated from small and mid-cap biotechs in 2018 (Figure 5). This number has grown steadily over time, and now almost half of new drug approvals originate from emerging biotechs (47% of 59 approvals in 2018).

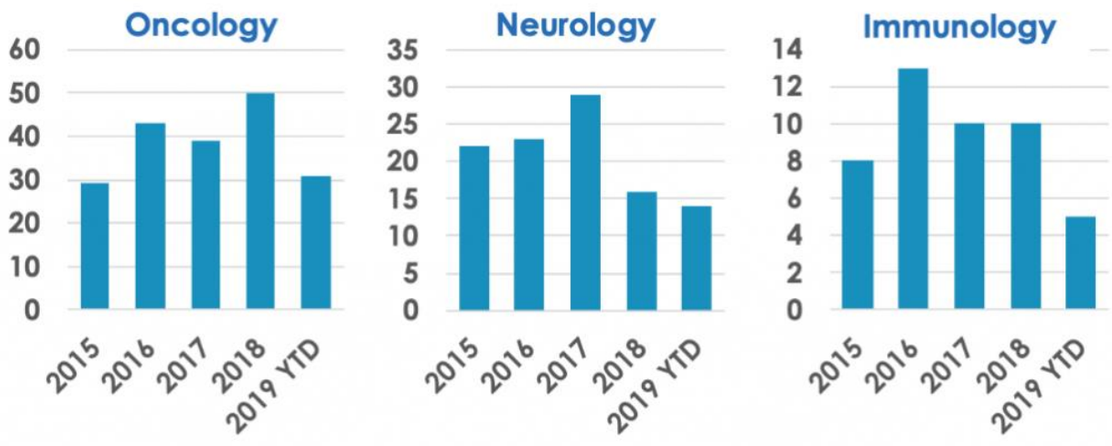


Source: IQVIA Pipeline Intelligence, Large Pharma revenue: >$10B, Large Biotech revenue: $5-10B, SMid revenue <$5B

As such, Big Pharma's R&D pipelines depend on accessing this kind of innovation, largely by gobbling up SMid caps at multi-billion dollar valuations.

In quick succession, we have seen Sanofi acquire Ablynx, GSK acquire Tesaro, Lilly acquire Loxo, and Pfizer acquire Array Biopharma. Roche is working on closing its takeover of Spark Therapeutics. Then there are the mega-mergers: AbbVie's acquisition of Allergan for $63 billion and the $74 billion agreement by BMS to acquire Celgene.

It is noteworthy that much of this activity overlaps directly with key strategic areas for Big Pharma. Oncology, neurology, and immunology are among the areas of highest SMid cap partnering (Figure 6).



Source: GlobalData, SMid-caps >$2B & <$50B as of 9/15/19

In the waters off the coast of South Africa, seal, dolphin, shark, and whale all thrive. A maturing ecosystem creates a virtuous cycle. It all starts with the sardine. We need to do our part to feed those little guys. The whole industry depends on it.