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The IPO Party Is Over – How Bad Is The Hangover?

by **Melanie Senior**

Over 100 biopharma companies piled onto public markets in 2021, raising a combined \$21bn. A sharp cool off has left many trading well below their listing price. What does it mean for biotech financing in 2022?

Public biotech stocks are suffering after the excesses of 2020 and 2021. Some see a welcome correction, others an indiscriminate blood bath. Biotech's coffers are stuffed with cash, cushioning the impact of the market downturn – for now. M&A is expected to provide another safety net, with an estimated \$500bn of strategic firepower waiting to be deployed as prices return to Earth.

But not all biotechs will escape the pain. The sector may still be front-of-mind in the wake of the pandemic, yet macro-economics, geopolitics and wider market mechanics may influence how quickly, and how high, it bounces back. "This will endure for a year or more," said one investor, pointing to non-specialist cash that has yet to leave the sector. In the meantime, biotechs need to "pace themselves," re-discover spending discipline, set clear milestones and dust off their business development manuals. Investors will top up reserves for their existing portfolio companies, and those with money to spare – of which there are many – will find juicy opportunities in 2022.

How The High Got So High

At the start of 2021, biotechs and other health-related companies fell over themselves to go public, riding the pandemic-wave. A record-breaking 130 biopharma companies listed that year, according to Biomedtracker, raising a combined \$21bn. That was 10% more than 2020, another record-setting year, both in total dollars raised and number of companies. It was *three times* the tally in 2019, the last full year pre-pandemic.

Listings were big, and fast. 2021's top three US biopharma IPOs, [*Sana Biotechnology, Inc.*](#), [*Zymergen Inc.*](#) and [*Recursion Pharmaceuticals, Inc.*](#), each raised over half a billion dollars on the

back of ambitious visions to turn gene- and cell-therapies mainstream and industrialize drug discovery using an expanding suite of gene-editing, screening and in silico tools. The top 10 US biopharma listings together raised over \$4.3bn; the top 10 Chinese and Asian biotechs were not far behind, raising over \$3.7bn.

Some companies were built, funded and fast-forwarded onto public markets in months, squeezing A, B and pre-IPO rounds into one. Investment firm Medicxi in January 2021 assembled 10 of its portfolio companies into [*Centessa Pharmaceuticals plc*](#), drawing over a dozen other investors into a \$250m A round and, four months later, a \$380m IPO on Nasdaq. (Also see "[*Centessa 'Creates Pharma Pipeline Overnight' Using Novel R&D Approach*](#)" - In Vivo, 3 Mar, 2021.)

The growing prominence in biotech of crossover investors and private equity players – for which an IPO is often the endgame – helped fuel this rush for a ticker symbol, as it became clear that any company, no matter what its assets, was more valuable when public. This also drove alternative listing routes, such as merging with special purpose acquisition companies (SPACs).

Meanwhile, drug approvals were happening at record pace, too: the US FDA waved through over 50 new drugs in 2021 (not counting emergency approvals for COVID-19 vaccines and therapies). Most used expedited pathways.

Then the music began to fade. Biotech indices including the Nasdaq Biotech Index and XBI started to fall in February, and, by the end of the year, the party was well and truly over (*see Exhibit 1*). Concerns over inflation and interest rate rises hit the whole market, but biotech dropped further. On average, 2021's large biopharma IPO class are now trading at 37% below their IPO price, according to Refinitiv data, versus 22% for all 2021 US listings.

Many individual companies have fared much worse, with bad clinical news harshly punished. Fibrogen's shares dropped by over 70% following mis-reported data and an FDA snub for lead

SPACs: Rout Or Rescue?

Special Purpose Acquisition Companies were popular in biotech through 2020 but the shine has come off. The average SPAC, after finding a target, performed even worse than normal IPOs during 2021, according to Pitchbook.

Opinions differ on the value that SPACs have brought to biotech. One Boston-based VC dismissed them as "a distraction" and "the manifestation of exuberance and excess capital."

Another believes SPACs could offer an alternative for some companies this year, as conventional IPOs dwindle. SPAC sponsors have two years, after raising capital, to find a merger partner. Dozens of health care focused SPACs have yet to find a target. Already in 2022, PureTech Health-founded Gelesis Inc.,

drug roxadustat, for anemia of chronic kidney disease. Gene therapy play *LogicBio Therapeutics, Inc.*, already down 90% at the end of 2021, went below a dollar this year after the FDA put a hold on a trial of its therapy for a rare metabolic disease.

Those with no clinical assets at all have also suffered: Zymergen cratered by more than 80%; Sana lost two thirds of its value. Some companies with un-tainted, later-stage programs appear less affected, but not all: Centessa has four clinical-stage programs and several others spanning various modalities and therapy areas, yet its value has halved since IPO. *EQRx, Inc.*, with five clinical programs and a mission to cut drug prices, promptly lost 60% after raising \$1.3bn through a SPAC merger in December.

“It’s a blood bath out there,” said one investor.

Crash, Or Correction?

Despite shocking share price falls, this downturn may be more correction than crash; a return to normal after the exuberance of 2020-2021. “Biotech is correcting after an unprecedented run-up,” said Jean-Francois Formela, partner at Atlas Venture in Cambridge, MA. Biotech has always been a risky sector, with volatile individual stocks and unending bull-bear cycles.

The question is whether the downcycle turns into a prolonged bear market. Much of the sector is well-placed to shoulder the blow – for now. Biotechs have stronger balance sheets than at any time in the past, so many can afford to wait before they need to raise more money. Average IPO proceeds in 2021 were about \$160m, double the average haul in 2017. That is enough to keep the lights on, even with (larger) companies now burning through cash faster than in the past. Centessa, for instance, has cash through to 2024, according to CEO Saurabh Saha.

Private fundraising also broke records over the last two years, buying VCs and their portfolios some insulation from the public market rout. Available private capital tripled over the course of the pandemic, according to Pitchbook and Silicon Valley Bank. US VC funds reached a record

which sells a weight management aid, raised about \$100m in a SPAC deal – though its stock has since fallen 40%. Another PureTech-founded entity, Akili Interactive (which sells a video game-based treatment for ADHD), announced plans to complete a \$400m SPAC transaction mid-year.

Others have failed to launch: Valo Health terminated a \$750m deal with a SPAC sponsored by Khosla Ventures in November and opted for a series C round instead.

UK-headquartered Benevolent AI, which uses AI to speed drug discovery, in December 2021 announced a merger with Amsterdam-listed SPAC Odyssey Acquisition, anticipated to raise over \$400m. The deal will be among Europe’s largest SPAC mergers – if it completes.

\$28.3bn, including \$1bn-plus mega-raises by Flagship Pioneering, Arch Venture Partners and OrbiMed. Bigger funds mean bigger funding rounds – 2021 saw B and C rounds of \$500m or more (EQRx and ElevateBio) and even seed deals in the tens of millions.

Formela noted that most companies in Atlas' portfolio had at least two years of cash. That gives them time before they are forced to raise further funds at a lower valuation that would dilute existing shareholders. And even then, Atlas and several other VCs, like Khosla Ventures and Abingworth Management, took advantage of the easy capital raising conditions in 2020 and 2021 to raise new “opportunity” funds – either to share some of the cream of crossover rounds or IPOs, or, in less rosy market conditions, to support their private portfolio companies for longer. These returning backers would benefit from lower valuations, in their follow-on investment, just as new investors would – making them both seller and buyer. Atlas raised a \$300m Opportunity Fund in October 2021.

“There’s a sufficient cushion in the private [biotech] market” to bridge the gap to public market rout, said Søren Møller, managing partner at Novo Seeds, which invests in early-stage companies from Novo Holdings’ evergreen fund.

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Caution In Late-Stage Rounds

Not all companies are protected, though. The downturn has hit some firms with late-stage, cash-hungry programs. [*Kaleido Biosciences, Inc.*](#) and [*Gamida Cell Ltd.*](#) are two examples of public companies cutting staff to eke out their cash a bit longer; others are raising debt.

Some private companies may find themselves in trouble too, since even private investors “are starting to behave differently,” according to Roel Bulthuis, managing partner at Amsterdam-based INKEF, which invests in early-stage European health care and technology firms. Money is moving away from later stage private rounds, and crossovers – having hijacked many B and C round discussions during 2020 and 2021 – are also less attractive. “People are more cautious,” said Bulthuis.

For now, it is difficult to evaluate whether – and how hard – the public market crash will impact private investment. Some investors, like Carl Gordon, managing partner at OrbiMed, do not think it’s a real bear market, since IPOs are still happening, albeit at a trickle. Formela, too, differentiates this from previous downturns when “there really was no [IPO] market at all.” Others are less sanguine. “Anyone who thinks they can raise a crossover round and then IPO in 2022 is delusional,” said Antoine Papiernik, managing partner at Sofinnova Partners.

Eventually, difficult IPO conditions, longer gaps between fundraisings and shallower (or no)

step-ups between rounds could hit venture capital fund performance, making it harder to raise new money to put to work. Such a scenario would require a 2-5 year downturn, though, reflects one banker-turned-biotech CEO. It is unlikely that the biotech sector will be punished for that long, having helped us out of the century's biggest health crisis (although there are also important macro-economic dynamics at play).

That gloomy hypothesis also fails to consider a much broader, deeper biotech investor base. "Capital markets look very different to 10 or even five years ago," said Atlas Venture's Formela. Granted, a few of the newcomer investors – including a retail component – may have contributed to the pandemic-linked exuberance. But many, such as pension funds, family offices and foundations, are long term players in health care and are likely to stay the course. In February 2022, for instance, SoftBank's Vision Fund 2 and RA Capital co-led a \$140m series C in Ventus Therapeutics, whose technology uncovers corners of proteins that might be druggable with small molecules. (In last year's markets, that C round might have been a crossover or IPO, even though the company's programs are still in discovery.)

Good News – More Discipline?

All in all, the feeling among the investment community is concern rather than panic. There is even relief in some corners. Undiscerning public markets create a flood of listings by low-quality or part-baked companies whose subsequent struggles may knock investor confidence across the board. On the private side, competition for deals grew as investors struggled to deploy capital fast enough from their ever-larger funds. That meant "they weren't always asking 'What will I do with the money? How will I create value?'" to get to the next step, said INKEF's Bulhuis. The challenge, he continued, was putting meaningful seed and A rounds to work, without creating crazy post-money valuations that would come back to haunt early investors in less exuberant markets.

A more sober listing environment means only those companies that are sufficiently mature, with a validated program or technology and a plan will be able to raise money – and that's no bad thing. It provides a more realistic valuation metric for earlier-stage companies and may also bring back more disciplined spending and capital allocation – a skill that endless cheap capital has eroded, and which some newer management teams may have little experience of. As long as the IPO window remains mostly shut, "investors will be looking closely at the size of funding rounds to ensure that companies have 18-24 months of cash, and a clear plan" to generate data required to build value, says one industry watcher.

Some biotech CEOs – perhaps wishfully – are hoping this is already the bottom of the cycle. "I and many of my colleagues are quite bullish about the [public markets in biotech] after a couple of turbulent years," said Daphne Zohar, CEO of London- and Nasdaq-listed [PureTech Health plc](#), whose pipeline includes four clinical-stage immune-modulatory drugs.

Dealmakers To The Rescue

Zohar and several investors point to M&A as the potential catalyst for a turnaround. Frothy valuations meant big M&A deals were virtually absent in 2021; overall M&A value was among the lowest on record, according to EY. Already, “we see increased M&A interest in our portfolio,” reported Novo Seeds’ Møller.

Several of the biggest deals that did occur in 2021 were in the R&D services sector, as industry seeks efficiencies from an expanding box of digital and biology-based tools. Thermo Fisher Scientific acquired Pharmaceutical Product Development (PPD) for \$17.4bn; ICON paid \$12bn for PRS Health Sciences. EQT’s \$8.5bn acquisition of contract research organisation Parexel was the largest ever private equity buyout of a pharma-related company, according to Pitchbook. EQT went on to buy Amsterdam-based venture firm Life Science Partners, illustrating PE’s growing interest in all corners of biopharma and life sciences, including early-stage investment. (EQT is now also in the running to buy [Novartis AG](#)’s generics unit, [Sandoz Inc.](#), according to the *Financial Times*.)

Most observers agree that dealmaking is likely to pick up in 2022. How much of that is M&A, versus the (often rich) licensing deals that were popular last year, remains to be seen. Several big pharmas need clinical stage assets to help plug multi-billion dollar holes left by patent expiries. A hawkish FTC is still a risk for those chasing larger deals: over a third of all US deals investigated in 2021, across all sectors, resulted in a complaint or abandonment – the highest share in 10 years, according to law firm Dechert.

Biotechs are already gearing up for deals as financing conditions tighten. When capital was cheap, they wanted to hang onto their assets. Now the balance of power between buyer and seller will be restored, suggested Medicxi co-founder and partner Francesco de Rubertis on a recent panel, adding that good quality companies should still get attractive deal-terms.

Some biotechs that missed the IPO gravy train have already turned to transactions. French neuromuscular rare disease-focused [Dynacure SAS](#) withdrew a planned \$100m IPO in July 2021, and in November signed a licensing deal with Nippon Shinyagu for its Phase I/II anti-sense oligonucleotide candidate, in exchange for \$5m upfront and up to \$82m in milestones.

Vigorous M&A cannot entirely replace a buoyant public market – there are too few buyers. But some exciting deals “could re-inject confidence,” said de Rubertis.

For now, the positives outweigh the negatives: biotech has more mature companies, more capital, more experienced management and a wider range of richer investors than ever before. “Quality companies will continue to get funded, even early-stage pre-clinical firms, if the science is differentiated and validated,” said Centessa’s Saha. Fundraising will be tougher than a year ago, but smart investors will take advantage of lower valuations. “I don’t think it’s going to be

terrible,” predicted OrbiMed’s Gordon.

Another investor said it would take a “real [macroeconomic] crisis” hitting public markets to turn the tables and damage early-stage investment in biotech. The world knows, perhaps now more than ever, that dismissing unexpected crises is unwise.