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Deals In 2023: Partnerships And Modest M&A

by **Melanie Senior**

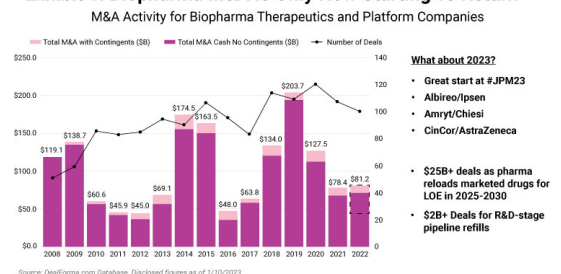
Mid-sized M&A, collaborations, creative financing, and biotech consolidation will feature in 2023. IPOs and follow-ons play bit-parts.

Dealmaking will continue to pick up in 2023, but don't expect mega-mergers. That's the message from many industry-watchers, chastened by a largely forgettable 2022 that failed to deliver the expected dealmaking frenzy as biotech valuations plunged. A more aggressive Federal Trade Commission (FTC), a still-fragile macro-economic environment, plus the uncertain specter of US drug price controls mean buyers are hesitant.

In 2022, total biopharma M&A reached about \$80bn – nearly a third of which came from [Amgen, Inc.](#)'s proposed \$27.8bn [Horizon Therapeutics plc](#) deal in December, according to DealForma. Had it not been for that, 2022 would have been the slowest M&A year since 2016.

What to expect for the remainder of 2023? The cautious view: more of what we've already seen so far. That's to say, mid-sized, bolt-on deals and partnerships as pharma selectively plugs pipeline gaps, but perhaps not (yet) the \$50bn-plus mergers required to address one of the steepest patent cliffs in the sector's history.

Exhibit 1: Biopharma M&A Is Only Now Starting To Return



Multi-billion-dollar drugs like [AbbVie Inc.](#)'s Humira, [Merck & Co., Inc.](#)'s Keytruda and [Bristol Myers Squibb Company](#)'s Opvirdo lose exclusivity this decade. But "there's still a couple of years before the cliff; a lot can change before they [pharma] have to pull the trigger," says Stephanie Léouzon, partner and head of Europe at investment

bank Torrey, noting the long-term disruption that mega-mergers entail.

In the deals that do occur, risk will be shared, through contingent value rights (CVRs) and other hedging structures, to bridge still-divergent valuation expectations. With few IPOs and follow-on public fundings expected during at least the first half of 2023, biotechs are becoming more willing product licensors, collaborators – and even sellers. They will need strong data to get the terms they want. Up-front cash and near-term milestones take priority over downstream value: a bigger share of tomorrow's pie is worthless if you go bankrupt today. There will be more consolidation among earlier-stage companies seeking to stay afloat.

Expect plenty of alternative financing set-ups – from royalty deals to venture debt, tranching investments and clinical co-development deals. Specialist venture capitalists will protect their own and demand more disciplined capital deployment. They'll also put new money to work (plenty have fresh funds). Indeed, monied private investors are among the most bullish, pointing out that post-crisis is the best time to invest. "It's the [mid- and late-stage asset] sale of the century," says Allan Marchington, managing director and head of life sciences at Intermediate Capital Group.

ICG co-led one of the biggest series Cs of the year so far, \$138m raised by France's rare diseases-focused [Amolyt Pharma](#). Yet these same investors remain highly discriminate. It's still a 'show-me' situation, cautions Marianne de Backer, CBO and global head of strategy, BD&L and Open Innovation, [Bayer AG](#). (De Backer, speaking on an Endpoints-hosted panel at JP Morgan in January, is set to take over as CEO of [Vir Biotechnology, Inc.](#) from April 2023.) Biotechs (and their backers) will be triaged into winners and losers. "Great companies will do fine," insists a US-based VC.

2023's dealmakers must also navigate a tougher commercial environment. If concerns around prolonged high inflation, a scaled-up Russia-Ukraine conflict and recession weren't enough, there's a new worry: the US Inflation Reduction Act. From 2026, it introduces price controls on top-selling US Medicare drugs. PS146868 The full implications of this wide-ranging law are unclear. But it has "ramifications throughout" dealmaking, pipeline modelling, and pricing decisions, warned Roel van den Akker, Pharmaceutical and Life Sciences deals leader at PwC in the US, at the JP Morgan conference. As private payers also push back more aggressively against high-priced drugs, Big Pharma may be re-thinking when, and on what, they spend their cash.

These headwinds are also catalyzing deals to boost R&D efficiency. Using AI to accelerate discovery, streamlining development with decentralized trials or digitalizing operations can help cut costs as future profits – and product lifespans – are curbed. (See Box: Accelerating R&D with AI)

Small M&A In A Buyers' Market

The year's first M&A deals were small, with buyer-friendly price tags, risk-mitigating CVRs, and a strong product focus.

Private [*Chiesi Farmaceutici S.p.A.*](#) bought rare disease-focused [*Amryt Pharma*](#) for \$1.25bn up front; [*Ipsen SA*](#) acquired niche liver disease company [*Albireo Pharma Inc.*](#) for \$925m and [*AstraZeneca PLC*](#) paid \$1.3bn up front for [*CinCor Pharma, Inc.*](#) and its Phase II hypertension lead. The first two included marketed orphan drugs – a risk-mitigated profile that mirrors some of 2022's biggest M&A transactions: Amgen's deals for Horizon and [*ChemoCentryx, Inc.*](#) (\$3.7bn), and [*Pfizer Inc.*](#)'s \$5.4bn [*Global Blood Therapeutics, Inc.*](#) purchase.

January's buyers capitalized on their targets' low 2H 2022 share prices and tied up to a quarter of the deal value to future milestones. Albireo shareholders received \$42/share -- double the recent share price, but only a tiny premium above 2022's peak - plus a further \$10 per share if rare liver disease drug Bylvy (odevixibat) achieves a second indication, biliary atresia. It was a similar story for Amryt.

CinCor shareholders won \$26 per share, 60% more than the company's January 2022 IPO price, and a promise of an additional \$10 per share if baxdrostat, an aldosterone synthase inhibitor that may lower blood pressure in treatment-resistant hypertension, achieves a regulatory submission. But they would have been better off selling earlier, according to an SEC filing. AstraZeneca was offering \$60-per share plus a \$6 CVR back in September, yet CinCor's team wanted more cash up front. Then baxdrostat flunked a trial and CinCor's value plummeted. Buyers can afford to wait (unless it's competitive).

[*Sun Pharmaceutical Industries Ltd.*](#)'s \$576m acquisition of [*Concert Pharmaceuticals, Inc.*](#) on January 19 also fit the buyer-market mold. It came complete with CVR, an almost-approved drug, and rescues Concert from a tight cash corner – even if the price, \$8/share, is barely over half the company's IPO price almost a decade prior. Deuruxolitinib is an oral JAK1/2 inhibitor for autoimmune dermatological disease alopecia areata, which causes baldness. An FDA submission is planned for the first half of 2023.

The biggest of these early 2023 deals won't hit \$2bn, even if the CVRs pay out. But they put 2023 on course to at least outshine 2022. That year there were only 14 deals worth over \$1bn, according to BioMedTracker. In 2021, the number was double that.

Partnerships Preferred

Biotechs don't want to sell at depressed prices, yet they need to eke out cash until the IPO and equity markets thaw. Hence the resurgence in partnering interest.

"We're getting three times as many inbound calls," reports Bayer's de Backer. It's a win-win:

Accelerating R&D With AI

biotechs get cash up front, and pharma have historically enjoyed significantly better returns from alliances than from M&A, according to analysis by EY.

Perhaps that's why median up-front licensing deal values in 2022, at \$30m, represented a ten-year high matched only by 2020, according to DealForma's Dokomajilar, speaking on a webinar sponsored by partnering platform provider Inova. This year so far, BioMedTracker reports 21 alliances worth more than \$10m in up-front cash, in line with the same period in 2022, see Table 1 below. Up fronts are expected to remain strong. Yet licensees are having to relinquish more downstream value to secure them.

Take [HUTCHMED \(China\) Limited](#): like many ambitious biotechs, it envisioned retaining a greater share of the fruits of its pipeline. The company has three marketed products in China. But tough conditions there and in the wider market – plus an FDA rebuff of neuroendocrine tumor treatment surufatinib in May – forced a 'strategic shift' in November 2022 to focus on advancing later-stage assets and to partnering outside of China.

With its share price languishing, HutchMed in January accepted \$400m up-front from [Takeda Pharmaceutical Co. Ltd.](#) in exchange for global development and commercialization rights ex-China, Macao and Hong Kong to colorectal cancer treatment fruquintinib, an oral VEGFR-1, 2, 3 inhibitor for previously-treated metastatic CRC patients. A rolling

Technology – including AI – may help save development dollars as drug prices are capped and monopolies shortened. Big-league newcomer [BioNTech SE](#) made an early investment into efficiency with its £362m (\$437m) purchase of UK-based AI and ML partner [InstaDeep Ltd.](#)

lush with Covid-19 vaccine cash, BioNtech hopes that buying its partner outright will digitalize and turbo-boost its entire business, not just accelerate new drug design and development. The vision is to become “a technology company where AI is seamlessly integrated into all aspects of our work” said CEO and co-founder Professor Ugur Sahin.

AI-biopharma transactions have risen sharply over the last decade, notes DealForma founder and CEO Chris Dokomajilar, though partnerships are more popular than acquisitions. High-profile advances such as OpenAI's chatbot Chat GPT or DeepMind's AlphaFold technology for predicting 3D protein structures mean more deals will likely follow.

AI's ability to come up with next differentiated drug may have been a little over-hyped, but it offers plenty more potential in trial design, planning, recruitment, and implementation. “We need to be even better” at applying AI across clinical development, said Najat Khan, Chief Data Science Officer and Global Head, Strategy & Operations, R&D at [Johnson & Johnson](#) during an Endpoints-moderated JPM

submission began in the US in December, where fruquintinib has Fast Track designation, and submissions in Europe and Japan are planned for 2023. The deal – which includes up to \$730m in potential milestones plus sales royalties - helps HutchMed fund the re-focused pipeline and buy time for shares to recover.

panel.

Takeda-Hutchmed is the biggest licensing deal so far this year, in up-front cash. But it pales in comparison to the \$4bn upfront (and a further \$2bn in milestones) that Takeda forked out for Nimbus' Phase 2b TYK2 inhibiting plaque psoriasis drug in December 2022. That was among the biggest single-asset deals of the last 15 years according to DealForma.

[*Neurocrine Biosciences, Inc.*](#)'s \$136m up-front cash (plus \$39m up front equity) for worldwide rights to a handful of [*Voyager Therapeutics, Inc.*](#)' CNS gene therapies is 2023's richest earlier-stage licensing deal so far: Voyager's most advanced program, for Parkinson's, is pre-clinical. It's a second-chance story. In 2021, Neurocrine pulled out of a prior Parkinson's project following a US clinical hold due to safety concerns. That program, which was in Phase II, cost Neurocrine \$165m up front in one of 2019's biggest deals.

This time, Neurocrine also gets rights to three other programs in rare CNS disorders. All three, plus the glucosylceramidase beta-1 (GBA-1) encoding therapy for Parkinson's, use Voyager's novel capsids (viral vectors) to carry the genetic material into cells. Voyager's capsids are good at penetrating the blood-brain-barrier; in October 2022 Pfizer exercised its option to license the technology for a CNS gene therapy program of its own.

Voyager, which has had setbacks, may not be able to co-fund development costs today. By the time the GBA-1 program completes Phase I, things might look different. So, it secured an option to share costs and profits with Neurocrine at that stage. If not, up to \$985m develop and milestone payments, plus commercial milestones and tiered royalties up to 20% on net US sales could come its way.

Other January deals reflect early bets by Big Pharma across a range of modalities. [*Roche Holding AG's Genentech, Inc.*](#) signed two small-molecule focused alliances, one with chemo-proteomics start-up [*Belharra Therapeutics Inc.*](#) (worth \$80m up front and up to \$2bn in bio-bucks) and another with oncogenic transcription factor-focused [*Kronos Bio, Inc.*](#) (\$20m; up to \$554m). AbbVie paid \$42m up front to use [*Anima Biotech Inc.*](#)'s mRNA biology modulators against oncology and immunology targets, and [*Eli Lilly and Company's TRexBio*](#) partnership will study regulatory T-cells to find new drug targets in immune-mediated diseases.

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Ruthless Meritocracy

On the financing front, 2023 is going to be a ruthless meritocracy: the best companies will survive – even thrive. The rest will perish or be forced to concede. Follow-on public money is available for those with good data: [Pliant Therapeutics, Inc.](#) raised \$287.5m in an outsized stock offering on January 24 at \$30 per share (almost double its June 2020 IPO price) thanks to positive Phase IIa efficacy data for idiopathic pulmonary fibrosis candidate bexotegrast, a dual integrin inhibitor. The company did the same in 2022, on the back of an earlier read-out from lower-dose cohorts in the same trial. That time it got \$230m at \$18.50/share.

Companies with compelling assets can also access alternative, non-dilutive sources of capital. Royalty financing provides up-front cash to biotechs in exchange for a share of future (or current) royalty streams. “We’ve seen a surge in opportunities since the fourth quarter of last year,” says Clarke Futch, CEO of [HealthCare Royalty Partners](#). “Companies may be looking to launch, or about to get approved, but they don’t like their share prices.”

Depressed shares make a sale unattractive, and equity financing too dilutive. Several quarters into the market downturn, management and boards have accepted that things aren’t going to change soon. [Atara Biotherapeutics, Inc.](#) in December 2022 secured \$31m from HealthCare Royalty as lead allogeneic T-cell therapy tabellecleucel (Ebvallo) launches in Europe, in exchange for a portion of the royalties and milestone payments due from European commercialization partner Pierre Fabre. Atara’s royalty share was already thinner: in September 2022, prior to the drug’s EU approval, the company tapped [Pierre Fabre](#) for an extra \$30m approval milestone. Ebvallo treats organ or bone-marrow transplant patients suffering from refractory Epstein-Barr virus-positive lymphoproliferative disease.

Venture debt – loans to VC-backed companies – is another option. Like royalty financing, venture debt has grown over the last decade from niche to mainstream. Loans to venture-backed firms across all US sectors have doubled to over \$30bn in the last five years, according to [Pitchbook-NVCA’s latest report](#). Health care’s share dropped last year but included deals like Horizon Technology Finance Corporation’s \$45m loan to inflammatory diseases-focused Evelo Biosciences [in December](#). Evelo pays interest only for three years, buying time while it generates three Phase II readouts during 2023. The Horizon loan replaces an existing debt facility that would have become payable in March 2023.

Biotechs can also opt to shift the cost, management - and risk - of clinical programs onto a specialist co-development partner. In January 2023, clinical co-development company Launch Therapeutics, set up the prior year by VC firm Abingworth and its owner Carlyle, announced a collaboration with [Pathalys Pharma, Inc.](#) to advance secondary hyperparathyroidism drug

candidate upacalcet through Phase III, registration and pre-commercialization. Pathalys gets a \$150m financing and equity package and Launch takes operational responsibility for the trials. Pathalys retains rights to the drug outside Japan and Asia, while Launch and its backers share in the drug's success – if it works. (Also see "[Bigger Money: Private Equity Grabs European VC](#)" - In Vivo, 21 Jun, 2022.)

Those providing the cash can command increasingly favorable terms. They also take on risk – including growing commercial risk. “Ten years ago, you could assume a 5% annual price increase in your model. That’s not the case anymore,” says HealthCare Royalty’s Futch. Only those with the most differentiated assets will access funds – whatever the source. “Last year we looked at 119 potential deals and signed seven,” cautions Futch.

Biotechs Join Forces To Stay Alive

Smaller companies are consolidating in their bid to find funds. Listed [Leap Therapeutics, Inc.](#) added cash and pipeline by merging with private [Flame Biosciences, Inc.](#), collecting the struggling group's clinical and pre-clinical antibodies plus \$50m net cash. Precision oncology firm [Enliven Therapeutics, Inc.](#) reverse-merged with listed [Imara Inc.](#), which had run out of road. Thanks to a concurrent \$165m private financing, newly-public Enliven has \$300m – enough until early 2026. Private biotech mergers can also trigger fresh funding: when cell therapy company [Ensoma](#) bought gene-editing minnow [Twelve Bio ApS](#) in January, Twelve's founding investor [Arix Bioscience Plc](#) co-led an \$85m financing round in the enlarged group.

If M&A and public markets stay dry, there will be more consolidation – not all of it validated by additional cash. Cancer vaccine firm [Elicio Therapeutics](#) took over listed [Angion Biomedica Corp.](#) after a failed IPO attempt last year and needed a \$10m bridge loan from its merger partner, whose programs were shuttered in mid-2022.

What Next?

There are whispers of a recovery in public biotech. Indices have been moving in the right direction - though it's hard to imagine things getting much worse. [Structure Therapeutics, Inc.](#) in early February pulled off that rare thing: an upsized, top-of-range IPO, worth about \$161m, followed by a share price rally. One good IPO doesn't make a trend. But there's appetite – and money - for the next innovation wave (apparently including Structure's oral GLP-1-targeting Phase 1b metabolic disease program), and some welcome a more disciplined, discriminate environment. “It may not be a blow-out M&A year, but there are lots of good data points coming, which means opportunities and partnerships,” sums up Torreya's Léouzon.

As for those big M&A deals: don't rule them out completely. “Pharma has significant capital. They may say they won't do M&A, but it's coming,” says ICG's Marchington.