JP Morgan **Conference 2023**

BY AMY BROWN AND JACOB PLIETH | JANUARY 2023

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Introduction

JP Morgan Healthcare Conference 2023 was the first in-person iteration of the event since 2020. After a rather lacklustre 2022 conference, did this year's event start the new year with a bang?

Well, no, not really. Day one saw a couple of interesting bolt-ons, all of which had their roots in Europe, but nothing major. More biotechs are coming to terms with reset valuations and the types of deals announced, all of which involved risk sharing, set the scene for the rest of the year. It is officially a buyers' market.

Still, a quiet start for M&A does not necessarily mean the remainder of the year will be slow. As small developers run out of cash, and larger groups get closer to patent cliffs, minds will focus. Deal making is the lifeblood of the industry and while it may not be pumping at full speed right now, it is not quite ready for a stent.

Aside from anaemic deal news flow, the conference was notable for incremental updates, with efforts to bury bad news from a couple of big names. In a not-at-all-scientific Twitter poll we ran, over 54% of the 700 respondents said "yes" to the question "Is this the worst JP Morgan ever". Ouch.

In this round-up, we sift through the key pieces of news and consider what it might mean for 2023 and beyond.

Don't get too excited...but don't be too despondent either.

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Day one sees buyers make the most of straitened times

BY AMY BROWN
JANUARY 09, 2023

Takeouts of Cincor, Albireo and Amryt emerge with contingent payment terms, as biopharma buyers flex their muscles.

Three billion-dollar bolt-on buyouts emerged on the first day of the JP Morgan healthcare conference, delivering more of a bang than last year's relatively quiet opener. But the terms involved should leave no one in doubt that this is now a buyers' market.

All involved contingent payments, a risk-mitigation strategy that is likely to become more common if poor market conditions persist. True, the target companies – Cincor, Albireo and Amryt – managed to extract ostensibly healthy premiums, but all three transactions come in the wake of poor share price performances.

In Albireo and Amryt's cases, investors are being asked to accept very little premium compared to where these two groups have traded in the past couple of years. And, while those who participated in Cincor's January 2022 IPO are getting a decent enough premium, shareholders who backed the group's secondary fundraising in August will be sitting on a loss.

With markets showing few signs of picking up, more developers will be faced with difficult choices in the coming months. Accept a risk-sharing structure, or grapple with potentially months more of share price stagnation? Acquirers' power will only grow if there is just one serious bidder at the table, which is possibly what happened in these three situations.

Perhaps investors should be encouraged to see that

deals are getting done. As well as the $3bn pledged in buyouts, the first day of JP Morgan also saw several licensing transactions emerging.

Another thread here is that all buyers are European – over to US biopharma to keep the M&A ball rolling in 2023.

ASTRAZENECA AND CINCOR

Astrazeneca's opportunistic move on Cincor looks likely to succeed – the UK pharma giant has offered to buy the mid-stage, single-asset company for an initial $1.3bn. The $26 per share price is 121% above Cincor's share price on Friday, but only 63% above the level at which the company floated almost exactly one year ago. Those who backed a $30 per share equity raise in August will be even more disappointed.

A further $500m is payable on submission "of a baxdrostat product" to the FDA or EMA as part of a $10 per share CVR (contingent value right).

In the wake of disappointing phase 2 data last year some might consider this a good outcome. Cincor is developing baxdrostat for treatment-resistant hypertension, but the failure of the Halo trial raised the risks for this project as it approaches pivotal development.

Baxdrostat had looked encouraging in a previous trial, and there is certainly a need for new options to bring down stubbornly high blood pressure. Astrazeneca now joins Johnson & Johnson as one of two big pharma names in resistant hypertension – the latter is partnered with Idorsia.

IPSEN AND ALBIREO

Baxdrostat was originated by Roche, and the second deal today, Ipsen's $952m buyout of Albireo, also concerns a big pharma cast-off. This buyout was struck mostly for Bylvay, an IBAT inhibitor that was spun out of Astrazeneca back in 2008, when Albireo was set up. The drug is being developed in various rare liver conditions and has been on the market since 2021.

Jitters around Bylvay's launch hit Albireo's stock last May, and it never really recovered. Ipsen's $42 per share offer represents a 104% premium to Albireo's one-month prior average share price; the biotech's stock touched a high of $37 last year, ahead of the correction.

As such, Albireo investors might be disappointed with the terms, particularly since the potential vesting of the $10 per share CVR could be a long way away. The payout hinges on FDA approval of Bylvay in biliary atresia by the end of 2027; the phase 3 Bold study recently completed enrolment in this setting. Data readout was targeted for the end of 2024, but today's statement implies that the trial might need upsizing.

Ipsen has been on something of a buying spree recently, snapping up Epizyme last June and buying rights to Genfit's Nash project elafibranor in late 2021.

CHIESI AND AMRYT

Finally, Amryt also found the approaches of a larger developer too tempting to ignore: the private Italian firm Chiesi has offered $1.3bn up front for the rare disease player. A further $225m is on the table, contingent on FDA approval of the epidermolysis bullosa (EB) product Filsuvez before the end of 2024 (worth $1.0 per ADS), and the receipt of a priority review voucher (worth a further $1.50 per ADS).

The $14.50 per ADS initial payment represents a 107% premium to Amryt's ADS price on Friday, and is almost bang on the stock's all-time high, touched in early 2021. The Ireland-listed group has seen its valuation drift since then, in line with the wider market but also owing to commercial and regulatory struggles with Filsuvez.

Payers baulked in Europe, where the EB product was approved in mid-2022, while the FDA has refused to grant a green light, a decision that Amryt has challenged. This now becomes Chiesi's problem, as does pushing the products that Amryt took over from Aegerion after that group collapsed into bankruptcy.

Licensing deal flurry offers limited cash up front

BY JACOB PLIETH
JANUARY 09, 2023

As well as three bolt-on deals with a European flavour day one of the JP Morgan healthcare conference today saw a flurry of smaller business development activities. However, none was enough to set the pulses racing: the biggest, a gene therapy-focused tie-up between Voyager and Neurocrine, was worth $175m in immediate cash, with $39m of this in equity, so it was hardly the sort of transaction deal bankers are desperate for as biotech enters an uncertain 2023. Lilly, Roche and Bayer signed discovery deals with Trexbio, Kronos and Recode respectively, worth a combined $75m in disclosed up-fronts. Meanwhile, Coherus picked up Klinge's biosimilar version of Eylea, and Autolus licensed its Car-T switch to Cabaletta, mirroring an earlier non-exclusive licence with Bristol Myers Squibb. Elsewhere two companies buried bad news as Calithera moved to liquidate in the wake of telaglenastat's failure, and Editas's chief medical officer stepped down as the company discontinued work on NK cells at a precarious time for this field. The fact deals are happening is positive, of course, but signs from 2023's first major investor conference are that buyers are increasingly able to dictate terms.

Selected licensing transactions on day one of JP Morgan

Deal source	Partner	Up-front	Deal summary
Voyager	Neurocrine	$136m*	Rights to Voyager's GBA1 gene therapy for Parkinson's disease & 3 gene therapies for rare CNS targets (follows previous deal over VY-AADC)
Trexbio	Lilly	$55m	Discovery of Treg-based therapeutics for immune-mediated diseases
Klinge	Coherus	€30m**	US rights to Klinge's FYB203, a biosimilar version of Eylea
Kronos	Roche	$20m	Use of Kronos's drug discovery tech against transcription factors selected by Roche
Autolus	Cabaletta	ND	Rights to Autolus's RQR8 safety switch for use in autoimmune disease project
Recode	Askbio (Bayer)	ND	Discovery deal combining Askbio's synthetic DNA & gene-editing nucleases with Recode's LNP tech

Notes: *plus $39m equity investment; **$32m; ND=not disclosed. Source: company releases.

Sutro makes its pitch to beat Immunogen

BY JACOB PLIETH
JANUARY 10, 2023

The group reckons it can target twice as many ovarian cancer patients, but an important disclosure shows that its case it not clear-cut.

Since Immunogen's Elahere got US accelerated approval for ovarian cancer last November Sutro has worked hard to make the case for its less advanced me-too project STRO-002. Yesterday Sutro upped the ante, but also revealed that its claim to superiority was not clear-cut.

Sutro's pitch is that twice as many patients will qualify for STRO-002 than are covered by Elahere's label. The company had earlier shown broad data ranges to support activity across folate receptor alpha (FRα) expression levels, and yesterday it split out the numbers. This confirmed that STRO-002's efficacy was driven by an effect in patients expressing the highest amounts of FRα.

This is important because if Elahere and STRO-002 are restricted to the same patient population Sutro's sole argument will be that its asset is safer. Elahere carries a boxed warning about eye toxicity, an adverse event STRO-002 has not really seen, and which at last November's Jefferies London healthcare conference Sutro put down to Elahere's poorly designed linker causing prolonged exposure to the toxic payload.

However, for its part STRO-002 has been associated with a 70% rate of serious neutropenia, including one death. This update came from the latest phase 1 data cut presented yesterday at an analyst event ahead of Sutro's presentation at the JP Morgan healthcare

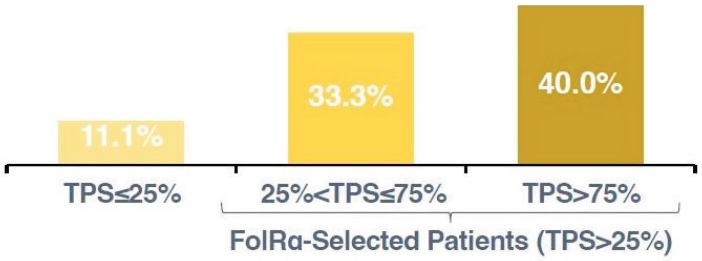
conference on Thursday; Immunogen's own JP Morgan pitch is scheduled for today.

HOW BROAD?

While Elahere is approved for FRα-high patients, representing 35-40% of the ovarian cancer population, Sutro has argued that STRO-002 has shown strong activity in >25% FRα expressers, accounting for 70-80% of patients.

The latest phase 1 dataset for STRO-002, which Sutro now calls luveltamab tazevibulin (luvelta), comprises 41 ovarian cancer subjects, and Sutro cited a 38% remission rate in >25% FRα expressers. But the group also split out those with the highest expression, >75%, who had a 40% remission rate.

Excluding this most efficacious subgroup, activity falls to 33%, yesterday's event revealed.
Luvelta efficacy by FRα expression. Source: Sutro presentation.



RECIST-Evaluable Patients	N=9	N=12	N=20
PR	1	4	8
ORR (95%, CI), %	11.1 (0.3, 48.3)	33.3 (10.0, 65.1)	40.0 (19.1, 63.9)

Luvelta efficacy by FRα expression.

Source: Sutro presentation.

That said, this might not be disastrous. Elahere's label cites 32% ORR, so on a cross-trial basis Sutro still wins out, though Elahere has a better median duration of response, at 6.9 months versus luvelta's 5.6 months.

There are further nuances; for instance Sutro uses tumour proportion scoring to grade FRα expression, while Immunogen cites results of Ventana's FOLR1 RxDx Assay to identify tumour cells with 2+ intensity.

ACCELERATED APPROVAL

Yesterday Sutro unveiled plans in the second quarter to launch a phase 2/3 study, Reframe, that would back an accelerated approval based on an interim read of luvelta's remission rates and safety. This same trial would later yield a final analysis of progression-free survival, against chemotherapy, and thus serve to confirm luvela's formal approval.

But Sutro's problem is that Immunogen will soon report data from Elahere's confirmatory Mirasol study, which could see the Immunogen drug gain full approval; once this happens the path for an accelerated nod for luvelta would close.

And then there is the question of recruiting patients into Reframe, a study that will not permit Elahere. How many patients, many of whom would be eligible for the Immunogen drug, will risk entering a trial where they might receive nothing better than chemo?

Recruiting quickly into Reframe will be key as the FDA cracks down on accelerated approvals. "We understand the FDA's position that a confirmatory trial needs to be substantially enrolled at the time of" an accelerated approval, Sutro said yesterday.

Battle of the anti-FRα ADCs				
	Elahere (mirvetuximab soravtansine; Immunogen)	Luveltamab tazevibulin (STRO-002, Sutro)		
Study	Soraya	STRO-001-GM1		
Population	FRα-high*	>25% FRα**	25-75% FRα**	>75% FRα**
ORR	33/104 (32%)	12/32 (38%)	4/12 (33%)	8/20 (40%)
Median DoR	6.9mth	5.5mth	5.6mth	5.5mth
Safety	61% rate of eye disorders, including 9% at grade 3+	31/44 (70%) grade 3+ neutropenia, incl 1 death		

Notes: *defined as 75% tumour cells with 2+ intensity, measured by Ventana FOLR1 RxDx Assay; **measured by tumour proportion score.

Source: prescribing info & Sutro presentation.

Novartis and Gilead's interim halt hopes wane

BY JACOB PLIETH
JANUARY 11, 2023

As 2023 got under way investors in Novartis and Gilead might have been looking for pleasant surprises from interim analyses of two key studies. Such hopes have been dashed, according to updates slipped out at the JP Morgan healthcare conference this week. Novartis's Kisqali is trying to break into adjuvant breast cancer, where Lilly's rival Verzenio is approved but where Pfizer's Ibrance failed in the Pallas trial. But Kisqali's Natalee study is now continuing to final readout in the second half of the year, having not been halted for efficacy at its two interim analyses, which came and went at 70% and 85% of disease progressions respectively. Meanwhile, the Enhance trial of Gilead's anti-CD47 MAb magrolimab in first-line high-risk myelodysplastic syndromes had an expected first interim analysis in the current quarter, but this too has passed without triggering a halt for efficacy. The CD47 mechanism has disappointed, and Enhance's focus now turns to a second interim analysis in the second half of the year.

Project	Kisqali	Magrolimab
Company	Novartis	Gilead (ex Forty Seven)
Trial	Natalee	Enhance
Setting	Adjuvant pre & postmenopausal ER+/Her2- breast cancer; (approved for 1st-line metastatic ER+/Her2- breast cancer)	1st-line, high-risk MDS; (also in pivotal trials for 1st-line TP53m AML (Enhance-2) & 1st-line unfit AML (Enhance-3), as well as other haem & solid cancers)
Interim analyses	1st at 70% of iDFS events (YE 2022, not halted) 2nd at 85% of iDFS events (H1 2023, not halted)	1st at unspecified threshold (H1 2023, not halted)
Status	Continues to final analysis (H2 2023), with iDFS as primary endpoint	Continues to 2nd interim analysis (H2 2023), with focus on OS (currently a co-primary endpoint along with CR rate); (NB had been on clinical hold in 2022)

Source: clinicaltrials.gov & JP Morgan presentations.

After this story was published Novartis clarified that the second interim analysis of Natalee had yet to take place.

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