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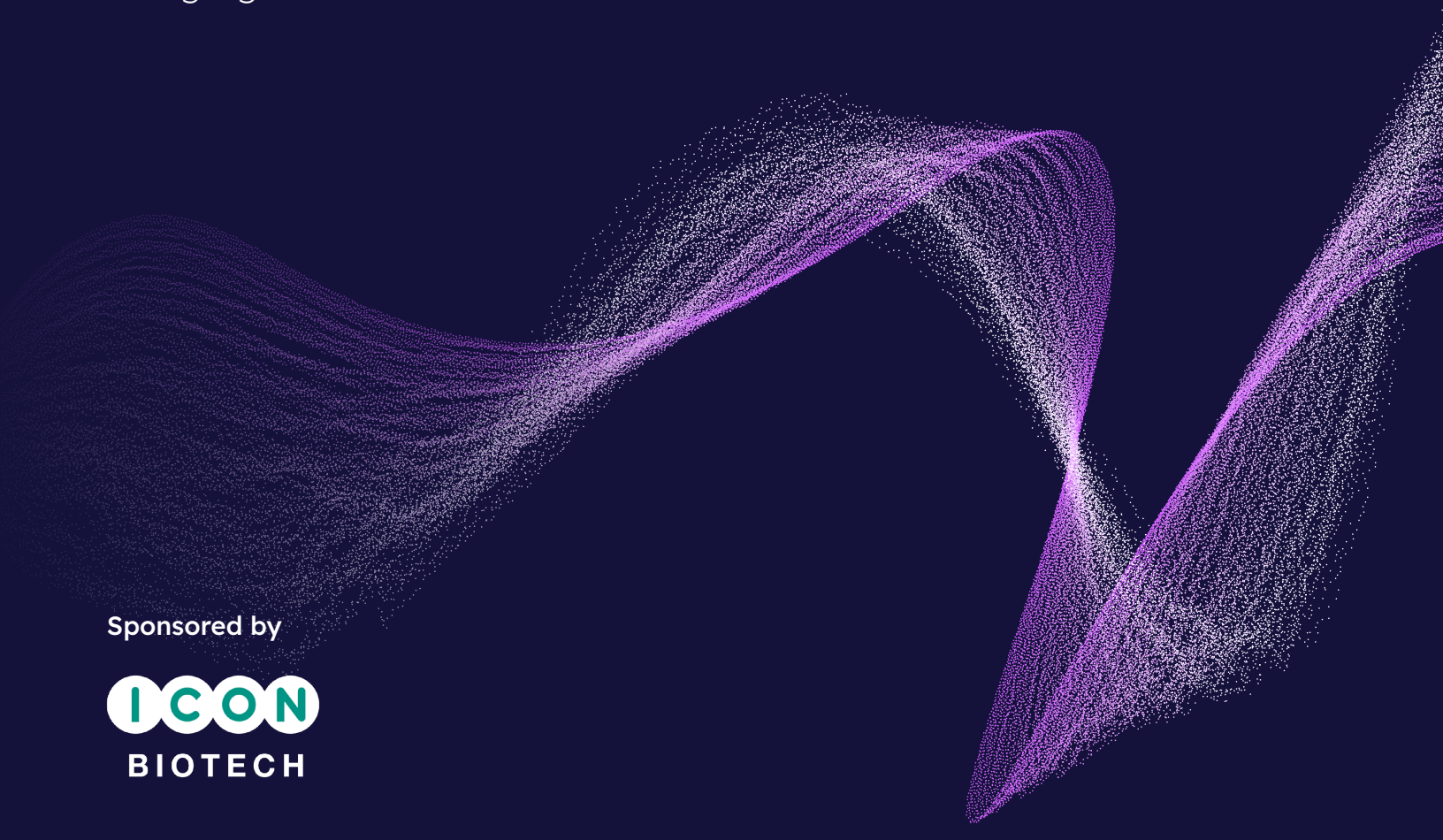

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Summary

The 42nd annual J.P. Morgan Healthcare Conference (JPM) was held in San Francisco, CA over 8–11 January 2024. This report collates the daily presentation highlights from the conference in a single destination. A complete list of events and catalysts that were announced or updated is included as a supplement to the report.

About the Author

Biomedtracker is an independent research service that offers proprietary clinical assessments and patient-based revenue forecasts of developmental drugs within a comprehensive and intuitive drug information database. Clients from the pharmaceutical, biotech, and investment industries rely on Biomedtracker for its insight on the likelihood of approval, commercial potential, and future data and regulatory catalysts for drugs within the competitive landscape of every important disease and indication. Over the last several years, Biomedtracker has become the leader in providing objective information alongside evidence-based clinical assessments and investment research on pipeline drugs worldwide. For more information on getting direct access to Biomedtracker, please email clientservices@citeline.com.

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Mega Cap

AbbVie

At the 42nd annual J.P. Morgan Healthcare conference, president and COO Rob Michael accompanied by the CCO Jeff Stewart and CMO Roopal Thakkar, started off their fireside chat with a victory lap, highlighting 2023 to be a strong year in growth across their five key therapeutic areas, including readouts from lead products Skyrizi and Rinvoq. Michael expects continued strong share gains for both Skyrizi and Rinvoq over 2024, attributing the anticipated momentum to be driven by fundamental commercial execution coupled with several key catalysts. The company's referral to fundamental commercial execution is pillared in light of the news this week that Skyrizi and Rinvoq secured the top two leading spots in pharmaceutical direct-to-consumer spending, with a collective over $700m spent on TV advertisement throughout 2023, testament to AbbVie's investment into their commercial execution. Key catalysts expected for the two powerhouse products include readouts from an unprecedented nine head-to-head trials across indications, alongside a fourth indication approval anticipated midway through 2024. AbbVie’s president specifically celebrated the drugs' dominance in the Crohn's disease market, with Skyrizi and Rinvoq capturing a third of patients in this market.

As AbbVie’s second largest therapeutic area, Michael also anticipates significant growth across its neuroscience platform. The approval of Vraylar in adjunctive major depressive disorder has stood as a strong growth driver for the company, and shares are expected to accelerate in the upcoming year. The oral CGRP receptor antagonist Qulipta has also seen promising growth, and the company plans to see expansion of this drug into international markets in 2024. The AbbVie panel championed a major year ahead for its neuroscience portfolio, expecting growth of over $1bn in 2024.

The panel then touched on the aesthetics market and the recovery which it saw in 2023. They detailed how the toxins market typically lags by a couple of quarters but is now recovering, with AbbVie's share position being stronger than before, with the company seeing share gains. This is mostly driven by the launches of new toxin products such as Volux and Skinvive. It was highlighted that the aesthetics market is seeing a trend to return to growth in 2024, and the company affirmed that toxins are following this trend, with two quarters of growth. In particular, the company cited confidence in its share performance, exemplified by its retention of share in the Botox market despite the launch of Daxxify.

As for the eye care market, AbbVie recognizes the longstanding stability of the market but anticipates a large transform to the pipeline with its Regenxbio partnership, believing the partnered gene therapy to be potentially highly transformative in wet AMD and diabetic retinopathy. The panel continued to underline the attractiveness of the market, stating the easy commercial access to top physicians.

The presenters also touched on two important deals under way for the company, and expressed that these were designed to provide growth in the next decade, reiterating AbbVie’s confidence

in its position and momentum in the current decade. They stressed AbbVie's plan for organizational focus on the closure of these deals, with attention channeled towards a smooth transition and integration of these new deals.

In concluding remarks, Michael and the team looked forward to another year of strong growth across all therapeutic areas, and stated their belief that their robust growth platform will help manage anticipated dilution from Humira biosimilar erosion. AbbVie enters 2024 in an optimistic position, with several key global catalysts anticipated.

Novartis

Novartis CEO Vas Narasimhan presented how Novartis has become a pureplay company in the last few years, focusing on only four therapeutic areas (oncology, immunology, neuroscience, and cardiovascular, renal, and metabolic) to achieve higher margins and maintain an attractive growth profile through maximizing shareholder value, with a 7% CAGR sales increase from 2018 to 2022. The company has upgraded its expected CAGR for 2022–27 from 4% to 5% based on the success seen with currently approved brands (with Entresto being the most successful with $5.9bn in reported sales) and the forecast success of various pipeline assets. It also executed over 15 successful strategic deals in 2023 alone, with the goal of enhancing its pipeline across core therapy areas and technology platforms.

Narasimhan began with a victory lap, highlighting the 10 positive Phase III readouts Novartis had in 2023, with examples including Kisqali in the adjuvant HR+/HER2- breast cancer setting, Pluvicto in the pre-chemotherapy metastatic castration-resistant prostate cancer (mCRPC) setting, and Fabhalta in paroxysmal nocturnal hemoglobinuria (PNH). The adjuvant HR+/HER2- setting is one which is relatively uncontested, with patients generally being treated with chemotherapies and endocrine therapies; it is also one of the largest patient populations across all three subtypes of breast cancer. While competitor Verzenio does have an approval for high-risk adjuvant patients, Kisqali has demonstrated efficacy in patients with both intermediate- and high-risk disease, a larger patient pool. A potential approval in 2024 for Kisqali will give Novartis access to a huge patient population, bringing with it the opportunity to generate billions of dollars in this setting alone.

As for Pluvicto, gaining an approval earlier in the mCRPC treatment algorithm can only be positive, but due to the high rates of crossover in the trial there was no OS benefit shown in the initial trial readout, although the crossover-adjusted OS is much more positive, with an HR of 0.80. Nonetheless, the FDA may want further data to validate the survival benefit, which could delay an approval and risks sullying physician opinion on Pluvicto in this setting.

At JPM 2024, Novartis announced its intention to strengthen its presence in rare diseases, and the positive readout for Fabhalta in PNH is a clear step toward this goal. Key endpoints that were met included improving quality of life for patients, improving hemoglobin levels, and reducing the need for blood transfusions, setting Novartis up for a new approval in the PNH space in 2024. Looking forward, Novartis is expecting to submit at least 15 key submissions to the FDA for approval between 2024 and 2027, with six of these expected in 2024, and three of these six submissions being in the cardiovascular, renal, and metabolic space.

Radioligand therapies in oncology, CAR-Ts in immunology, and siRNA in neuroscience and cardiovascular indications are three key technologies that Novartis believes may unlock significant mid-to-long-term growth across its four core therapy areas. The company is establishing itself as a leader in radioligand therapy technology after the success of Pluvicto, and positive readouts being reported from a second radioligand therapy, Lutathera. The future for Novartis is expected to remain focused on these novel technologies. Label expansions, expected for many of its current blockbuster brands, are forecast to generate further billions for Novartis as access to larger and newer patient populations is granted. Overall, Novartis's restructuring and streamlined focus is paying off, as seen with the strong CAGR seen in historical years and the upgraded CAGR forecast for the years ahead.

Novo Nordisk

Novo Nordisk is proud to celebrate its 100th year anniversary, with CEO Lars Fruergaard Jørgensen announcing the company's accelerated growth and momentum, particularly in its 25-year stint in the obesity space. The company's revenues grew over 50% in 2023, setting a comfortable platform entering 2024. The questions rounds started around the topic of demand outstretching supply in this space, particularly with the launch of Wegovy in the market. Jørgensen commented on the US having additional volume channels and looking to speed up manufacturing of the drug with significant additional capacities in 2024. Having a significant product scaling up in the market for the first time, Novo Nordik is currently treating 40 million patients globally, growing at roughly 4 million additional patients a year. First launched in the US, Wegovy has seen exponential demand from patients and practitioners. Although Europe saw a slightly different uptake case, there has still been increasing clinical evidence building value for treating obesity. This has been a turning point for the company, with obesity now being treated as a disease with severe health consequences. Jørgensen also drew attention to medical intervention playing an important role in the healthcare system which was previously designed for acute care and is now progressing into long-term treatment. The topic around payers, benefits, and cost was also highlighted, with obesity being a strain on cost due to an aging population which is increasingly obese. There was particular emphasis on developing a weight-centric approach in addressing this higher BMI morbidity population.

With Wegovy costing $16,188.24 annually, and the price remaining high on a net basis, Novo Nordisk did not see this as a problem as supply improves. Jørgensen consequently drew further attention to the value in treating patients in the US healthcare system first, who generally have a faster adoption to innovation. Although social media hype grew demand for the drug excessively, steady robust demand for Wegovy will continue, with a focus on clinics and physicians understanding the drug's mechanism of action. With unconstrained launches seen in the current market, Novo Nordisk is governing controlled future launches as already seen in Germany and the UK in 2023 with the idea of catering to patients with greater needs and making sure the vulnerable have access to treatment rather than an out-of-pocket opportunity. Though too early to indicate, Novo Nordisk believes that patients will have a higher stay time on the drug compared to previous drugs as there is a strong incentive for them to remain on treatment. Jørgensen also welcomed the healthy competition from Zepbound (Eli Lilly) and did not see this as a challenge, paying greater attention to the education on its value to the health system, with Novo Nordisk focusing on topline growth over competitors.

Gears were then switched into the diabetes space, where the market has seen a shift to addressing co-morbid cardiovascular (CV) diseases, with semaglutide so far proving to be the only molecule in market showing 20% CV risk reduction. Novo Nordisk was encouraged by the drug's added value and benefit brought to the disease area. Although the GLP-1s have been favored in the market with strong weight loss results, market penetration for semaglutide has been seen to be in the mid-teens in the US and low teens in the EU, with usage now also occurring in China. Jørgensen believed this will continue to move significantly higher in the near future, with the drug having opportunity to move into background treatment regimens.

Another topic particularly highlighted in the area was the underlying growth of patients with type 2 diabetes developing a secondary disease from obesity. Focusing on treating obesity here would be key in driving change to prevent future co-morbidity events taking place. Although the US currently shows a higher rate of obesity than the rest of the world, growth trends are expanding at the same rate, with the volume of opportunity increasing for treatment. Mounjaro is also set to relaunch, which will proceed to fuel market growth, providing choices of treatment in clinics for type 2 diabetes patients and physicians.

The presentation closed with Jørgensen drawing attention to the next generation of innovation, in particular CagriSema, which has been in the pipeline for almost 25 years, as well as Phase III results updates in 2024. Beyond the focus on its major therapeutic area of diabetes and obesity, the company has started investing and driving M&A into the CV and metabolic space as well as in rare diseases including hemophilia, most recently in sickle cell disease, to target long-term growth.

Large Cap

Alnylam Pharmaceuticals

Alnylam Pharmaceuticals began its presentation by focusing on past and present achievements in both commercial and clinical aspects, highlighting its strong financial position with an annual rise of 39% in combined net product revenues, and emphasizing its diversified portfolio. Following the introduction of five medicines over a span of less than four years, the firm concluded 2023 on a positive note, with a year-end cash and investment balance of around $2.4bn. These results were funded by the success of its RNA interference platform, which seeks to target the genetic cause of disease by silencing the expression of genes that cause specific rare diseases. Alnylam's current commercial portfolio consists of Oxlumo (lumasiran) for primary hyperoxaluria type 1, Givlaari (givosiran) for acute intermittent porphyria, and Onpattro (patisiran) and Amvuttra (vutrisiran) for hereditary transthyretin (ATTR) amyloidosis. While the majority of these assets are focused on genetic treatments with limited patient numbers, current pipeline assets diversify the company's focus into three other therapeutic areas: cardiometabolic disease, infectious disease, and CNS and ocular diseases.

Time was taken to reflect on the positive clinical results obtained in 2023, including the pipeline asset zilebesiran in partnership with Roche, which is aimed at treating both hypertension and Alzheimer's disease. Positive Phase II results from the KARDIA-1 trial in mild-to-moderate

hypertension were discussed alongside other Phase II plans to comprehensively treat hypertension, even in resistant forms, to inform a Phase III CV outcomes trial. If these trial data are positive, this could lead to a launch in the US, UK, EU, and Japan by approximately 2030.

Alnylam presented its clinical projections for 2024, which encompassed the initiation of six clinical studies, the submission of three new investigational New Drug Applications (INDs), the possibility of filing a supplemental New Drug Application (sNDA) for Amvuttra, and the release of Phase II findings for zilebesiran. Amvuttra's forthcoming submission will be supported by results from the HELIOS-B study, which are anticipated in early 2024, for the treatment of cardiomyopathy in patients with ATTR amyloidosis. This announcement was underscored by the presentation of previous benefits of Amvuttra from the APOLLO-B Phase III trial in ATTR-CM, where there was a clear reduction in disease biomarkers, early separation of mortality curves, and evidence for disease stabilization. The comprehensive development of zilebesiran is to be furthered with two Phase II trials: KARDIA-2 in combination with a single antihypertensive in patients with mild-to-moderate hypertension, and KARDIA-3 in combination with more than two antihypertensives in uncontrolled hypertension. The commencement of a Phase III trial for ALN-TTRsc04 in ATTR amyloidosis is expected to occur in late 2024. Additionally, Phase II and Phase I trial initiations for ALN-APP, targeting the treatment of cerebral amyloid angiopathy and Alzheimer's disease, respectively, are also planned.

Beyond the mid-to-late-stage assets, Phase I assets ALN-KHK and ALN-BCAT are expected to commence studies in early 2024 in type 2 diabetes and hepatocellular carcinoma, respectively. Furthermore, partnered programs in hemophilia A and B (fitusiran) with Sanofi and hepatitis B and D (elebsiran) with Vir Biotechnology are under way, with an FDA filing anticipated for fitusiran in 2024 and Phase II data reporting for elebsiran throughout 2024.

Amgen

Amgen’s long-term growth strategy relies on drug sales from an array of diseases within general medicine, oncology, inflammation, and rare disease, with the latter representing a newly created therapeutic area arising from the 2023 acquisition of Horizon Therapeutics. Growth will stem from Amgen’s marketed products across these areas, as well as from its pipeline, with the biosimilars business being integrated into each of these four main disease area pillars.

Being a hot area in general medicine, MariTide’s (maridebart cafraglutide) Phase II obesity study completed enrollment in 2023. Results will be released in 2024, which Amgen believes will show a differentiated profile. Additionally, the company has AMG 786 in Phase I, as well as about a half a dozen medicines in preclinical for obesity and related co-morbidities. In cardiovascular disease, Amgen markets PCSK9 Repatha, which is being evaluated in a Phase III prevention trial in high-risk patients. In the pipeline, olpasiran is enrolling in a study evaluating patients with high levels of Lp(a). Amgen expects that osteoporosis drugs Evenity and Prolia will continue to perform well through to the end of the decade.

Demonstrating the company’s success in oncology, the JPM presentation highlighted the fact that one in five cancer patients receives an Amgen medicine. Blincyto and Vectibix achieved record quarterly sales in Q3 2023, while Kyprolis, Nplate, and Xgeva each performed at blockbuster levels in 2023. Additionally, existing brands include Kanjinti, Mvasi, and Riabni,

which are biosimilar versions of trastuzumab, bevacizumab, and rituximab, respectively.

2024 will also provide several readouts from Amgen's oncology portfolio. Amgen is expanding on success in acute lymphoblastic leukemia from its first bispecific T-cell engager (BiTE) molecule, Blincyto, by moving it into earlier front-line treatment settings and developing a subcutaneous formulation. Commercial small molecule KRAS G12C inhibitor Lumakras is being evaluated in a variety of different combinations in Phase III non-small cell lung cancer and colorectal cancer settings. With a PDUFA date of 12 June 2024, priority review of tarlatamab is under way in advanced small cell lung cancer. Early clinical studies demonstrated a 40% response rate and a six-month survival rate of 73% for the drug in these patients, and the company heralded this as the first T-cell engager to demonstrate activity in a common solid tumor. In Phases III, II, and I are bemarituzumab for gastric cancer, AMG 193 addressing PRMT5-mutated cancers, and bispecific T-cell engaging therapy xaluritamig in prostate cancer, respectively. Amgen is also developing ABP 206, a biosimilar version of Opdivo, along with two additional undisclosed biosimilars.

Amgen has been involved in the inflammation market for decades with Enbrel and from the 2019 acquisition of Otezla. Partnered with AstraZeneca, Amgen's more recently approved respiratory drug, Tezspire, is available for patients who struggle with uncontrolled severe asthma, but other studies are under way. Tezspire is additionally being evaluated in chronic rhinosinusitis, eosinophilic esophagitis, and COPD. Amgen also highlighted its potential first-in-class anti-OX40 antibody rocatinlimab, being evaluated in the Phase III ROCKET program in atopic dermatitis. A Phase II study of this drug in asthma will also be initiated. Amgen's biosimilar versions of infliximab, Avsola, and adalimumab, Amjevita, are available, while the company is also developing biosimilars to Stelara, Soliris, and Eylea.

Finally, Amgen's rare disease program was highlighted with four commercial medicines: Tepezza for thyroid eye disease, Krystexxa for gout, Uplizna for neuromyelitis optica spectrum disorder, and Tavneos for ANCA-associated vasculitis. Bekemv is available as a biosimilar version of eculizumab. A Phase III Japanese study evaluating Tepezza in chronic and low clinical activity score study for thyroid eye disease is enrolling, while the company is also pursuing a subcutaneous formulation of that medicine. Phase III data for Uplizna are expected in myasthenia gravis and IgG4-related disease. Dazodalibep has begun enrolling in a Phase III Sjogren's syndrome study, while Phase II programs are being pursued for daxdilimab in lupus, dermatomyositis, and myositis, and for AMG 670 in idiopathic pulmonary fibrosis and systemic sclerosis.

Amgen's JPM presentation also touched on investments in harnessing AI and a brief summary of efforts towards good corporate responsibility.

Argenx

During its JPM 2024 presentation, Argenx outlined its current achievements and future objectives. It emphasized the success of two commercial products, Vyvgart and Vyvgart Hytrulo, which generated $1.2bn in revenue in 2023. Recognition was given to the CIDP team for timely submissions and progress in various indications. The company's focus on pioneering FcRn biology to create novel targets and leveraging antibody drugs was also highlighted.

The presentation stressed the importance of real-world impact, showcasing the transformation in the lives of patients like Mike, diagnosed with myasthenia gravis, who experienced significant improvements with Vyvgart. The commitment to expanding innovation access through programs like the My VYVGART Path and positive evaluations by health technology assessment bodies outside the US further underlined the company's efforts.

In the CIDP segment, the company emphasized stellar trial data, high patient compliance, and successful rollover into the open-label extension. The exclusive license for Halozyme's ENHANZE technology aims to enhance the patient treatment experience. Also introduced was empasiprubart for multifocal motor neuropathy, showcasing a 91% risk reduction for intravenous immunoglobulin rescue. The preclinical model for ARGX-119 targeting MuSK in congenital myasthenic syndrome displayed promising results.

Four new pipeline assets were unveiled: ARGX-213, targeting FcRn; ARGX-109, an ultra-potent IL-6 blocker; and ARGX-121 and ARGX-220, first-in-class novel target antibodies. The company emphasized a robust pipeline strategy.

Key milestones anticipated for 2024 included global approvals for Vyvgart, CIDP launch, prefilled syringe development, Phase II data readouts, and progress on the four new pipeline assets. The company maintained strong financials, with a cash position of $3.2bn and a planned cash burn of around $0.5bn, positioning itself toward financial self-sufficiency.

In conclusion, the Argenx presentation provided a comprehensive overview of its current position and future plans. The company highlighted its achievements, ongoing projects, and anticipated milestones across various therapeutic areas. The emphasis on real-world impact and commitment to broadening innovation access added depth to the strategic initiatives outlined in the presentation. The company's strong financial standing and disciplined investment in R&D reflected its stability and trajectory toward financial independence.

Baxter

Baxter chairman and CEO Joe Almeida kicked off the presentation speaking about Baxter's steadfast mission of saving and sustaining lives. The company operates in markets that grow 3–4% per year. It has a global diversified and market-leading portfolio of medical products and infusion therapies (YTD 2023 sales of $3.7bn), healthcare systems and technologies (YTD 2023 sales of $2.2bn), and pharmaceuticals (YTD 2023 sales of $1.7bn). Baxter's products serve over 350 million patients annually in over 100 countries. Its portfolio includes infusion systems, IV therapies, hemostats and sealants, positioning devices and ancillaries, and specialty injectables. Baxter is on track to deliver differentiated product innovations.

Its kidney care business includes a market-leading portfolio within essential renal segments including chronic therapies (YTD 2023 sales of $2.7bn) and acute therapies (YTD 2023 sales of $0.6bn). Baxter is continuing to progress on the planned separation of its kidney care segment and is making progress towards the target of July 2024 for the proposed spin-off. This would create two leading healthcare companies with robust product portfolios. The separation is expected to enhance value creation through accelerated revenue and operating income growth opportunities for both companies. Baxter plans to host an investor conference in mid-2024 to

discuss forward-looking strategies and financial objectives for the two companies.

Almeida said the company is seeking to achieve carbon neutrality for direct operations by 2040 by reducing greenhouse gas emissions, implementing strategic water and waste plans, and integrating a sustainable procurement strategy.

The company finalized its operating model, and in Q3 2023 it began reporting across four verticalized global segments, replacing a prior structure of nine businesses operating across three geographic regions. It completed the divestiture of the BioPharma Solutions business at the end of Q3 2023. It is continuing momentum in 2024 and beyond.

Becton, Dickinson and Company

CEO Tom Polen focused the presentation on Becton Dickinson's (BD's) performance in 2023 and what advancements the company hopes to make in its 2025 strategic goals. The presentation kicked off by highlighting how the company exceeded its 5.5% revenue growth profile. This was made possible by shifting the company's portfolio into higher growth spaces.

Polen highlighted that over the last two years, BD has been able to launch over 50 new products with around 60% of R&D funds being used to target those higher-growth spaces. The company has also invested $2bn towards completing six new acquisitions – all of which focused on targeting these higher-growth markets. The strong revenue growth profile was aided by the company streamlining its portfolio by 20% when compared to 2019, as well as reducing its footprint by 20% at multiple sites where consolidating plans are either under way or completed. Finally, in the last two years BD also delivered on the company's number one priority of obtaining FDA clearance for the updated Alaris system.

The presentation then focused on the future. This includes BD investing over $1bn in R&D, with 25 key product launches anticipated for fiscal year 2024 – and this puts BD in line with its goal of 100 new product launches by 2025. This will not only put the company on track to double its incremental revenue from new products by full-year 2025, but will also create a gradual margin increase for BD.

This growth profile can be attributed to investments in growth platforms – BD's PureWick portfolio is one such example. PureWick, which initially was intended for use by females in a hospital setting, was later launched for home use as PureWick DryDoc, and has now become the market's leading platform for non-invasive urine management. In 2023, the male version was launched for hospital settings, and this is now on track to be one of the fastest growing product launches in the company's history. Additionally, through BD's acquisitions of GSL and Parata Systems, the company has built a pharmacy automation business. With around $700m in revenue, BD pharmacy automation is another key driving factor for the company's continued revenue growth.

Looking ahead, Polen noted that the company was "well positioned" to achieve its 2025 goals. The company is relying on Project Recode to deliver savings, and with the highly anticipated relaunch of the BD Alaris infusion system expected soon, continued growth is likely.

The presentation ended with Polen stating that he was pleased with the progress and results delivered so far and he was "even more excited about the future." This excitement was built on delivering consistent 5.5% growth by targeting high-growth markets, executing a simplification strategy to drive double-digit earnings per share, and finally by adjusting margin expansion to 25% by the end of 2025.

BeiGene

John Oyler, BeiGene's co-founder and CEO, began the presentation with an overview of the company's history, highlighting the complexity of the company and the major differences between BeiGene and competitors. Oyler reiterated the belief that BeiGene is built differently to deliver impactful medicines while addressing affordability through strategic cost and time advantages. The presentation kicked off with a visual of the dramatic improvements of five-year survival rates for most cancers in the US and how the modalities being used at BeiGene have contributed to this effect. Oyler also touched on the fact that almost one in four Americans have difficulty affording co-payments or treatments, and medicines are not typically accessible to the rest of the world until patent expiry. The industry has seen clinical trial costs quickly rise in recent years, becoming approximately 75% of the total cost of medicines. BeiGene has focused from inception on reducing major clinical costs through multiple avenues and has continued to invest internally to also meaningfully reduce research and manufacturing costs.

In the first three quarters of 2023, BeiGene generated $1.8bn in revenue, a 76% increase over the previous year. In 2024, the company will be opening a new facility in Princeton, New Jersey, and it currently has over 50 potential medicines in its pipeline, which it intends to expand.

In terms of BeiGene's pipeline updates, Oyler focused mainly on Brukinsa, sonrotoclax, and Tevimbra, describing sonrotoclax as a better molecule preclinically than Brukinsa. Sonrotoclax is a BCL2 inhibitor that is already in the pivotal stage of clinical trials, with a $4bn BCL2i class projection for 2028. BeiGene plans to initiate a global pivotal trial of sonrotoclax in combination with Brukinsa in patients with previously untreated chronic lymphocytic leukemia in 2024. The primary endpoint of this planned trial will be PFS up to approximately nine years, with multiple secondary endpoints. The trial anticipates enrollment of 640 participants.

The outlook for BeiGene's pipeline in 2024 is heavily focused on Tevimbra in multiple indications. Oyler announced catalysts that are expected in 2024, including a European approval decision for Tevimbra in non-small cell lung cancer, a European supplemental filing in both gastric cancer and esophageal cancer indications, as well as PDUFA decisions in esophageal cancer for both first- and second-line treatment. As of the end of 2023, Tevimbra has treated more than 750,000 patients globally, and brought in $144m in third quarter revenue.

BeiGene anticipates bringing multiple new solid tumor programs to the clinical space in 2024. The main three assets it will be focusing on are CDK4i, EGFR CDAC, and FGFR2b ADC molecules. These new pursuits will add to the over 50 assets that BeiGene currently holds within its portfolio.

Oyler concluded the presentation with a discussion including clarification of misperceptions that the company is currently facing, demonstrated cost and time advantages, the company's

transition from cash-consuming to cash-generating, and with that foundation in place, Oyler stated that his belief that BeiGene is rapidly transitioning into a leading oncology company in the industry, looking forward to an exciting and transformational 2024.

Bristol Myers Squibb

Newly appointed CEO Chris Boerner kicked off this year's JPM conference by highlighting his company's efforts to write the next chapter in its history, with a focus on maximizing performance through to 2025, on navigating a transition period, and on driving growth in the late 2020s.

Bristol Myers Squibb currently stands as a leader in three major therapy areas, namely oncology, hematology, and cardiovascular disease, and is an increasingly growing presence in immunology and neuroscience. Its legacy portfolio – which includes Eliquis, Revlimid, Pomalyst, and Sprycel – is expected to generate a strong cash flow and provide the flexibility to invest in the growth of assets in development, with Bristol Myers Squibb boasting a robust pipeline of 12 assets in registrational stage and over 30 assets in early-stage development. With almost $25bn in 2023 sales from its legacy portfolio, the revenue is expected to fund the diversification and strengthening of the company's "growth portfolio," with a focus on areas of significant unmet need.

Bristol Myers Squibb plans to build on its leadership status in oncology by extending durability in immuno-oncology through the launch and further expansion of subcutaneously delivered Opdivo and Opdualag. Following its acquisition of Mirati Therapeutics, planned to close by H1 2024, Bristol Myers Squibb will also add targeted agent Augtyro (repotrectinib) to its list of brands. Additionally, licensing agreements and collaborations (e.g., SystImmune, Tubulis, and RayzeBio) will deepen Bristol Myers Squibb's platform capabilities, introducing ADCs, cell therapies, and radiopharmaceuticals to the pipeline. Approved for the treatment of second-line and beyond large B-cell lymphoma, Breyanzi is the only CAR T-cell therapy to have shown efficacy in chronic lymphocytic leukemia/small lymphocytic lymphoma, and its FDA priority review and March 2024 PDUFA date boost Bristol Myers Squibb's hopes for a significant increase in the treatment's target population, and with a significant increase in manufacturing capacity planned for 2024, hopes for an increase in revenue. Following manufacturing issues in 2022 and 2023, which constrained the growth of Breyanzi and Abecma and prevented patients from accessing these therapies, Boerner reiterated his company's plans to ramp up manufacturing capacity for CAR-Ts in 2024.

In cardiovascular disease, Bristol Myers Squibb is banking on the growing opportunities presented by Camzyos and MYK-224 in cardiomyopathies and heart failure, while a collaboration with Johnson & Johnson is expected to extend the company's success in thrombosis through the oral factor XIa inhibitor milvexian.

Bristol Myers Squibb will also grow its presence in immunology, through maximizing the existing core indications for Sotyktu, Zeposia, and Orencia, through seeking label expansions for Sotyktu and Zeposia, and through developing new assets cendakimab, CD19 NEX T, and an LPA1 antagonist. The company's hopes for leadership status in immunology rely on Sotyktu, which is currently approved for moderate-to-severe plaque psoriasis and which had a very successful

launch, gaining a 25–30% market share of new oral prescriptions within the first months post-launch. Boerner highlighted plans to broaden formulary access for Sotyktu, focusing on growing the drug's volume, and presented the drug's significant expansion opportunities in psoriatic arthritis, lupus, Sjogren's syndrome, and alopecia areata, which are not only characterized by significant unmet need, but would also boost the drug's target population beyond its current label.

With the acquisition of Karuna Therapeutics announced in December 2023, Bristol Myers Squibb will also strengthen its neuroscience portfolio, with KarXT, a potential first-in-class treatment for schizophrenia and as adjunctive therapy and first-in-disease treatment for Alzheimer's disease psychosis, now becoming part of Bristol Myers Squibb's pipeline and widening its existing footprint in this therapy area.

With blockbuster drugs Revlimid, Eliquis, and Opdivo significantly impacted by patent expirations and the US Inflation Reduction Act, Bristol Myers Squibb is entering a "significant period of transition," as acknowledged by Boerner during his presentation, but the company's focus on a renewed and reinforced pipeline through licensing opportunities, partnerships, and bolt-on opportunities may offer much-needed momentum for growth.

Cytokinetics

Robert Blum, CEO of Cytokinetics, presented the recent activities of the company and the strategic plans for 2024. Cytokinetics' mission is to discover and develop new medicines for cardiovascular and neuromuscular diseases of impaired muscle function, with a research focus on muscle biology, specifically the structure of the sarcomere, which utilizes myosin for muscle contraction.

A highlight of 2023 for the company was the positive topline Phase III results reported for the SEQUOIA-HCM trial which investigated its lead compound, aficamten, in symptomatic obstructive hypertrophic cardiomyopathy (oHCM). Results showed that when the drug was added to the standard of care, such as beta-blockers, non-dihydropyridine calcium channel blockers, and disopyramide, it significantly improved heart failure symptoms based on improvement in both KCCQ-CSS and NYHA functional class, and was safe and well tolerated with an overall incidence of adverse events similar to placebo. A key milestone during 2024 will be the full results readout from SEQUOIA-HCM, which will be presented in Q2. Further clinical development will continue for aficamten during the year, with patients currently being enrolled in the ongoing MAPLE-HCM Phase III trial, which is the second Phase III trial for aficamten in oHCM, while enrollment will also continue for the pivotal ACACIA-HCM Phase III trial in non-obstructive HCM (nHCM).

Cytokinetics is preparing for regulatory interactions with both the FDA and EMA during 2024. In Q1, a meeting with the FDA is planned to review the results from SEQUOIA-HCM, in addition to a pre-NDA meeting. The company also plans to meet with the EMA in H1 2024, and during H2 2024 expects to submit an NDA and MAA to the FDA and EMA, respectively, for aficamten in oHCM. Blum also mentioned plans to continue to pursue approval of omecamtiv mecarbil in reduced ejection fraction heart failure in Europe, with an EMA review currently pending. In terms of the company's emerging pipeline, it currently has two compounds, CK-586 and CK-136, which

are both in Phase I development for heart failure.

Genmab

In his JPM 2024 opening remarks, Genmab's CEO Jan van de Winkel reiterated his company's focus to evolve into a "fully integrated biotech innovation powerhouse," focusing on improving the lives of patients through "innovative and differentiated antibody therapeutics." The company's vision is that by 2030, its antibody drugs will transform the lives of cancer patients.

In addition to its eight approved drugs, which are either fully owned or are owned by third parties but were created by Genmab or incorporate Genmab's innovation – Tivdak, Darzalex, Rybrevant, Kesimpta, Tepezza, Tecvayli, Epkinly, and Talvey – the company also boasts an innovative clinical pipeline, with 11 agents in Phase II and Phase III trials, as well as others in early clinical development. The eight approved drugs are expected to yield $2.3bn–$2.4bn in 2023 revenue, which will sustain the company's efforts to further develop and expand its pipeline.

Co-developed with AbbVie, bispecific antibody Epkinly/Tepkinly is now approved in the US, Europe, and Japan for relapsed/refractory (R/R) diffuse large B-cell lymphoma (DLBCL), and with a subcutaneous delivery that distinguishes it from its bispecific competitors, is considered a great addition to the treatment armamentarium. Following the drug's accelerated approval in the US, Genmab is now pushing Epkinly's development plan further, with five Phase III trials across two indications (DLBCL and follicular lymphoma [FL]), in both the front-line setting (which, with a larger target population, is more lucrative than third-line DLBCL, the drug's current label) and the R/R setting. Genmab is also expanding the drug's early-phase development to other indications beyond DLBCL and FL, with chronic lymphocytic leukemia and B-cell non-Hodgkin's lymphoma included in its trials.

Tivdak, the first fully owned Genmab product to receive regulatory approval (in September 2021), is also the first and only antibody-drug conjugate to be approved by the FDA under the accelerated program for second-line recurrent or metastatic cervical cancer with disease progression on or after chemotherapy. In a bid to expand Tivdak's commercial outlook, Genmab is pursuing a broadening of its label to include early lines of cervical cancer as well as other solid tumors.

Additionally, through its collaboration with BioNTech, Biogen is hoping to further the development of bispecific checkpoint immunotherapy acasunlimab (DuoBody-PD-L1x4-1BB, currently in Phase II development in non-small cell lung cancer and endometrial cancer), bispecific immunotherapy GEN1042 (DuoBody-CD40x4-1BB, currently in a Phase I/II trial in solid tumors), and GEN1053 (HexaBody-CD27), a HexaBody technology with potential in solid tumors.

In an attempt to add to its Darzalex franchise, Genmab is also developing the fully owned investigational agent GEN3014, a HexaBody technology that, like Darzalex, targets CD38 and has shown promising data in preclinical models for multiple myeloma, DLBCL, and acute myeloid leukemia (AML). Developed under an exclusive worldwide license and option agreement with Janssen, the drug is being assessed head-to-head with Darzalex in a Phase I/II trial in R/R

multiple myeloma and R/R AML. The drug's very high affinity for CD38 may lead to significant efficacy, but it may also be a negative, as its ability to kill CD38-positive cells more potently may also be associated with significant toxicity. This may indeed be problematic, as CD38 expression is found on a variety of cells, including on cardiomyocytes.

In closing, van de Winkel indicated that the company's revenue for 2023 is expected to be $2.3bn–$2.4bn, and with Darzalex net sales of $9.8bn–$10bn, the company expects an operating profit of $706m–$846m.

Gilead

CEO Daniel O'Day started the presentation highlighting Gilead's headway to a good start to 2024, with the year being of great importance for the company. The company continues to focus on three main therapeutic areas: inflammation, oncology, and HIV. Having seen flat development previously, the last four years have seen Gilead's portfolio double in size, with a strong margin for expansion at an accelerated growth rate of 8% YOY. This should be a catalyst robust year for Gilead, with over 12 clinical trials in progress, five or more of which will be seeing Phase II results. O'Day was proud to announce that the company's core and legacy portfolios are continuing to perform well, and there has been a tremendous increase in portfolio diversification, having 88% growth in the pipeline since 2019, enjoying a season of durable growth output with no significant patent expirations. He continued to highlight the company's position to deliver 10 new transformative therapies by the end of 2030, and, most importantly, that oncology is on track to contribute a third of sales by the end of 2030.

Initially focusing on oncology, O'Day stated that this therapeutic area of the business was currently annualizing over $2bn in revenues, performing at double-digit growth and showing promising clinical momentum due to a solid team and strong network partnerships. Trodelvy is leading the way with 30 trials under way and with plans for approvals globally as well as expanding into new indications of non-small cell lung cancer and triple-negative breast cancer. Trials in 2025 onwards will also see combination therapy of IO and chemotherapy.

Emphasizing Yescarta and Tecartus, O'Day proceeded to place focus on Gilead's position as the global leader in cell therapy, with significant opportunity in the market. Yescarta currently stands as the only CAR-T therapy with FDA approval, having seen long-term results in large B-cell lymphoma. In collaboration with Kite, the company now draws focus on accelerating manufacturing time of these products to see improvement to a turnaround time of less than 16 days in the US by the end of 2024. Additionally, Gilead is also under way with four Phase I studies and a comprehensive pipeline of novel CAR-T agents in the preclinical and clinical stages, to include potential combination with next-generation targets such as immune-mediated tumor killing and immunotherapy agents. O'Day followed on to emphasize how 2025 and 2026 would see a new era for Gilead on broader base therapeutics.

Leading the way into HIV, Biktarvy has maintained its position as the global leader in treatment, annualizing $12bn and maintaining >47% US market share in Q3 2023 while still holding exclusivity to 2033. Innovation also heavily continues with lenacapavir, a biannual injection for prevention which has made significant headway to enter clinics in 2024, and five new launches to be seen in combination with daily oral therapy by the end of 2025.

With five Phase III updates, as well as over eight HIV treatments and 10 oncology updates to be seen in 2024, O'Day is confident that Gilead is moving into a new era of consistent sustainable growth due to its diverse and established portfolio.

GSK

GSK CEO Emma Walmsley kicked off the JPM 2024 presentation celebrating the double-digit sales and adjusted operating profit growth seen up to Q3 2023. Last year at the 2023 JPM conference, Walmsley stressed that GSK was confident it would meet its ambitious goals laid out for the next decade after the company's FY2022 revenue guidance was raised twice. She now reiterated that GSK is on track to achieve these goals going forward, promising to deliver an over 5% sales CAGR and an over 10% adjusted operating profit CAGR as well as over £10bn in cash generated from operations during 2021–26 through focusing on four core therapy areas: infectious diseases, HIV, respiratory/immunology, and oncology.

GSK has an extremely strong presence in infectious diseases, with a newer development being the first approval of an RSV vaccine for older adults. In 2023, blockbuster vaccine Arexvy gained an approval for older adults, and the company increased its presence in China through partnering with Zhifei on its Shingrix vaccine for shingles. In the HIV space, GSK is a world leader after winning the first approval for a long-acting HIV medicine and now predicts a CAGR of 6–8% during 2021–26 in this therapy area alone. Flagship agent Dovato is facing a patent cliff in 2028, but GSK is confident that patients will transition to cabotegravir, offsetting this future loss.

The respiratory therapy area was discussed, as it is an area with significant growth opportunities for GSK. Three pivotal trial readouts in the respiratory space are expected in 2024 for Nucala in COPD, depemokimab in severe asthma, and camlipixant for chronic cough, all of which are expected to generate billions of pounds in revenues. Moving to oncology, Walmsley heralded PD-1 inhibitor Jemperli as the backbone of the company's immuno-oncology research after it was given approval in endometrial cancer; Phase III non-small cell lung cancer data for this asset are expected in 2024 as well. New approvals and data readouts are expected in 2024 for oncology assets Ojjaara and Zejula, with GSK aiming to strengthen its presence in this therapy area by investigating additional pipeline assets at the earlier stages.

Walmsley stated she was "thrilled" with the momentum seen within GSK after the large structural changes in 2022, reiterating that it currently stands by its 2023 guidance of a >10% adjusted operating profit CAGR and a >5% sales CAGR from 2021–26 for now, although Walmsley hinted at a potential update to this guidance in GSK's 2023 full-year financial results, expected to be released at the end of January.

H. Lundbeck

H. Lundbeck's new CEO Charl van Zyl doubled down on the company's commitment to neuroscience. During the JPM presentation, he set the context around the direction of the company and the outcome of a strategic review. A primary objective is for the company to remain disciplined in capital spend and allocations, firstly deriving growth from existing assets.

The current commercial portfolio focuses on Rexulti and Vyepti, while the emerging pipeline is more weighted to the early stage, so Lundbeck will look to external innovation to bolster its late-stage pipeline and build a more sustainable pipeline for the long term. Van Zyl confirmed a 30–32% adjusted EBITDA target long term, excluding potential business development activities.

To grow Rexulti in its new indication of agitation associated with Alzheimer's disease dementia, Lundbeck will invest in opportunities to expand the breadth of the drug's prescriber base coverage by increasing awareness through additional sales force, but also increasing awareness of the option for treatment of this specific agitation indication among caregivers and at long-term care facilities. For both Rexulti and Vyepti, a CGRP-targeted treatment for migraine, Lundbeck expects to deploy patient resource managers to offer guidance, offer more directed healthcare professional engagement to enhance diagnosis, expand advanced analytics to improve patient support, and improve patient access. The company estimates that these measures could double the revenue from these two franchises to over 60% by 2028, growing the overall revenue during that time. The plan is also to prioritize from a geographic perspective to invest predominantly in the US.

On business development, Lundbeck is expected to engage in multiple deals, rather than one single deal, to complement the company's pipeline. In order to focus these efforts, three key areas will be considered for M&A or partnership opportunities. The first is that Lundbeck will build on the company's established psychiatry core business, will reinforce its neuro-specialty position to follow existing infrastructure within the chronic migraine space, and establish a rare (but not ultra-rare) neurology disease franchise.

Incyte

Incyte CEO Hervé Hoppenot opened the company's presentation by reviewing where it stands today, as well as what it plans to achieve over the next seven years to 2030. He cited his expectation that Incyte's commercial expertise in oncology and inflammation and autoimmunity and strong R&D engine would fuel long-term growth. He pointed out an approximate 17% revenue CAGR and operational profitability over the past five years, attributing that to new product launches and growth of existing products plus royalty revenues. He also emphasized the 15% growth for the first nine months of 2023, highlighting JAK1/JAK2 inhibitor Jakafi (ruxolitinib), with net sales of $1.9bn, and Opzelura (ruxolitinib cream), with sales of $229m for the 2023 year-to-date time period.

He mentioned the securing of small biotech exception status (through Medicare's Inflation Reduction Act) for ruxolitinib, through which Jakafi will be exempted from selection for price negotiation until 2029, as well as a Part D catastrophic coverage phase-in through 2030, which will have a meaningful impact in the years 2025 to 2031.

Hoppenot detailed each of the company's three main clinical franchises: myeloproliferative neoplasms (MPNs)/graft-versus-host disease (GVHD), hematology and oncology, and dermatology, noting the creation of the dermatology group during 2020–21, which is now a commercial organization led by Opzelura. He highlighted the emerging dermatology opportunity and the intent to maximize the potential of ruxolitinib cream (Opzelura) beyond its launch in atopic dermatitis and vitiligo two years ago, and to expand JAK1 inhibitor povorcitinib into

multiple indications with high unmet need. For Opzelura, the primary endpoint was met in its randomized, placebo-controlled, Phase II trial evaluating it in adults with hidradenitis suppurativa (HS). Phase II data will be submitted for an upcoming scientific meeting in 2024, while a Phase III study is currently under evaluation. A Phase II study assessing the efficacy and safety of oral povorcitinib in prurigo nodularis met its primary endpoint across all three treatment dose groups, with Phase III studies in HS and vitiligo currently enrolling.

Also announced were key pipeline updates that could support significant future launches anticipated by 2030, including both indication expansions of commercialized medicines and those with proof-of concept data, and advancing novel medicines to drive sustainable long-term growth. Progress across the MPN/GVHD pipeline includes axatilimab (for which a BLA was submitted in third-line and beyond cGVHD); mCALR (a mAb for which a Phase I trial is ongoing in myelofibrosis and essential thrombocythemia [ET]); and JAK2 inhibitor V617F (in MF, polycythemia vera [PV], and ET). Within the oncology pipeline, a Phase I study demonstrated early efficacy of CDK2 inhibitor INCB123667 as a monotherapy or combination therapy for late-stage cancers.

In his closing remarks, Hoppenot restated Incyte's emphasis on sustaining and driving growth by continuing to execute commercially and advancing multiple programs. He, along with other company executives, also answered questions addressing topics including the following: Jakafi as its largest opportunity, listing guidance for the drug to have $3bn in revenues by 2028, particularly looking to PV, an underpenetrated indication; Opzelura's adoption in existing and new indications; and the possibility of broadening through potential partnerships, using its $3.5bn of cash on its balance sheet to bring in assets complementary to its three core therapy areas that leverage its expertise.

Legend Biotech

Much of the JPM presentation for Legend Biotech focused on the company's sole commercial product, Carvykti, a CAR-T product targeting BCMA and approved for fifth-line or later (US) or fourth-line or later (EU and Japan) multiple myeloma (MM). Q3 2023 sales of Carvykti were $152m ($140m in the US, $12m in the EU). In the US, sales increased by 23% for Q3 2023 compared to Q2 2023, while in the EU the increase was 300%, which was driven by launch in Germany. Carvykti competes with Bristol Myers Squibb's Abecma, with Legend officials saying Carvykti is being given to two thirds of MM patients receiving CAR-T, with Abecma being given to the remaining third. This is despite Abecma being first-to-market, and is likely due to the high efficacy seen in clinical trials for Carvykti. Legend has a collaboration with Johnson & Johnson, with the two companies splitting sales 50/50 in the US, Europe, and Japan, and 70/30 in favor of Legend in China. Following a $350m upfront payment from Johnson & Johnson, Legend has received $330m in clinical and regulatory milestone payments and is eligible for additional milestone payments. Legend ended Q3 2023 with $1.4bn in cash.

Legend aims to exit 2025 with the ability to manufacture 10,000 doses of Carvykti per year with the help of two manufacturing facilities in each of three regions: the US, EU, and China. A manufacturing site in Raritan, New Jersey is GMP operational and supplies commercial product for the US, EU, and Japan, while a site in Somerset, New Jersey provides clinical supplies for

pipeline programs. A site in Ghent, Belgium will start clinical production in January 2024 with commercial production expected in H2 2024. A second site in Belgium is under construction and will be used for Carvykti commercial supply. The two Chinese facilities are in Nanjing; one is GMP operational and generates clinical supplies for Chinese clinical trials and will support the potential launch of Carvykti in China, while a second site is under construction and will be used for Carvykti commercial supply production. A Johnson & Johnson facility in Switzerland is producing lentivirus in-house and the supply is sufficient to cover current needs. Additional lentivirus supply is expected to be available from Johnson & Johnson facilities in the US and Netherlands in 2024 and 2025, respectively. Finally, a three-year contract manufacturing deal with Novartis was signed in Q2 2023 and is on track to produce clinical materials in H1 2024.

On 3 January 2023, Legend announced the closing of an exclusive global license agreement with Novartis to advance certain DLL3-targeted CAR-T therapies, including LB2102, an investigational therapy for small cell lung cancer. Legend will conduct the Phase I trial for LB2102 in the US while Novartis will conduct all other development for the licensed products. Legend contributed the binder for the CAR-T product while Novartis will contribute the T-Charge platform which allows for a two-day manufacturing process. The deal provided a $100m upfront payment with milestones up to $1.01bn and tiered royalties on net sales.

Other Phase I assets include autologous CAR-Ts targeting GPC3 for liver cancer, claudin 18.2 for gastric, esophageal, and pancreatic cancer, and CD19xCD20xCD22 for lymphoma. An autologous CAR-T targeting GCC for colorectal cancer is ready to enter the clinic soon. Legend also has an allogeneic CAR-T targeting BCMA using a gamma-delta T-cell receptor in a Phase I trial for MM.

In the near term, Legend is focusing on advancing Carvykti into earlier lines of therapy. Following positive results from CARTITUDE-4, Carvykti is currently under regulatory review for second-line or later MM in the US and EU, with decisions expected by 5 April 2024 and Q1 2024, respectively. The second-line setting is estimated by Legend at 80,000 patients compared to 20,000 patients for the currently approved setting. A survey of community and academic center physicians carried out by Legend found that the physicians expected to prescribe Carvykti to one third of second-line patients – this includes the 15–20% of second-line patients who are high risk, as well as younger patients who are attracted by the one-and-done nature of the therapy which allows them to travel and otherwise live a normal life post-treatment. One challenge in treating these patients is that 80% of second-line patients are seen in the community setting. Legend noted that approximately one third of current Carvykti use is in the community setting, but it expects that patients will demand this therapy from their physicians, which will increase use in the community.

Carvykti is also being evaluated in the front-line setting, with CARTITUDE-5 enrolling patients not intending to undergo a transplant, and CARTITUDE-6 enrolling transplant-eligible patients. CARTITUDE-5 has completed enrollment outside of the US and is expected to complete US enrollment in H1 2024. Enrollment is ongoing for CARTITUDE-6.

In December 2023, the label for Carvykti was modified to include a new item in the black box warning of secondary hematologic malignancies (this item was previously in the warning and precautions section). During the Q&A, a company official noted that while CARTITUDE-1 reported 10% of patients having secondary malignancies, these were heavily pretreated patients and the

historical rate of secondary malignancies for such patients was 3% per year. The official further remarked that since CARTITUDE-1 patients have been followed for several years, this may explain the high rate of secondary malignancies.

Neurocrine Biosciences

Neurocrine Biosciences is a neuroscience company that has been in business for 32 years, mostly as an R&D company, but has become a fully integrated commercial company in the past six years. As with other companies in this space, Neurocrine highlights the heterogeneity of the field, subdividing it into neuropsychiatry, neuroendocrinology, and neuroimmunology. The company's lead product, Ingrezza, became the first treatment for tardive dyskinesia and is also approved to treat chorea associated with Huntington's disease. CEO Kevin Gorman touted the multi-billion-dollar franchise, which has annual net sales guidance for 2023 falling between $1.82bn and $1.84bn, that is growing by over 20% each year, even after six years on the market. Additional growth is expected as Neurocrine estimates that Ingrezza has only treated about 10% of the total addressable population. Neurocrine has settled on four ANDA litigations to extend Ingrezza's exclusivity out to March 2038. Neurocrine is in a neuroendocrine partnership with AbbVie with elagolix, also known by the brand name Orilissa in women's health (co-packaged as Oriahnn). Commercial products also include formulations of hydrocortisone, Alkindi and Efmody, from the acquisition of Diurnal.

Looking at the pipeline, the Neurocrine CEO really focused on the potential of crinecerfont, for which two Phase III studies, one adult and one pediatric, reported results in 2023, beating the company's expectations in congenital adrenal hyperplasia (CAH). A large part of the Neurocrine JPM presentation detailed the pathophysiology and complications in the treatment of CAH, including video testimony from endocrinologists and patients. The company believes this will be a life-changing medicine, and expects to file an NDA later in 2024, with breakthrough therapy designation having been granted in 2023. As with Ingrezza, Neurocrine has been focusing efforts on adding more patents to the Orange Book over the next two years for crinecerfont, and is confident in intellectual property protection until at least 2035.

Neurocrine has 14 compounds in clinical development in 17 different indications. In 2024, the company expects five Phase II readouts, two from Efmody in CAH and adrenal insufficiency, and three in neuropsychiatry, including AMPA potentiator NBI-1065845 for major depressive disorder and DAAO inhibitor luvadaxistat for cognitive impairment in schizophrenia. The early-phase muscarinic pipeline was particularly emphasized during the JPM presentation, with the Cerevel acquisition called out as validation for a focus on this mechanistic approach. More specifically, Phase II data are expected from M4 agonist NBI-1117568 in schizophrenia. Earlier in the pipeline, NBI-1076986 is an M4 antagonist to be evaluated in movement disorders, while three other agonists have different preferences for M1 or M4. The muscarinic system has several receptors and Neurocrine is exploring different types of agonism and antagonism of this pathway. In 2024, Neurocrine expects to advance four Phase I programs for muscarinic compounds as well as a Phase I program for a next-generation VMAT2 inhibitor.

As of the end of September 2023, Neurocrine has $1.5bn in cash and investments to help propel the company in achieving its goal of becoming a leading neuroscience firm. The company is

expanding its global reach with commercialization in Europe. In 2025, the company plans to advance two gene therapy programs into clinical development.

Regeneron

Looking back at 2023, Regeneron CEO Leonard Schleifer noted the following key achievements: (i) FDA approval and successful launch of Eylea HD (a reformulation of Eylea that allows for less frequent intraocular injections) for wet age-related macular degeneration (wet AMD), diabetic macular edema, and diabetic retinopathy; (ii) positive pivotal data for Dupixent in eosinophilic COPD leading to a submission to US and EU regulatory authorities for a possible sixth indication; and (iii) BLA submissions for the CD3 bispecifics odronextamab (targeting CD20 for DLBCL and follicular lymphoma) and linvoseltamab (targeting BCMA for multiple myeloma). Combined sales for Eylea HD and Eylea reached $1.46bn for Q4 2023, with Eylea HD sales accounting for $123m in its first full quarter after the August 2023 launch. With >750,000 patients on therapy globally, Dupixent global sales grew 34% and reached nearly $8.4bn for the first three quarters of 2023. Potential new indications for Dupixent provide an opportunity to add up to 1 million additional eligible patients in the US. Schleifer concluded his introduction by noting that Regeneron is building an oncology pipeline driven primarily by Libtayo combinations and that Libtayo is poised to exceed $1bn in sales in 2024.

The CSO, George Yancopoulos, spoke next and began by discussing the combination of fianlimab (an anti-LAG-3 antibody) and Libtayo. Following results in first-line metastatic melanoma that compared well to historical data for Opdivo monotherapy and Opdualag (Opdivo combined with relatlimab), a Phase III trial was initiated in the same setting, with data expected in H2 2024. The fianlimab + Libtayo combination is also being evaluated in a Phase III trial for adjuvant melanoma and in Phase I trials for advanced non-small cell lung cancer (NSCLC) and perioperative liver cancer. In 2024, Regeneron expects to initiate Phase I trials for this combination in the perioperative setting for the following indications: melanoma, NSCLC, cutaneous squamous cell carcinoma, and head and neck squamous cell carcinoma.

Yancopoulos next discussed CD28 co-stimulatory bispecifics. He noted that Libtayo combined with a PSMAxCD28 co-stimulatory reported remarkable efficacy in prostate cancer patients but was associated with serious immune-related adverse events. Regeneron is now aiming to combine PSMAxCD28 with a PSMAxCD3 bispecific, with enrollment for this combination starting in H1 2024. Other co-stimulatory bispecifics in the clinic include EGFRxCD28 for multiple solid tumor indications (expansion cohorts with Libtayo expected to initiate in H2 2024), MUC16xCD28 for ovarian cancer (initial dose escalation results with Libtayo have been presented and expansion cohorts are expected to initiate in 2024; a dose escalation cohort with ubamatamab, a MUC16xCD3 bispecific, is enrolling patients); CD22xCD28 for DLBCL (currently enrolling dose escalation cohorts including with odronextamab); and CD38xCD28 for multiple myeloma (a Phase I study will be initiated in 2024 which will include a combination with linvoseltamab).

Shifting to immunology, Yancopoulos presented preclinical data highlighting the potential for linvoseltamab combined with Dupixent to reverse severe allergy. Dupixent inhibits class switching to IgE antibodies which are involved in allergies. As such, Dupixent is effective in

preventing emergence of new allergies but does not affect pre-existing allergies. Linvoseltamab, on the other hand, effectively eliminates BCMA-expressing cells including long-lived plasma cells and has been shown to reduce serum IgE in multiple myeloma patients. Once the patients stop linvoseltamab, the IgE antibodies return, but in monkey models, administering linvoseltamab with Dupixent resulted in a persistent reduction of serum IgE. A clinical trial with the two-drug regimen is expected to initiate in 2024 for patients with severe food allergies.

Yancopoulos also highlighted Regeneron's obesity program. Trevogrumab is a an anti-myostatin, and in non-human primates, combining trevogrumab with semaglutide led to greater fat loss and less lean mass loss compared to semaglutide monotherapy. Pending results from a safety and tolerability trial of high dose trevogrumab in healthy volunteers, a Phase II trial of trevogrumab + semaglutide ± garetosmab (anti-activin A) will initiate in mid-2024. Regeneron's obesity program is also seeking to target GPR75. Exome sequencing of ~640,000 individuals revealed that gene variants in GPR75 are associated with reduced risk of obesity. Individuals with at least one inactive copy of the GPR75 gene had lower BMI and, on average, tended to weigh about 12 pounds less. Regeneron is pursuing three modalities to target GPR75: (i) an siRNA in collaboration with Alnylam; (ii) a small molecule in collaboration with AstraZeneca; and (iii) an antibody approach.

Regeneron continues to work on new genetic medicines. Regeneron is combining Veopoz, an anti-C5 antibody, with cemdisiran, a C5 siRNA. The siRNA markedly decreases C5 production by the liver, allowing much lower levels of antibody to be used to completely block the residual C5. In an exploratory cohort from an ongoing Phase III trial, patients with paroxysmal nocturnal hemoglobinuria (PNH) treated with this combination achieved greater control of intravascular hemolysis compared to the current standard of care. For the first time, normal levels of lactose dehydrogenase levels were achieved in PNH patients.

This approach of combining an anti-C5 antibody with C5 siRNA is being extended to geographic atrophy and dry AMD, with two Phase III trials beginning this year. Recently approved approaches inhibiting complement are approved for slowing progression of geographic atrophy but must be delivered directly into the eye and come with the risk of severe eye inflammation and even blindness. Regeneron's systemic approach will have the advantage of being safer and more convenient.

Yancopoulos mentioned two CRISPR gene editing programs: (i) a collaboration with Intellia on NTLA-2001 that is entering Phase III for transthyretin amyloidosis (ATTR) with cardiomyopathy; and (ii) a gene insertion program targeting factor IX that is expected to enter the clinic in 2024 to potentially cure hemophilia B.

Finally, Regeneron is also developing AAV gene therapies. DB-OTO is a gene therapy that is delivered to the inner ear to rescue hearing in infants with OTOF-related hearing loss. DB-OTO selectively expresses functional OTOF in the inner ear hair cells of patients, enabling the ear to transmit sound to the brain. Preliminary results from the first patient treated continue to show improvements in auditory responses at week 4 and week 12 compared to baseline. The child started with profound hearing impairment (treatable with cochlear implant), and DB-OTO improved hearing at week 12 to moderate hearing loss range (treatable with a hearing aid). These studies pave the way for GJB2/DB-103, a gene therapy for GJB2-related hearing loss in

the IND stage.

Sanofi

At the 42nd annual J.P. Morgan Healthcare Conference, Sanofi showcased its strategic R&D portfolio with a vast pipeline of potential blockbuster opportunities driving long-term value. CEO Paul Hudson began the presentation by highlighting Sanofi's great success in the immunology space and its flagship Dupixent. Despite being a later entrant as the fifth advanced therapy, Dupixent quickly became a blockbuster and is now expected to gross €13bn in 2023. Currently, Sanofi's leading immunology franchise, with blockbuster antibody Dupixent at its core, has been driving the company's sustained growth. Dupixent is projected to continue its strong performance and to deliver low-double-digit net sales growth from 2023 to 2030, supported by a potential new approval in COPD as well as greater penetration in approved indications. Additionally, recently launched and future assets are expected to contribute over €10bn of annual sales by 2030, driven by late-stage assets such as tolebrutinib, itepekimab, amlitelimab, frexalimab, and rilzabrutinib, as well as currently marketed brands such as Sarclisa, Tzield, and Altuviiio. In addition to a broad immunology portfolio, Sanofi expects its vaccine pipeline to also generate over €10bn sales by 2030, spearheaded by the launch of Beyfortus, an RSV vaccine for use in infants.

While much of the company's momentum will continue to depend on Dupixent, Sanofi emphasized its efforts to increase its R&D investment to prepare ahead of Dupixent's loss of exclusivity. The company highlighted a strategic transformation through R&D featuring potential multi-indication assets such as amlitelimab, frexalimab, and the oral TNFR1si SAR441566, intended to address unmet patient needs in markets with low penetration of advanced therapies. Each of these "pipeline-in-a-product" assets is slated to become a potential blockbuster with a peak sales potential of over €5bn. The company stated that its commitment to R&D will yield an expected 25 mid-to-late-stage readouts and up to 19 regulatory submissions in the next few years. Starting in 2024, Sanofi expects a steady stream of pipeline news to flow, with the first regulatory submissions expected for tolebrutinib in multiple sclerosis and rilzabrutinib in pulmonary indications such as asthma and immune thrombocytopenic purpura. Similarly, amlitelimab, frexalimab, and SAR441566 are expected to enter the registrational stage in 2027. Lastly, Hudson noted that Sanofi's R&D will lead to a 50% increase in the number of Phase III studies between 2023 and 2025. The additional R&D investment will also double the size of the vaccines business by the end of 2030 and assist the company's foray into the PCV market segment.

With the ambition to become a pureplay immunology powerhouse, Hudson reiterated Sanofi's intention to spin off its Consumer Healthcare unit. The company hopes to enable greater management focus and capital allocation to the needs of the Biopharma business, further optimizing the cost structure. Subject to market conditions, the separation could be finalized at the earliest in Q4 2024 through a capital markets transaction, creating a new publicly listed entity.

In his closing remarks, Hudson noted a potential low-single-digit decline in 2024 as the result of the decision to support the full realization of its pipeline's potential and long-term value creation.

However, Sanofi expects a strong rebound in business earnings per share growth in 2025, driven by continued sales growth supported by its leading franchises, the full benefit from planned efficiency initiatives, and its expectation of relatively stable R&D expenses post 2025. Overall, 2024 will be an inflection point for Sanofi as the company enters its next chapter with the goal of becoming a tech-powered immunology leader.

Teva

In his first year as CEO, Richard Francis headed a transformative growth strategy which saw Teva return to revenue growth and settle on track to meet its financial targets for 2027. By the end of 2022, Teva was in a less than ideal position, with negative topline evolution and the company's focus centering on debt repayment and settlement of litigation. However, at the 42nd annual J.P. Morgan Healthcare Conference, Francis exhibited the company's feats in delivering across all pillars of its implemented growth strategy. The four pillars supporting the strategy are to deliver on growth engines, step up innovation, sustain its generics powerhouse, and focus the business.

Francis outlined three key assets which have helped deliver on the growth engines, namely Austedo, Uzedy, and Ajovy. Some of the 2023 milestones for these assets which helped deliver on growth included the launch of Austedo's improved profile with once-daily dosing in May 2023, the launch of Uzedy in May 2023, and achievement of Medicaid and hospital formulary approvals for Uzedy. Both Austedo and Ajovy demonstrated improved market share year-over-year, with 32% and 24% increases in US revenues for Austedo and Ajovy, respectively. Long-term goals for delivering on growth engines were also presented, predominantly focusing on continued growth through geographic and market share expansion. For Austedo, a sizable goal was set of more than $2.5bn in revenue by 2027 across tardive dyskinesia and chorea associated with Huntington's disease, but the company expressed confidence in achieving this goal, and reaffirmed that Austedo was on track to reach the $1.2bn 2023 sales target. Teva's strong biosimilar pipeline is also anticipated to continue contributing to revenue growth in the short term, having already generated global revenue of over $1bn since the franchise launched. The company currently has 16 biosimilar assets on the market and expects five more products to launch by 2027, including a biosimilar for Humira.

The company celebrated its progress in step up innovation, particularly rejoicing in the pipeline acceleration of key late-stage assets as well as partnerships with industry-leading players. Teva's late-stage pipeline has two agents in Phase III trials, namely TEV-'749 and TEV-'248. TEV-'749 has completed enrollment and is anticipating a Phase III readout in the second half of 2024, with Francis championing the product's potential to change the treatment landscape for schizophrenia. TEV-'248 is a combination therapy of an inhaled corticosteroid and a short-acting beta agonist, the two most widely used molecules in respiratory conditions, and the company estimates at least 30% of the 10 million potential patients to use this combination regimen, generating a market potential of $2.5bn. Teva also partnered with Sanofi in 2023 for the anti-TL1A agent TEV-'574, which is under Phase II investigation. Sanofi's experience in immunology was highlighted as a core strength in the development of this product, and a market potential of $28bn is proposed. The company is also building upon its early-stage pipeline to strengthen its leading position in neuroscience and immunology.

While the generics space has been an area Teva is experienced with, the new CEO expressed that the company had not met its full potential here yet, outlining Teva to have a strong commercial footprint, deep pipeline, and quality manufacturing, all of which have not been optimized previously. Going forward, the company plans to focus the pipeline more on high-value products, excluding lowest-contribution products to move away from broader coverage and towards a more specified and intensive development of high-generating assets. In turn, Teva expects to move from more than 80% coverage of loss of exclusivities to 60%. Continued network optimization is also a focus for Teva in 2024, with the goal to reduce operational sites from 52 to 40–44 by 2027. In 2023, progress was made towards this goal with the closure of three sites. An operational excellence plan is anticipated to roll out to help achieve this goal. With these plans in motion, the company hopes to launch 13 complex generics with a combined brand value of approximately $10bn in 2024 and 2025.

Francis also outlined the progress Teva made last year on the fourth pillar of the growth strategy: to focus the business. The carve out of Teva API as a standalone unit is under way, with a new CEO and management team now dedicated to the business. The company anticipates expected growth of approximately 6–7% in the upcoming year.

In his closing remarks, Francis commended the efforts of all of Teva's team in their willingness for change and to drive the company back into growth. Francis reiterated the financial targets of 2027, confidently affirming the company to be on track to achieve a mid-single-digit CAGR, 30% operating income margin, 2.0x EBITDA, and 80% cash-to-earnings by 2027.

Vertex Pharmaceuticals

Vertex Pharmaceuticals gave insight into numerous updates on upcoming clinical milestones at the J.P. Morgan Healthcare Conference. The company is working to expand its leadership in cystic fibrosis while simultaneously expanding its reach into other areas of need such as post-operative and neuropathic pain management.

Pivotal Phase III programs of VX-548 for the treatment of moderate-to-severe pain in abdominoplasty and bunionectomy, as well as a single-arm safety and effectiveness trial, have all been completed. Vertex expects data readouts from these studies in early 2024. Along with acute pain, the next steps for VX-548 are to engage in an End-of-Phase II meeting with regulators with a goal of attaining a broad peripheral neuropathic pain label and advancing the compound into pivotal development in diabetic peripheral neuropathy, while enrolling and dosing patients in a Phase II study in lumbosacral radiculopathy. Another candidate, VX-993, is also being studied for acute and peripheral neuropathic pain indications. Vertex plans to advance the oral formulation of VX-993 into a Phase II study in acute pain and initiate a Phase I study of the intravenous formulation for the same indication. A Phase II study of VX-993 in peripheral neuropathic pain is planned as well.

Vertex announced that enrollment has been completed into the Phase IIb portion of a pivotal Phase IIb/III trial of inaxaplin, the first potential medicine to target the underlying cause of APOL1-mediated kidney disease. The company expects to select a dose and begin the Phase III portion of the study in the first quarter of 2024, with an interim analysis of the study planned at 48 weeks, and a potential path to file for accelerated approval in the US. A final analysis will be

conducted at two years of treatment.

A Phase I/II trial of VX-880, an investigational allogeneic human stem cell-derived islet cell therapy for the treatment of type 1 diabetes, has been fully enrolled. Efficacy from the trial continues to show curative potential, and safety data are consistent with immunosuppressives, perioperative period, and past medical history. Notably, however, two participants in the trial have died due to causes unrelated to VX-880, and Vertex has placed the study on a protocol-specified pause.

Mid Cap

Acadia Pharmaceuticals

Steve Davis, CEO of Acadia Pharmaceuticals, led this year's JPM discussion which centered on the company's three operational pillars – the commercial franchise, pipeline assets, and the company's positive cash flow.

Beginning with a focus on Acadia's two commercialized products, Davis reviewed Daybue (trofinetide), which was approved in April 2023 as the first marketed therapy for the rare disease Rett syndrome, a genetic neurodevelopmental disorder that occurs primarily in females following a near-normal development in the first two years of life. Acadia licensed North American rights to the drug from Neuren in 2018 and then gained exclusive global rights in July 2023. Of the 5,000 diagnosed patients in the US, more than 800 have already been prescribed Daybue, with $170m–$177.5m in expected revenue for the first eight months on the market. ACADIA plans a global expansion with filings in Canada, Europe, and Japan expected in 2024–25.

Nuplazid (pimavanserin) is Acadia's oldest marketed product, launched eight years ago as the first and only approved treatment for Parkinson's disease psychosis (PDP). The drug generates over $300m in annual cash flow, and the company has seen growing new patient starts recently due to real-world evidence studies showing, among other metrics, that Nuplazid exhibits significantly lower mortality rates in PDP patients compared to other antipsychotics on the market.

In a review of pipeline projects, Davis again discussed pimavanserin and its implication in treating negative symptoms of schizophrenia. These chronic symptoms include social withdrawal, restricted speech, lack of emotion, loss of motivation, and blunted affect. While first-line schizophrenia therapies treat positive symptoms, there are no FDA-approved therapies for the negative symptoms, which, when left untreated, can lead to long-term disability and caregiver burden. The ADVANCE-2 Phase III trial is under way, with results expected in Q1 2024. Also in Phase III is ACP-101, a nasally administered therapy indicated for hyperphagia in patients with Prader-Willi syndrome. Rounding out the pipeline discussion, Davis also reviewed ACP-24, a 5HT2A blocker in Phase I for Alzheimer's disease psychosis, with development based on data from Nuplazid, which is also an 5HT2A blocker.

Davis closed with a 2023 recap highlighting the Daybue launch, revenue growth from Daybue

and Nuplazid, and the company's achievement of cash flow positivity, while looking forward to upcoming late-stage development results, global product expansion, and continued work on pipeline projects.

Alkermes

Richard Pops, CEO of Alkermes, started the presentation by highlighting the accomplishments of 2023 that led to Alkermes's position as a profitable, pureplay neuroscience company in 2024. Key achievements include the completed separation of the oncology business which streamlined the operational structure and laid the groundwork to expand neuroscience drug development. Patent litigation over Vivitrol was resolved favorably, and financial expectations were raised when the company prevailed in arbitration with Janssen resulting in additional cash flow and a strong balance sheet. The proprietary commercial product portfolio grew in net sales by 20% year-over-year.

One of Alkermes's strategic priorities for 2024 is to deliver strong commercial growth and profitability. This is driven by four core products that demonstrate strong, consistent growth generating >$1bn: Lybalvi (oral, once-daily treatment option for schizophrenia and bipolar I disorder), Aristada (long-acting injectable [LAI] for the treatment of schizophrenia), Vivitrol (LAI for the treatment of alcohol dependence and opioid dependence), and Vumerity (novel oral fumarate for the treatment of relapsing forms of multiple sclerosis).

Alkermes will leverage its neuroscience drug development capabilities this year to advance its investigational orexin 2 receptor agonist ALKS 2680 for the treatment of narcolepsy. The Phase Ib proof-of-concept study is under way and topline results of the first-in-human study were presented at the World Sleep Meeting in October 2023. Results showed strong efficacy and safety/tolerability, and the company is planning a Phase II narcolepsy type 1 study initiation in the first half of 2024. The Phase Ib narcolepsy type 2 and idiopathic hypersomnia proof-of-concept data are also expected during H1 2024. Alkermes plans to advance other internal development candidates in psychiatry and neurology and will explore external pipeline opportunities as well.

Alkermes is entering 2024 with a strong foundation for growth. The company is starting the year with ~$800m in cash and investments, while separating its oncology business will result in significant R&D expense savings. The company is planning for significant cash generation from continued revenue growth from its core commercial products and is expected to be operating cost neutral in 2024.

Amphastar Pharmaceuticals

Amphastar, a bio-pharmaceutical company that develops, manufactures, and markets technically challenging generic and proprietary products, presented the company overview and outlook at the 42nd annual J.P. Morgan Healthcare Conference. CEO Jack Zhang started the presentation highlighting the fundamental factors that have led the company to success. Firstly, Amphastar has a fully integrated "One-Stop" business model that allows for control over quality and compliance at each stage of the product cycle, from R&D to manufacturing and marketing.

Secondly, the company adopts a dual-strategies growth model of in-house pipeline development and strategic acquisitions. Lastly, Amphastar follows a "three H" principle: insist on high quality, emphasize high efficiency, and rely on high technology to develop pipelines. By adopting all of the above, its portfolio of market-ready drugs has expanded over the years, leading to the diversification of its revenue base and high net income margins.

CFO Bill Peters continued the presentation, covering pipeline and product updates. Baqsimi, Primatene MIST, and Amphastar's generic Glucagon Injection Kit are expected to be key growth drivers in 2024. Baqsimi, a novel intranasal glucagon product with IP protection, is a category leader in ease of use due to being the only non-injection glucagon approved by the FDA. The American Diabetes Association recommends that patients at increased risk for level 2 hypoglycemia be prescribed glucagon. Approximately 7 million people are treated with insulin, and only about 0.7 million (~10%) of these patients currently utilize glucagon, showing the growth potential of the product. Primatene MIST, a proprietary and patent-protected over-the-counter epinephrine inhalation product, was launched in December 2018 and continues to demonstrate its popularity with patients, accounting for 17% of Amphastar sales in 2022. The company is expecting to continue the success of these products in 2024 through the implementation of advertising campaigns and promotions.

In terms of its development pipeline, Amphastar anticipates a number of R&D milestones to occur within 2024. In addition to two recently submitted regulatory filings, the company is expecting three new approvals in AMP-002, AMP-008, and AMP-015 (teriparatide) and four new regulatory filings later this year. The news is not expected to slow down beyond 2024, as the company is placing a greater focus on developing proprietary and biosimilar products. Its 2025 pipeline is expected to comprise of 50% proprietary, 35% biosimilar, and 15% generic, compared to 21%, 16%, and 63% in 2021, respectively. With a solid financial foundation and diverse pipeline, Amphastar will be looking forward to future news and expanding its market-ready portfolio.

Apellis Pharmaceuticals

Apellis Pharmaceuticals' CEO Cedric Francois provided an overview of 2024 plans for the company, which are centered around novel treatments targeting the complement cascade, including its two approved pegcetacoplan injectable products, Empaveli for paroxysmal nocturnal hemoglobinuria (PNH) and Syfovre for geographic atrophy (GA).

Francois stated that there were four key priorities for Apellis in 2023: 1) increase access to Syfovre in the US; 2) expand Syfovre's geographic footprint beyond the US; 3) maximize Empaveli opportunities for PNH and evaluate pegcetacoplan for C3 glomerulopathy (C3G) and immune-complex-mediated membranoproliferative glomerulonephritis (IC-MPGN); and 4) advance the company's early pipeline. With respect to the first priority, Q4 revenues for Syfovre exceeded market expectations, suggesting likely success, based on data showing a slowing of GA progression over time, few episodes of retinal vasculitis, and positive physician feedback. For the second priority, there are no approved treatments outside the US, and as a result this remains a high unmet need. The CEO noted that the company expects a negative opinion from the EMA's Committee for Medicinal Products for Human Use (CHMP) regarding Syfovre, although

Francois reports that the company will appeal. The appeal process will be interesting to follow as the pivotal trial data were mixed (one positive and one negative trial), although Apellis highlighted new analyses demonstrating functional improvements in vision that combined with specialist feedback on Syfovre use may convince the regulator.

On a more positive note, safety data for Empaveli, including no cases of meningococcal infections and low thrombosis rates, will be reassuring for prescribers. Moreover, FDA approval of a new device for injecting Empaveli offers a more convenient administration for patients, which will be important as new orally administered competitors are expected to provide competition in 2024. In addition, early data for pegcetacoplan in patients with C3G and IC-MPGN are promising; there are currently no approved treatments. Pegcetacoplan showed reduced C3 complement deposition in glomeruli within 12 weeks in 13 patients from the Phase II NOBLE trial evaluating the drug in patients with C3G or IC-MPGN and who had undergone kidney transplants. The ensuing Phase III VALIANT trial is expected to have topline results in mid-2024. Apellis is also looking to expand its therapeutic area coverage with the development of gene edited therapies for other rare diseases.

Arrowhead Pharmaceuticals

Arrowhead Pharmaceuticals' president and CEO Christopher Anzalone provided this year's JPM presentation, summarizing the company's ongoing pipeline work, partnering initiatives, and plans for the year ahead. Before discussion shifted to specific projects in development, Anzalone briefly discussed Arrowhead's modular RNAi system consisting of libraries of targeting ligands, linker chemistries, and stabilization chemistries. The platform has allowed the company to discover candidates with enhanced pharmacokinetics that can act outside of the liver.

Anzalone noted that the company has its projects separated into four main verticals – cardiometabolic, pulmonary, liver, and neuromuscular. Cardiometabolic and pulmonary are two areas in which Arrowhead plans to largely retain development and commercialization rights in-house, but the company is still evaluating preclinical CNS projects and whether those will be partnered out. The two wholly owned candidates leading the cardiometabolic pipeline are plozasiran (ARO-APOC3) for familial chylomicronemia syndrome (FCS) and hypertriglyceridemia, and zodasiran (ARO-ANG3) for homozygous familial hypercholesterolemia and atherosclerotic cardiovascular disease. Phase III development for plozasiran in FCS should wrap up in Q2 2024, while Phase III development for zodasiran is planned to start in Q1. Pulmonary candidates entering Phase II this year include ARO-RAGE for asthma, ARO-MMP7 for idiopathic pulmonary fibrosis, and ARO-MUC5AC for COPD/asthma.

Of the 16 total candidates in Arrowhead's pipeline, four are partnered – one in Phase III with Amgen (olpasiran for cardiovascular disease), one in Phase III with Takeda (fazirsiran for alpha-1 liver disease), and two Phase II projects with GSK (JNJ-3989 for hepatitis B virus and GSK4532990 for NASH). Anzalone noted five targets that the company is potentially looking to partner: ARO-PNPLA3 (NASH), ARO-C3 (complement-mediated disease), ARO-DUX4 (facioscapulohumeral muscular dystrophy), ARO-DM1 (myotonic dystrophy type 1), and ARO-CFB (complement-mediated disease).

The company is following a "20 in '25" initiative, with the goal of having 20 individual drugs in

clinical trials or at market in 2025. Anzalone noted that Arrowhead has seen almost $1bn in partnership money over the past six years, which has helped fund ongoing development activities. The company also recently grossed $450m through a public offering, which was the first time the company had raised money publicly in five years. Looking forward, he anticipates multiple product launches in the next five years and substantial opportunities for additional partnering deals.

Ascendis Pharma

Jan Møller Mikkelsen, president and CEO, highlighted the company's recent activities, pipeline developments, and plans for 2024. The presentation kicked off with mentions of the US-approved Skytrofa for pediatric growth hormone deficiency (GHD) and the EU-approved Yorvipath for adult chronic hypoparathyroidism.

Mikkelsen noted that Skytrofa, which had previously received orphan drug designation both in the US and EU, had accumulated around €64m in revenue by Q4 2023, and Ascendis anticipates the drug will eventually bring in around €320m–€340m by the end of 2024. These figures are bolstered by the recent achievements of the company which include the completion of the Phase III enliGHten trial in a pediatric population with GHD which showed that of those who completed treatment, 59% met or exceeded their average parental height standard deviation score (SDS), with mean Skytrofa treatment duration of 3.2 years. For those who completed treatment, the baseline mean height SDS at the beginning of the open-label extension trial was -1.6, compared to mean height SDS of -0.4 (achieving height similar to their parents) at their final study visit.

Following these results, Ascendis announced plans to submit a supplemental Biologics License Application to the US FDA for the adult GHD indication in Q2 2024. Furthermore, Ascendis announced the Clinical Trial Application submission for the Phase II COACH trial – which is a combination trial of Skytrofa and TransCon CNP – with topline results of the trial expected in Q4 2024.

The presentation also highlighted Ascendis's commercial organization of the launch of Yorvipath. Following its EU approval, the company anticipates launching Yorvipath in Germany in January 2024 with an initial list price of €105,000 per patient per year. Looking beyond this, Ascendis also plans to expand into the next major markets across Europe by the end of 2025, where the company estimates there are over 100,000 additional adults with chronic hypothyroidism who could benefit from the use of Yorvipath. The company plans to do this by providing commercial products through early access routes, such as "named patient," until commercial reimbursement is established.

Focusing on the US market, the FDA has set a PDUFA date of 14 May 2024 for Yorvipath, and if approved, Ascendis expects a US product launch in Q3 2024. Ascendis is hopeful of a rapid efficient launch in the US due to an experienced commercial team already in place through the company's established, proven endocrinology disease infrastructure.

Towards the end, the presentation focused on growing Ascendis's commercial presence in the rest of the world. This focused on VISEN's exclusive licensing agreement for TransCon hGH, TransCon PTH, and TransCon CNP in China, as well as Teijin's exclusive licensing agreement for

TransCon hGH, TransCon PTH, and TransCon CNP in Japan. In China, VISEN's TransCon hGH Phase III and TransCon CNP Phase II trials have now been completed, whereas in Japan the Phase III PaTHway trials have been completed. The presentation also highlighted that Ascendis has expanded its global reach through exclusive distribution agreements with geographical market leaders, and as of January 2024 the company has established three regional agreements.

The presentation concluded by introducing Vision 2030, which was broken down into three sections. The aim of Vision 2030 is for Ascendis to become a leading endocrinology rare disease company, to create value in additional therapeutic areas through innovative business models, and finally to outperform industry drug development benchmarks with the company's product innovation algorithm.

Azenta Life Sciences

Azenta remains an established life sciences company with a unique portfolio of end-to-end sample management, holding a strong track record in developing and serving an attractive high-end growth market. Leading the company for over 13 years, CEO Stephen S. Schwartz addressed the crowd with confidence on the company's growth forecast for the next 10 years, creating value in the sample management space. The company currently (in the fiscal year ending Q4 2023) performed at 2% organic growth, outperforming the market, with positive free cash flow and 25% YOY growth aided by the completion of the acquisition of Ziath, Ltd. a year earlier. Azenta ended the year with $600m in revenue and a balance sheet well positioned to add value. Schwartz forecasted 5–8% growth alongside the next 6–8 quarters of strong pipeline growth. The company announced a $1.5bn share buyback plan 14 months ago, with $950m in shares already purchased and the remainder to be completed in 2024. It also recently announced a governance change, having nominated three additional directors to the board with operational and scientific specialties.

Watching momentum build in a $10bn market size, Azenta has reached sustained growth of $700m ($10m in 2011), barely penetrating the surface with over 10,000 customers in 150 countries. Primarily focused on growth and innovation, the company has realigned its drive and is prioritizing investments into its sales organization, hoping to see results in the next couple of years. With strong growth prospects and tailwinds due outsourcing ~50% of its R&D, Azenta has seen 2x growth over a five-year period and is confident of similar results in the next three years, forecasting long-term growth in the cell and gene therapy space as well as being a leader in the cryogenic technology space.

Schwartz also discussed the three additional segments reported by the company: 1) added samples management solutions, bringing in $300m in revenues in 2024; 2) multiomics segment adding to scientific capabilities, generating $250m with considerable scale; and 3) B Medical, a vaccine delivery capability enabling access to remote and critical parts of the world, generating $113m. As a growth company, Azenta is planning to reach $2bn in revenues over the next five years, with a 2024 forecast of a 75% increase in adjusted EBITDA, adding revenue on top.

BridgeBio Pharma

BridgeBio Pharma CEO Neil Kumar commenced the company's JPM Healthcare Conference presentation with unwavering optimism for the year ahead and the company's long-term journey to becoming a fully integrated pharmaceutical company. Kumar briefly outlined the company's R&D engine and promising genetic medicine pipeline before moving on to key priorities for 2024, principally the commercial launch of acoramidis for ATTR-cardiomyopathy (ATTR-CM).

Following a brief introductory overview, Kumar went into great detail regarding the company's confidence in acoramidis, its potential to significantly improve patient outcomes as well as relevant advancements in patient identification and market landscape developments. BridgeBio submitted the NDA for acoramidis in December 2023 and announced in its presentation that it expects to submit marketing authorization to the EMA in the near future. An outline of previous data from the Phase III ATTRibute-CM trial was presented before two new pieces of encouraging data were teased, the first of which interestingly showed a correlation between stabilization in serum TTR, serum TTR, and survival rates. Secondly, cardiovascular MRI preliminarily showed that acoramidis may lead to actual disease regression in some patients, as evidenced by a decrease in extracellular volume of the heart. The presentation then moved on to BridgeBio's commercial and marketing strategy for acoramidis, mentioning its strong position with deep expertise and strong relationships with experts in the cardiovascular field.

Kumar used the rest of the presentation to discuss the company's late-stage pipeline with potential best-in-class and first-in-class therapies for rare diseases, mainly its achondroplasia and limb-girdle muscular dystrophy programs. BridgeBio is aiming for a best-in-class FGFR3 inhibitor with its low-dose once-daily oral sachet FGFR inhibitor infigratinib and has recently initiated Phase III study, with enrollment expected to complete in the first half of 2024. Regarding the limb-girdle muscular dystrophy program, BridgeBio is developing BBP-418, a first potential therapy for this disease, and expects enrollment to be completed in the Phase III trial in the first half of 2024.

Kumar emphasized that launching acoramidis is the company's first and most important goal for 2024, as well as focusing on progressing its achondroplasia and muscular dystrophy assets. BridgeBio is poised at the cusp of making a significant impact in the field of genetic medicine, with a promising late-stage pipeline focusing on unmet needs and a strong positioning ahead of the launch of acoramidis.

Denali Therapeutics

Denali Therapeutics is on the verge of transitioning from a purely development company whose only source of revenue comes from partnering agreements with large-cap biotech companies to having its own products to commercialize while continuing its profitable partnerships to further develop its technology and pipeline. Denali has divided its strategy into two phases, termed Peak 1 and Peak 2. Peak 1 consists of its current programs of small molecules and the first of its newer transport vehicle (TV) platform drugs. Peak 2 will consist of all TV-enabled drugs specifically targeting Alzheimer's disease and Parkinson's disease. Denali is estimating potential profits of up to $10bn for Peak 1 programs and over $10bn for Peak 2 programs.

For Peak 1, Denali is expecting to complete enrollment of its Phase II/III COMPASS study of DNL310 for Hunter syndrome and Phase II/III HEALEY study of DNL343 for the treatment of amyotrophic lateral sclerosis (ALS). Denali is also expecting first data from its Phase II HIMALAYA study of DNL788 for ALS, and further data from DNL310 for Hunter syndrome. For Peak 2, Denali heavily emphasized the advantages of the blood-brain barrier-crossing technology of its TV-enabled drugs, showing advantages of distributing capabilities, superior plaque reduction, less vascular localization, and fewer ARIA events in mice. Overall, Denali has solid backing from partners such as Biogen, Sanofi, and Takeda, and has capitalized $1.12bn with runway into 2027.

Immunovant

CEO Peter Salzmann highlighted the significance of IgG autoantibodies in causing autoimmune diseases. The once-considered undruggable nature of autoantibodies, due to patient-specific variations by polymorphism, was overcome with the discovery of the neonatal Fc receptor (FcRn). Immunovant harnesses its anti-FcRn technology to bind and inhibit FcRn, resulting in the degradation of IgG antibodies. Salzmann further emphasized the significant potential of targeting FcRn, which is evident from two approvals for myasthenia gravis (MG) and ongoing clinical trials involving FcRn for 21 additional indications. The reduction of IgG levels in clinical trials serves as a well-established biomarker that can expedite development programs. Immunovant's assets possess three distinct attributes: 1) the convenience of self-subcutaneous injection for frequent and long-term use; 2) a notable correlation between deep IgG reduction and enhanced clinical efficacy; and 3) tailored dosing strategies that align with the induction and maintenance dosing patterns of the top 10 immunology drugs.

Immunovant's leading asset, batoclimab, is currently undergoing three pivotal studies for the treatment of MG, thyroid eye disease (TED), and chronic inflammatory demyelinating polyneuropathy (CIDP), as well as a proof-of-concept study for Graves' disease (GD). In the MG trial, batoclimab offers dosing flexibility to physicians due to the highly variable nature of the disease. The topline data for MG are expected to be available in H2 2024. Similarly, topline data for treating CIDP are anticipated in H1 2024. Batoclimab has the potential to become a pioneering treatment for TED, as it effectively targets anti-TSHR autoantibodies associated with this condition. While positive findings were already released last year, the topline results for TED are expected in H1 2025. In December 2023, Immunovant released positive proof-of-concept data of batoclimab for treating GD. Comprehensive topline data for this disease are anticipated in H1 2025. To address concerns about potential LDL elevation caused by batoclimab, Immunovant has developed the next-generation product IMVT-1402. The Phase I study of IMVT-1402 has recently concluded, demonstrating minimal impact on albumin and LDL levels. The composition of matter patent for IMVT-1402 is expected to extend until 2043. Leveraging the knowledge gained from batoclimab, IMVT-1402 is positioned to be a first-in-class treatment for GD and a best-in-class option for MG and refractory rheumatoid arthritis.

When questioned about the decision to pursue batoclimab in different indications with concerns about LDL, Salzmann provided different responses based on the specific indication. The GD trial of batoclimab aims to establish the optimal dosage and efficacy, which will inform the potential of IMVT-1402. Once positive data for GD are obtained, Immunovant plans to transition that

program to IMVT-1402. In addition to IGF-1R drugs, batoclimab offers a competitive advantage in treating TED through its unique mechanism and fixed-duration regimen, addressing an unmet need in the disease. For MG patients treated with an induction and maintenance approach, Salzmann anticipated favorable response in IgG reduction to a lower dose of batoclimab during the maintenance period, with minimal impact on analytes. In the case of CIDP, the company may switch to IMVT-1402 for registration if it observes a dose response with batoclimab.

Insmed

Insmed's CEO William Lewis began the presentation with confidence surrounding the upcoming year for Insmed and the company's anticipated milestones. This upcoming year is believed to be a transformational year for the company, with the greatest growth and expansion in the company's history expected in 2024. This anticipated success is built upon the four pillars of the company – Arikayce, brensocatib, treprostinil palmitil inhalation powder (TPIP), and its early-stage research – all of which were touched on during the presentation.

Arikayce experienced 24% YOY growth in its fifth year since the launch of the drug, and the company anticipates continuing the trend of double-digit growth through 2024, with its revenue guidance expectations falling at $340m–$360m. Lewis touched on the Phase IIIb ENCORE front-line study that is currently ongoing for Arikayce for newly diagnosed Mycobacterium avium complex (MAC) disease, with enrollment completion expected in 2024 and topline data following in 2025. If this trial achieves success and leads to a label expansion in all patients with MAC lung disease and newly diagnosed nontuberculous Mycobacteria (NTM) MAC, it could result in the expansion of the Arikayce commercial opportunity by 3–5 times and lead to the growth of Arikayce to a greater than $1bn peak sales product.

Lewis described the upcoming Phase III ASPEN topline readout as one of the most impactful and anticipated events to occur in Insmed's history. This data readout will be key in determining the future for brensocatib and whether this year will be as transformative for the company as hoped. If the ASPEN trial shows success with statistical significance between $p<0.01$ and $p<0.05$, the company will file for approval for the bronchiectasis indication, for which there are no currently approved treatments. Not only that, but this could result in awareness and potential for broader use of the DPP-I pathway to treat other diseases. Lewis mentioned that competitor Boehringer Ingelheim has already started pursuing development of a DPP-I drug for bronchiectasis following the success of Insmed's Phase II brensocatib WILLOW study. Insmed also plans to expand this once-a-day convenient chronic oral treatment with uses in chronic rhinosinusitis without nasal polyps, being studied currently in the Phase II BiRCh trial, and hidradenitis suppurativa.

Insmed's TPIP therapy for pulmonary arterial hypertension (PAH) and interstitial lung disease-related PH (PH-ILD) was the last major update out of the four pillars. Lewis reminded listeners that highly encouraging blinded data generated from its Phase II TPIP program were released in October 2023. A KOL described the hemodynamic changes as stunning. In the upcoming months, a topline readout for the Phase II PH-ILD study is expected before the end of Q2 2024. The presentation outlined what the company would define as success in regard to this study, and if the study is successful Insmed plans to move straight to Phase III development. TPIP has the potential to be the prostanoid of choice in the PH-ILD and PAH markets, and if it

moves forward it would be the only inhaled prostanoid that with once-a-day administration with a slow release of TPIP for continuous treatment day and night.

Lewis closed the presentation by highlighting the company's research capabilities for its early-stage pipeline and outlined important upcoming momentum-building catalysts through 2025. He mentioned that the company has over 30 preclinical programs with high potential in the future once it goes past these upcoming important milestones, and low ongoing expenditure for its early pipeline.

Intra-Cellular Therapies

Intra-Cellular Therapies' CEO Sharon Mates presented the company's progress over 2023 at the 42nd annual J.P. Morgan Healthcare Conference, predominantly focusing on the continued successful launch of Caplyta. Mates highlighted the exceptional Rx growth of approximately 85% seen with Caplyta in 2023 compared to 2022. The execution of this was attributed to increased breadth and depth of prescribing and a strong market access position. Caplyta initially launched in March 2020 for schizophrenia. The agent then later saw a significant increase in net sales following its additional launch in bipolar depression in December 2021, with the growth of sales attributed to a strong underlying Rx demand. Mates celebrated Caplyta's compelling product profile by underlining the agent's proven efficacy, favorable safety profile, and convenient dosing. Caplyta's once-daily dosing, with no titration required, was once received with skepticism from physicians but has since proved to be an undeniable advantage for the drug, particularly through the COVID-19 pandemic in which it became apparent that a non-titration therapy offered a considerable relief of treatment burden. The agent's competitive edge was also displayed as Mates recognized Caplyta as the first and only treatment indicated for bipolar I and II depression in adults, as both a monotherapy and as an adjunctive therapy with lithium or valproate. The 2023 financial year net sales guidance for Caplyta has been estimated at $460m–$470m.

In the upcoming year and onwards, the company is focused on advancing growth for Caplyta by both maximizing its use in its current indications and by expanding across the mood disorder spectrum. The company plans to drive growth in its current indications by investing in prescriber education and broad national advertising. The company plans to educate over 43,000 prescribers through experienced sales specialists, peer-to-peer medical education programs, and robust digital promotion. Intra-Cellular Therapeutics also plans to enhance visibility to potential patients with bipolar disorder through television and social media campaigns. Plans to establish Caplyta across depressive disorders are already under way, with a comprehensive Phase III program investigating the agent in adjunctive major depressive disorder (MDD). The large antipsychotic market is estimated to represent 67.8 million Rxs, of which Caplyta currently addresses 50% with its approvals in bipolar depression and schizophrenia. An approval for adjunctive MDD would expand the market substantially for Caplyta, increasing this 50% addressable market to 80%. The company has planned four studies in the comprehensive adjunctive MDD Phase III program, namely Study 501, Study 502, Study 505, and Study 503. Mates stated that the company is on track for topline data readouts for Study 501 and Study 502 in Q1 and Q2 2024, respectively. Caplyta is also under Phase III investigation for pediatric indications.

In the presentation, Mates also highlighted the roadmap for the company's early-stage pipeline. Agents of particular interest include the PDE1 inhibitors, which are currently in a Phase II development program for Parkinson's disease but may also help broaden the company's therapeutic portfolio beyond neurological diseases via initiation of a cancer immunotherapy program. The company's preclinical portfolio of non-hallucinogenic psychedelics was also championed. It was suggested that these agents have the potential to treat mood and other neuropsychiatric disorders without the liabilities of hallucinations and cardiac valvular pathologies of known psychedelics. The company hopes to enter human testing in late 2024 and early 2025 with lead product ITI-1549.

Jazz Pharmaceuticals

Jazz Pharmaceuticals' chairman and CEO Bruce Cozadd provided an overview of the company and disclosed business and financial updates on the first day of the 42nd annual J.P. Morgan Healthcare Conference. The Jazz Pharmaceuticals presentation segmented the company into three primary areas: commercial, pipeline, and corporate development.

As a part of the commercial update, Jazz expects double-digit percentage revenue growth across combined key growth drivers including Xywav, Epidiolex, and Rylaze. This expectation also includes meeting 2023 total, neuroscience, and oncology revenue guidance released in its Q3 2023 earnings announcement. Total revenue guidance for the year ending 2023 remains in the $3.75bn–$3.875bn range, with 49% of revenue so far driven by oncology and Epidiolex, and the remaining attributed to sleep revenue. By 2025, it is hoped that revenue will approach $5bn, with 60% of revenues driven by oncology and Epidiolex.

On the corporate development front, Jazz remains active with $1.6bn in cash and is targeting opportunities to drive topline revenue growth and diversification in 2024 heading into 2025. It highlighted recent agreements and acquisitions that have already set the stage for this growth strategy, namely the acquisition of GW Pharma in 2021 and the zanidatamab licensing agreement with Zymeworks in 2022.

For pipeline updates, Jazz expects multiple near-term catalysts and emphasized the importance of zanidatamab, which recently had its BLA submission initiated for potential accelerated approval in second-line biliary tract cancer. Jazz expects to complete the BLA submission in the first half of 2024. Jazz also announced that it has increased enrollment in the zanidatamab Phase III HERIZON-GEA-01 trial from 714 to 918 to improve statistical power for OS analysis, while maintaining the late 2024 PFS topline readout target based on the original enrollment total, which would maintain an earliest possible time to approval based on PFS and increases the probability of success of OS with two interim readouts and a final OS readout.

Jazz expects a Phase III topline PFS readout for Zepzelca, already approved for second-line use, in extensive stage first-line small cell lung cancer in combination with Tecentriq (atezolizumab) in collaboration with Roche by late 2024 or early 2025. Jazz also expects to have a topline data readout from the Phase IIb suvecaltamide essential tremor study late in the first half of 2024. Topline data are also expected for Epidiolex in the second half of 2024 from the pivotal Phase III trial for Dravet/Lennox-Gastaut/tuberous sclerosis complex in Japan. The company then noted that early programs such as JZP815 and JZP898 are continuing to advance in Phase I studies.

Madrigal Pharmaceuticals

Following NDA acceptance and the granting of priority review in September 2023 for its primary asset resmetirom, an oral thyroid hormone receptor-beta agonist, Madrigal Pharmaceuticals is on track to shift into a commercial pharmaceutical company. Bill Sibold, the newly appointed CEO, focused his presentation on the upcoming PDUFA decision in non-alcoholic steatohepatitis (NASH) for resmetirom in March 2024 and how the company has prepared for its commercialization.

The presentation kicked off with a personal story from a patient advocate. The story highlighted the significant unmet need in NASH and its heavy burden on healthcare systems, accentuated by a lack of disease awareness and therapeutic options. Sibold highlighted that the opportunity to position Madrigal as the leading biopharmaceutical company in NASH will be driven by resmetirom becoming the first foundational therapy for NASH with significant fibrosis. He then stressed that Madrigal is ready to achieve this goal, promising to capitalize on the first-to-market status of resmetirom to ensure an effective specialty launch, supported by an experienced commercial team and backed by robust clinical data.

Looking at the clinical data, Sibold again noted resmetirom's profound effects on both key endpoints of interest to regulators: (i) a one-stage improvement in fibrosis without worsening of NASH; and (ii) NASH resolution without worsening of fibrosis. In addition, resmetirom also demonstrated meaningful improvements on non-invasive fibrosis biomarkers and lipid measures. Rounding out the discussion, Sibold emphasized the favorable safety profile of resmetirom. Most discontinuations were GI-related (diarrhea, characterized as loose stools), but were limited to the first 12 weeks. Overall, resmetirom showed a satisfactory safety profile, fitting its position as a chronic therapy.

Looking forward, Madrigal is expecting to rapidly launch resmetirom upon approval in 2024. Sibold hopes to draw from his personal experience launching Dupixent to establish a path from diagnosis to fulfillment for resmetirom, ultimately securing clear market access. Commenting further on the launch execution, Sibold noted that the company will initially target hepatologists and gastroenterologists. Importantly, liver biopsy is not seen as an access barrier. Pricing, however, will be an ongoing crucial discussion with payers ahead of launch. Beyond 2024, Madrigal also hopes to achieve full approval for resmetirom and to secure additional label expansion in compensated cirrhosis patients.

Nuvalent

Nuvalent creates precisely targeted therapies for patients with cancer by focusing on chemistry and structure-based drug design. CEO Jim Porter started the presentation by explaining how the company is differentiated from others through its relationships with the physician-scientists responsible for developing early-generation kinase inhibitors, allowing for insight into the limitations of these therapies and the unmet needs within the market. For example, first-generation kinase inhibitors often hit off targets, leading to dose-limiting adverse events. Investigators at Nuvalent believe that more selective inhibitors allow for deeper and more durable responses and, consequently, have the potential to become best in class.

The company disclosed its lead programs for ROS1+ and ALK+ non-small cell lung cancer (NSCLC), as well as the supportive preclinical data, in 2021. In 2022, Nuvalent demonstrated clinical proof of concept for its ROS1+ program, disclosed a third novel program for HER2 exon 20 insertion-positive NSCLC, and initiated two global Phase I/II studies, ARROS-1 (for NVL-520 in ROS1+ NSCLC) and ALKOVE-1 (for NVL-655 in ALK+ NSCLC). In 2023, clinical proof-of-concept data were demonstrated for the ALK+ program, the HER2 program was advanced to IND, and the Phase II portion of the ARROS-1 trial was initiated, which is designed to support registration in previously treated ROS1+ patients. Nuvalent ended 2023 with approximately $719.9m in cash, cash equivalents, and marketable securities.

The speaker largely focused on the company's ROS1+ and ALK+ programs in the presentation, and highlighted the potential for its assets to supplant the current first-line standard of care for these NSCLC subtypes. There are currently five approved therapies for ALK1+ NSCLC, with alectinib as the first-line standard of care and lorlatinib as second-line standard of care. However, there is no clear standard of care for third-line patients, many of whom have ALK compound resistance mutations not treatable by current therapies. Despite having higher activity levels, lorlatinib does not get front-line use because it hits an off target called TRK in the CNS, which can lead to a broad spectrum of nervous system disorders. The unmet needs in ROS1+ NSCLC are comparable. There are three approved therapies, with the standard of care being crizotinib, which is not highly brain penetrable, so many patients with CNS disease, as well as ROS1+ resistance mutations, will progress. The other two therapies face the same issue as lorlatinib regarding TRK off-targeting.

The Phase I portion of the ALKOVE-1 trial is designed to understand the safety of NVL-655, an ALK-selective, TRK-sparing inhibitor for ALK+ NSCLC, and to establish a recommended dose to progress to Phase II. Preliminary Phase I data released in 2023 showed activity in patients with diverse single ALK resistance mutations and patients with diverse compound ALK resistance mutations. Additionally, the drug induced intracranial responses in patients with TKI-refractory ALK+ NSCLC, suggesting strong brain penetrance, and demonstrated selective ALK inhibition compared to off-target TRK, leading to a favorable safety profile.

In preliminary Phase I data, after treatment with NVL-520, a ROS1-selective, TRK-sparing inhibitor, activity was observed in patients with ROS1+ NSCLC, including after exhausting approved and investigational therapies. Additionally, activity was observed in patients with ROS1+ resistance mutations and in patients with a history of CNS metastases. NVL-520 demonstrated a clean safety profile, with no dose reductions or treatment discontinuations due to adverse events.

In 2024, Nuvalent aims to progress the Phase II ARROS-1 trial with registrational intent and to initiate the Phase II portion of the ALKOVE-1 trial, designed to support registration in previously treated ALK1+ patients, while also releasing Phase I/II data from both the ROS1+ and ALK+ programs. Additionally, the company expects to initiate a Phase I trial for its HER2 program and to launch the first-line ALK+ development strategy. Nuvalent is aiming for its first pivotal data release in 2025 and for at least one of its products to gain approval by 2026.

PTC Therapeutics

Matthew Klein, CEO at PTC Therapeutics, described an eventful 2023 for the company, with a total unaudited net product revenue of $661m, representing 23% YOY growth, largely driven by its Duchenne muscular dystrophy (DMD) franchise, Translarna and Emflaza, which together generated an unaudited net product revenue of $610m. Translarna growth was driven by new patients in existing geographies, as well as geographic expansion, and Emflaza growth was attributed to continued new prescriptions, high compliance, and more favorable access. Many changes were implemented within the company in 2023, including reductions of operating expenses and headcount by approximately 25% and 30%, respectively, the refocusing of the company's R&D portfolio, and the strengthening of its balance sheet. Additionally, the company reported positive clinical data from the Phase III APHENITY trial of sepiapterin in adult and pediatric patients with phenylketonuria (PKU), the Phase IIa PIVOT-HD trial of PTC518 in Huntington's disease (HD), and the Phase II/III MOVE-FA trial of vatiquinone for Friedreich's ataxia.

Focusing on sepiapterin, APHENITY met the primary endpoint by showing statistically significant reductions in blood phenylalanine levels in patients with PKU. Sepiapterin treatment enabled increased dietary phenylalanine intake in these patients and was well tolerated, with no serious adverse events. The results support the potential for sepiapterin to address a broad PKU population, including those who are treatment-naïve, those who have failed on current therapies, and those who are not well controlled by current therapies.

PTC518 has several key attributes that could potentially drive its differentiation in the HD market. It is orally bioavailable, it penetrates the blood-brain barrier, it is titratable and reversible, and it can reduce HTT mRNA and protein in the CNS and periphery. PTC released 12-week data from Part A of the PIVOT-HD trial in June 2023 which showed a dose-dependent lowering of mHTT protein levels in peripheral blood cells, with a 30% reduction for the 10mg cohort and a 21% reduction for the 5mg cohort, compared to a 12% increase in mHTT protein levels for the placebo group. Additionally, targeted PTC518 exposure in the CSF was reached at week 12 and was consistent with or higher than free plasma drug levels, demonstrating the drug's ability to cross the blood-brain barrier. These CSF results are important as PTC is primarily focused on mHTT reduction in the brain, as opposed to peripheral blood cells.

Key regulatory and clinical milestones expected in 2024 include MAA and NDA submissions for sepiapterin in PKU, a BLA submission for Upstaza in aromatic L-amino acid decarboxylase deficiency, and 12-month Part B data from the PIVOT-HD study for PTC518 in HD (which will include blood, CSF, and radiographic biomarkers). Additionally, the company expects topline results from the CARDINALS study for utreloxastat in amyotrophic lateral sclerosis (ALS), a Type C regulatory meeting with the FDA for vatiquinone in Friedreich's ataxia, and EU Committee for Medicinal Products for Human Use (CHMP) supplemental filing results for Translarna in DMD. Total revenue guidance for 2024 is $600m–$850m, with the low end of the guidance representing a potential negative CHMP opinion for Translarna in DMD, and the highest estimate representing a positive opinion.

Recursion Pharmaceuticals

Recursion Pharmaceuticals, a data-driven AI-based company, excels in conducting in silico experiments to assess the success of pipeline compounds targeting specific protein targets. During the JPM presentation, the CEO Chris Gibson unveiled the timeline of clinical readouts for its five programs, comprising four rare disease programs and one oncology program. Notable highlights include a Phase II readout for cerebral cavernous malformation in Q3 2024, Phase II safety and preliminary efficacy readouts for neurofibromatosis type 2 and familial adenomatous polyposis in Q4 2024 and H1 2025, respectively, a Phase II safety readout for Clostridioides difficile infection in 2024, and a Phase II safety and preliminary efficacy readout for AXIN1 for APC-mutant cancers in H1 2025. Recursion's therapeutic discoveries have garnered significant partnerships, including collaborations with Roche in the neuroscience space and Bayer in undruggable oncology targets. Additionally, Recursion has formed alliances with Nvidia for computation and machine learning/AI, Tempus for real-world data, and Enamine for chemical synthesis.

During the presentation, Gibson showcased Recursion's latest platform, LOWE (Large Language Model-Orchestrated Workflow Engine). LOWE integrates multiple modules developed by Recursion, covering protein target identification, compound optimization, and in vivo drug metabolism and pharmacokinetics (DMPK). Phenomics, for instance, enables high-throughput screening, with 2.2 million weekly experiments across 50 human cell types, with CRIPSR/Cas9 knockouts treated with 2 million compounds, generating over 1 billion cell images to correlate biology and chemistry. The DMPK module optimizes compounds using predictive models and in vivo validation, ensuring suitable pharmacokinetics. InVivomic prioritization uses machine learning to evaluate compounds and doses for animal studies, providing insights into safety and toxicity profiles. By combining real-world patient data from TEMPUS and leveraging Nvidia’s supercomputer, LOWE enables the examination of phenotypes affected by genetic and chemical perturbations, thereby informing the identification of the most promising chemical candidates for subsequent animal and clinical studies with minimized risk.

In 2023, Recursion achieved significant milestones including advancing multiple Phase II trials, establishing partnerships with prominent pharmaceutical and technology companies, acquiring Cyclica and Valence, and developing the advanced LOWE platform with enhanced calculation capabilities. As of 2024, Recursion begins with a strong financial position, holding $390m in cash. Its plans for the year include filing an IND application for ovarian cancer, commencing two Phase II studies, and unveiling clinical readouts for two Phase II programs. Furthermore, Recursion aims to forge new partnerships to further expand its pipeline in the cardiovascular domain.

Sarepta Therapeutics

At the 42nd annual J.P. Morgan Healthcare Conference, Sarepta Therapeutics, a leading developer of RNA-based gene therapies, showcased its progress over the last seven years and gave an outlook for the near future. CEO Doug Ingram started with an overview of company progress from 2017. Sarepta started with one technology platform – RNA, a pipeline of six, and revenue of $5m. Fast forward to today, Sarepta now has three technology platforms (RNA, gene

therapy, and gene editing), a pipeline of over 40 drugs with four on-market therapies, and an estimated 2023 revenue of $1.145bn that is now bringing in profit.

Sarepta continues to push the boundaries of gene therapy in challenging conditions such as rare neuromuscular diseases, particularly Duchenne muscular dystrophy (DMD). The presentation centered on Elevidys (delandistrogene moxeparvovec-rokl), a single-dose, adeno-associated virus (AAV)-based gene transfer therapy for intravenous infusion designed to address the underlying genetic cause of DMD. Elevidys was first granted approval in the US in June 2023 for the treatment of ambulatory pediatric patients aged 4–5 years with DMD with a confirmed mutation in the DMD gene. Sarepta is looking to expand the label to DMD patients without restriction to age or ambulatory status based on results from EMBARK (Study SRP-9001-301), a global, randomized, double-blind, placebo-controlled, Phase III clinical study in patients with DMD aged 4–7 years. EMBARK achieved statistical significance on all prespecified key secondary endpoints, showing that the functional benefits of Elevidys are not limited to a particular age group. The company expects an approval decision in August 2024.

In addition to the update on Elevidys, Sarepta also expects to announce clinical data for its next-generation RNA-based therapy SRP-5051 for DMD in 2024, in addition to executing R&D productivity, including a novel new capsid and approaches to clearing pre-existing antibodies. By 2030, Sarepta is poised to become a big biotech, focusing on cutting-edge genetic medicine.

Shockwave Medical

Shockwave Medical's CEO Doug Godshall described the progress of the company during 2023 and the outlook for 2024 and beyond. Shockwave is a medical technology company that produces intravascular lithotripsy (IVL) catheters which modify calcium through a specific form of sonic pressure waves. These catheters are used to target complex calcified anatomies, while minimizing complications, and the company considers the technology to be simple to use, which allows it to be easily integrated into clinical procedures.

Godshall enthusiastically described the company's current portfolio, which currently has three catheter products (Shockwave L6, Shockwave M5+, Shockwave S4) for use in peripheral arteries, and two catheter products (Shockwave C2, Shockwave C2+) for coronary arteries. Since 2017, these IVL catheters are estimated to have treated >400,000 patients worldwide. Shockwave's pipeline quadrupled between 2021 and 2023, with 27 development programs ongoing in 2023 versus just seven in 2021. The company has made significant progress in gaining Medicare reimbursement for its products, and in 2023 coronary inpatients were able to receive reimbursement. Reimbursement access is set to be expanded to include coronary physicians in 2024, with the aim of providing reimbursement to coronary outpatients in the future. In terms of the long-term financial outlook of the company, Godshall expects that between 2024 and 2026, the company will experience a 25% CAGR in revenue and will receive over $600m in R&D investment. A key milestone for the company during 2024 will be setting up a new production facility in Costa Rica.

SpringWorks

CEO Saqib Islam began the SpringWorks presentation by highlighting the company's 2023 achievements which will set the stage for continued success in 2024. Most notable was the launch of the Ogsiveo (nirogacestat), the first and only FDA-approved therapy for adult patients with desmoid tumors requiring systemic treatment, with the potential to become the standard of care. The FDA had previously granted breakthrough therapy, fast track, and orphan drug designations for the oral gamma secretase inhibitor, and approval was based on the results of the Phase III DeFi trial which demonstrated a 71% reduction in the risk of disease progression and statistically significant and clinically meaningful improvements in patient-reported outcomes. The company expects to submit a Marketing Authorization Application for desmoid tumors in Europe in H1 2024. There are advanced expansion opportunities for Ogsiveo as a monotherapy in ovarian granulosa cell tumors (initial data for a Phase II study are expected in the second half of 2024) and with a BCMA combination therapy in multiple myeloma. Nirogacestat has a durable patent portfolio of 10 Orange Book-listable patents, with the latest expiring in 2042.

Islam also discussed positive topline data from the pivotal Phase IIb ReNeu trial evaluating SpringWorks' other lead program, mirdametinib, an investigational oral MEK inhibitor, in pediatric and adult patients with neurofibromatosis type 1-associated plexiform neurofibromas (NF1-PN). Data demonstrated a confirmed objective response rate of 52% in pediatric patients and 41% in adult patients. The deep and durable responses support a potential best-in-class profile in pediatric NF1-PN patients. Mirdametinib was granted fast track and rare pediatric disease designations by the FDA, and orphan drug designation by both the FDA and European Commission. Within the first half of 2024, the company plans to submit an NDA to the FDA for children and adults with NF1-PN, as well as present detailed ReNeu trial data at a major medical conference.

Other milestones anticipated for SpringWorks' emerging pipeline include data from a Phase I trial of SW-682 (TEAD inhibitor) in Hippo mutant solid tumors in the first half of 2024, and additional data released for brimarafenib as a monotherapy in MAPK-mutant solid tumors in the second half of the year.

Islam emphasized that a solid foundation and clear drivers are in place for long-term success – the first product launch is under way, with a near-term approval path for a second asset, durable IP protections, a deep pipeline of late- and early-stage oncology programs with several near-term catalysts, and a capital-efficient operating model and strong balance sheet.

Summit Therapeutics

At the J.P. Morgan Healthcare Conference, Summit Therapeutics emphasized its 2024 focus to execute on Phase III clinical trials and expand the company's clinical development plan, with its overall mission of improving quality of life, increasing potential duration of life, and resolving serious medical healthcare needs.

CEO and president Maky Zanganeh began the presentation by highlighting the company's lead compound, ivonescimab. In 2023, Summit in-licensed ivonescimab from its partner, Akeso, a

leading biopharma company in China with extensive manufacturing capabilities.

Ivonescimab is intentionally designed to improve the safety and efficacy standard of two established and approved targets: PD-1 and VEGF. Ivonescimab's cooperative binding increases the binding strength of each target in the presence of the other target, allowing for strong, simultaneous blocking of both PD-1 and VEGF, which are present at their highest concentrations in and around tumors. Ivonescimab's tetravalent structure enables higher avidity in the tumor microenvironment with over 18-fold increased binding affinity to PD-1 in the presence of VEGF in vitro, and over four times increased binding affinity to VEGF in the presence of PD-1 in vitro. This tetravalent structure, the intentional novel design of the molecule, and bringing these two targets into a single bispecific antibody with cooperative binding qualities have the potential to direct ivonescimab to the tumor tissue versus healthy tissue. The intent of this design is to improve upon previously established efficacy thresholds, in addition to side effects and safety profiles associated with these targets.

Clinical Phase II data for ivonescimab in combination with chemotherapy in first-line advanced/metastatic squamous non-small cell lung cancer (NSCLC) demonstrated median PFS of 11.1 months, exceeding that seen in the Phase III KEYNOTE-407 trial of standard-of-care pembrolizumab in combination with chemotherapy by approximately three months. Additionally, the 24-month OS rate of 64.8% surpassed that seen in KEYNOTE-407 by a significant amount. Data from another Phase II study in second-line or later EGFR progressors also showed positive efficacy and safety when compared to previous trials.

The data generated from Phase II have supported Summit's decision to advance ivonescimab into two global Phase III clinical trials. HARMONi intends to evaluate ivonescimab combined with chemotherapy compared to a placebo + chemotherapy in patients with EGFR-mutated, locally advanced or metastatic non-squamous NSCLC who have progressed after treatment with a third-generation EGFR TKI, and HARMONi-3 is designed to evaluate ivonescimab combined with chemotherapy compared to pembrolizumab combined with chemotherapy in patients with first-line metastatic squamous NSCLC. Both studies were initiated in 2023.

Ivonescimab is the only Phase III PD-1/VEGF bispecific antibody in Summit's licensing territories of the US, Canada, Europe, and Japan. Beyond Phase III, there are no approved PD-1/VEGF bispecific antibodies within these territories, leaving a favorable market opportunity within these regions.

Ultragenyx Pharmaceutical

Ultragenyx announced new financial guidance for 2024 of $500m–$530m, a growth expectation of 16–23% over the previous year's guidance. This reflects the overall trend of the company as it has four products on the market for five indications, six late-stage studies ongoing, and plans to reach approvals for another 3–7 indications in the next five years. In 2023, growth was attributed to an increase in sales of Crysvita and Dojolvi, and that is expected to continue with growth estimates increasing for both ($375m–$400m and $75m–$80m, respectively). As such, the company finally expects to reach profitability by 2026.

In terms of pipeline development for 2024, Ultragenyx anticipates data from its DTX401

program for glycogen storage disease type Ia and UX701 for Wilson disease in the first half of 2024. The company will also be pursuing an accelerated review path with the FDA for UX111 for the treatment of Sanfilippo syndrome type A by pushing for FDA approval of biomarker data. Finally, the company expects to complete enrollment for its Phase III programs for DTX301 for the treatment of ornithine transcarbamylase deficiency and the Phase III ORBIT and COSMIC studies of UX143 for osteogenesis imperfecta in 2024.

Xenon Pharmaceuticals

Xenon's president and CEO Ian Mortimer began with a financial overview, reporting $640m in cash at the end of Q3 2023, and confirmed that the company is prepared to support both its extensive epilepsy and major depressive disorder (MDD) Phase III programs.

The company's primary asset, XEN1101, is a Kv7 potassium channel opener in trials for both epilepsy and MDD. Modeled after the notably successful Phase IIb X-TOLE trial, the registrational Phase III X-TOLE 2 and 3 studies address focal onset seizures, which comprise roughly 60% of epilepsy patients. In X-TOLE, XEN1101 produced a 52.8% decrease in monthly focal seizure frequency at the 25mg dosage, 46.4% in the 20mg arm, 33.2% in the 10mg arm, and 18.2% in the placebo group, demonstrating not only statistically significant efficacy but also a clear dose response. These results were particularly impressive given that the patient population was quite severe, with many prior drug failures and a median of 13.5 seizures per month at baseline. An open-label extension (OLE) program for X-TOLE is ongoing concurrently with the Phase III program, fleshing out the safety and tolerability profile. X-TOLE 2 will complete enrollment in the second half of 2024, with topline data available six to eight months later and an NDA filing soon thereafter.

To round out Xenon's epilepsy coverage, the ongoing X-ACKT trial for XEN1101 in primary generalized tonic-clonic seizures will either contribute to the aforementioned NDA or be the basis for a supplementary NDA, depending on timing. Success in this indication is estimated to unlock an additional 30% of the epilepsy market. Additionally, both the X-TOLE OLE and X-ACKT have begun accepting patients as young as 12 years of age, and the company is actively working on a pediatric formula for children aged under six years, who may not be able to handle an oral pill.

Mortimer also provided an update on XEN1101 in the MDD population. Topline results from the Phase II X-NOVA study read out in November 2023 and, although the drug failed to meet the primary endpoint of change in MADRS score at week 6, efficacy signals were seen at some of the secondary endpoints such as HAM-D and the Snaith–Hamilton Pleasure Scale. Interestingly, tolerability was even better in the MDD population than in epilepsy, although this may have to do with the fact that the drug was assessed as an adjunctive therapy in epilepsy and as a monotherapy in MDD. At worst, the X-NOVA results support the use of XEN1101 in epileptic patients with depression, which is a common co-morbidity. However, Xenon did indicate that it hopes to initiate a Phase III trial later in 2024 using HAM-D as the primary endpoint, pending the outcomes from an End-of-Phase II meeting with the FDA. Whether or not a third MDD trial will be needed is still being discussed internally and will be addressed at this End-of-Phase II meeting as well.

While most of the presentation revolved around XEN1101, the company did briefly reference its

preclinical pain program targeting NAV1.7. Candidates for this target will likely enter IND-enabling studies in 2024 and 2025, but Xenon emphasized that its efforts are primarily focused on the late-phase programs.

Small Cap

Agios Pharmaceuticals

Agios Pharmaceuticals reinforced its status as a frontrunner in the field of cellular metabolism treatments for rare diseases by reviewing its advancements from 2023 and outlining upcoming projects until 2026. Its only currently approved asset, Pyrukynd (mitapivat) for pyruvate kinase deficiency, continues to be the backbone of its pipeline programs, with Agios exploring its usage in sickle cell anemia and thalassemia. Additionally, the existing indication for pyruvate kinase deficiency is anticipated to be broadened to include pediatric usage through the Phase III ACTIVATE trial. The topline results of this trial are projected to be announced by the end of 2024, with an estimated approval date in 2026. Mitapivat is a pyruvate kinase activator whose mechanism of action increases ATP levels, which prevent dehydration and ion loss in sickle red blood cells and decrease 2,3-DPG, which promotes oxygen unloading, minimizing sickling and hemolysis.

During 2023, the company reported positive topline results from the Phase III ENERGIZE trial for a currently underserved population with non-transfusion-dependent (NTD) alpha- or beta-thalassemia. This patient population makes up approximately two thirds of the disease group; however, this segment has been largely neglected by treatment guidelines in favor of the more severe, transfusion-dependent population. Agios Pharmaceuticals believes this translates to >1 million patients worldwide, with 18,000 to 23,000 in the US and five major European markets (France, Germany, Italy, Spain, UK) alone. Given the fragmented approach and limited availability of specialist treatment choices, individuals with NTD disease are generally more prone to experiencing long-term consequences that can negatively impact their quality of life, cause organ damage, and lead to early death. The Phase III results presented are very promising, with 42.3% of patients achieving a hemoglobin response (defined as an increase of ≥1g/dL in average hemoglobin concentrations) as a primary endpoint, and improvements on two additional secondary endpoints (fatigue and average change in hemoglobin concentration) versus placebo. The data are expected to be submitted for a regulatory filing alongside results from the ongoing Phase III ENERGIZE-T study in transfusion-dependent thalassemia patients, which has a readout expected in mid-2024, for a potential broad thalassemia label approval in 2025.

The development of mitapivat in sickle cell disease has also progressed, with positive data reported from the Phase II portion of the RISE-UP study and the Phase III portion under way. A data readout from the Phase III part of the study is expected in 2025 for potential approval in 2026. As with its treatment of thalassemia, a dose-dependent statistically significant increase (~50% of patients) in hemoglobin response rate was observed in the mitapivat group compared to placebo. Positive secondary endpoints such as an improvement in vaso-occlusive crises may help with an accelerated US approval, as the FDA has been more hesitant to grant new

marketing authorizations with Pfizer's Oxbryta (voxelotor), a hemoglobin S polymerization inhibitor, already on the market.

Meanwhile, Agios's early-stage pipeline remains active, with a positive Phase IIa study of AG-946 for lower-risk myelodysplastic syndromes, an IND filed for a PAH stabilizer for the treatment of phenylketonuria, and a licensing agreement with Alnylam for novel siRNA-targeting TMPRSS6 for the potential treatment of polycythemia vera. The company remains well funded to achieve its ongoing clinical programs until 2026.

Akebia Therapeutics

Akebia Therapeutics, a fully integrated biopharmaceutical company in renal diseases, reaffirmed its focus on realizing profitability by reviewing achievements from 2023 and outlining upcoming projects for 2024 and beyond. Kicking off the presentation, CEO John Butler confidently addressed the crowd on Akebia's path to profitability, relying on continued financial discipline and meaningful near-term product growth to fund scientific innovations. The company currently expects approximately $170m in 2023 preliminary unaudited net revenue, with further growth in 2024 for Auryxia, an agent approved for hyperphosphatemia and iron deficiency anemia. While March 2025 marks the loss of exclusivity for Auryxia, Akebia highlighted a potential upside due to phosphate binders being added to the bundle, thus meaning eligibility for reimbursement from the Transitional Drug Add-on Payment Adjustment (TDAPA) program.

The presentation then transitioned to anemia management in dialysis patients, as this is an area with significant growth opportunities for Akebia. With a PDUFA date of 27 March 2024 approaching, Butler noted the significant $1bn US market opportunity if vadadustat is approved. Vadadustat, a hypoxia-inducible factor prolyl hydroxylase inhibitor, was initially approved in Europe and Japan as Vafseo for the treatment of anemia associated with chronic kidney disease in adults on dialysis. Beyond Europe and Japan, vadadustat also recently secured approvals in Australia and Taiwan in November 2023. Potential US approval in early 2024 will initially expose vadadustat to ~558,000 chronic kidney disease patients on dialysis, of whom the majority are reimbursed through TDAPA bundle payment. Upon FDA approval, Akebia anticipates obtaining TDAPA designation for vadadustat within six months of post-filing acceptance to drive adoption quickly. On launch preparation, Butler boldly underscored Akebia's commercial readiness, noting a strong embedded commercial team and supply chain readiness with adequate manufacturing and logistics setup. The CSL-Vifor partnership will be crucial to ensure access to vadadustat, as the agreement continues to provide access to up to 60% of US dialysis patients and leverages CSL-Vifor's exclusive distribution arrangements. Furthermore, international market collaborations with Medice in Europe and Mitsubishi Tanabe in Japan will provide additional upside, with a potential European launch for vadadustat in the first half of 2024.

Beyond the approval of vadadustat in dialysis patients, Butler emphasized the potential of vadadustat in the non-dialysis population. All-cause mortality risk was a discussion point, where Butler stressed that the significantly higher risk in these pre-dialysis patients remains even after treatment with erythropoiesis-stimulating agents (ESAs) after dialysis. Stating that anemia may not be optimally managed in patients transitioning to dialysis, Butler expressed that vadadustat could offer a unique opportunity to manage risks ahead of dialysis. In addition, data from the

Phase III FOCUS study were reiterated, demonstrating how vadadustat is comparable to Roche and Vifor's ESA Mircera (methoxy polyethylene glycol-epoetin beta) when used three times weekly, a pattern of administration that aligns with dialysis sessions. This adds to the convenience of vadadustat in that it could be used at the same time as dialysis, but its oral formulation also means that it could be prescribed and administered at home, adding to the opportunity for further label expansion post approval.

Shifting gears towards pipeline and scientific development, Butler introduced two novel HIF-based compounds, AKB-9090 and AKB-10108, specializing in HIF stabilization in acute care indications. Stabilization of HIF leads to the release of erythropoietin, increased extracellular adenosine signaling/glycolytic activity, and decreased inflammatory responses that collectively lessen renal ischemia reperfusion injury and promote resolution of lung injury. Both assets are expected to enter clinical development shortly, with AKB-9090 ready to enter Phase I in 2025.

Butler closed out the presentation by emphasizing Akebia's significant savings since 2022 by reducing its operating expenses on a quarterly basis. Additionally, a loan agreement with Pharmakon was renegotiated, extending maturity to March 2025 and deferring payments through October 2024 on the principal balance of $35m. In his concluding remarks, Butler looked forward to an exciting 2024 with significant cash generation from the continued revenue growth of Auryxia and vadadustat, should it be approved, alongside pipeline expansion opportunities.

Akero Therapeutics

The end of Q4 2023 saw Akero Therapeutics formally become a late-stage company, with its main asset efruxifermin, a long-acting Fc fusion modified fibroblast growth factor 21 (FGF21) agonist, advancing into a Phase III program entitled SYNCHRONY for non-alcoholic steatohepatitis (NASH) patients. With a broad Phase III program focused on both pre-cirrhotic (F2–F3) and cirrhotic (F4) NASH populations, Akero is well poised to evaluate fibrosis improvement and NASH resolution across a wide spectrum of patients to support potential accelerated approval for efruxifermin in the US, Europe, and other pharmaceutical markets.

Akero's president and CEO Andrew Cheng highlighted the recent milestones of the company and strategic goals for 2024 and beyond. Efruxifermin has demonstrated statistically significant responses on both key endpoints of interest to regulators: (i) one-stage improvement in fibrosis without worsening of NASH; and (ii) NASH resolution without worsening of fibrosis, in the Phase IIb HARMONY study and Phase II BALANCED study for pre-cirrhotic NASH, which support its advancement to Phase III development. The first patients in the Phase III program received their first doses in December 2023. Two parallel, randomized, placebo-controlled trials have commenced: SYNCHRONY Histology evaluating the efficacy and safety of efruxifermin in patients with biopsy-confirmed pre-cirrhotic NASH, and SYNCHRONY Real-World assessing safety and tolerability of efruxifermin in patients with non-invasively diagnosed NASH or non-alcoholic fatty liver disease/metabolic dysfunction-associated steatotic liver disease (NAFLD/MASLD).

A highlight for Akero in 2023 was the readout from an expansion cohort, known as cohort D, in the Phase IIb SYMMETRY study in cirrhotic NASH patients. The results showed higher levels of liver fat reduction and greater improvement in lipids for patients treated with efruxifermin in

combination with GLP-1 receptor agonist (RA) treatment compared to GLP-1 RA treatment alone (GLP-1 RAs are also being investigated for NASH). The data provided early evidence on the usage of efruxifermin in NASH patients with type 2 diabetes, which given how frequently type 2 diabetes also presents in NASH patients, could increase efruxifermin's favorability for adoption. While efruxifermin narrowly missed the primary endpoint of fibrosis improvement in the SYMMETRY study, given multiple extenuating circumstances including high placebo response and treatment duration, alignment with the FDA on the design of the planned SYNCHRONY Outcomes study in cirrhotic patients would be a meaningful catalyst in early 2024. As proposed to the FDA, SYNCHRONY Outcomes will evaluate fibrosis improvement based on histology to support accelerated/conditional approval in both the US and Europe, along with long-term clinical outcomes to support full approval. The trial is expected to be initiated in the first half of 2024.

Further clinical development will continue for efruxifermin, with Week 96 data from the HARMONY study anticipated in March 2024. In addition, a highlight in early 2025 will be the long-term Week 96 readout from the SYMMETRY study. Overall, Akero Therapeutics is positioned for a transformative year in 2024. With strong financials and a broad Phase III program, the company presents exciting opportunities for investors and patients as a major player in NASH.

Allogene Therapeutics

In his JPM presentation, CEO David Chang outlined a significant shift in Allogene's business priorities. Allogene's allogeneic CAR-T platform will now focus on four priorities: (i) CD19-targeted cemacabtagene ansegedleucel (cema-cel) as first-line consolidation for large B-cell lymphoma (LBCL); (ii) cema-cel for relapsed/refractory chronic lymphocytic leukemia (CLL); (iii) ALLO-329, targeting CD19 and CD70 for autoimmune diseases; and (iv) ALLO-316, targeting CD70 for renal cell carcinoma (RCC).

The lead program is cema-cel for first-line LBCL. Cema-cel was previously being developed for third-line or later LBCL, but this setting has become saturated. However, the first-line LBCL setting has challenges of its own, namely that the standard of care, R-CHOP or the more recently introduced Polivy-R-CHP, is very effective, with ~60% of patients being cured. As such, the strategy for cema-cel will rely on Foresight Diagnostics' minimal residual disease (MRD) assay to identify the 30% of patients who are at high risk for relapse after responding to standard first-line chemotherapy (another 10% of patients are refractory to first-line therapy and go to second line). Allogene has announced a partnership with Foresight Diagnostics to develop the investigational MRD assay. Chang presented data showing that Foresight's assay (which has a sensitivity of one in 106 cells) is an improvement over the currently approved MRD assays (clonoSEQ and CAPP-Seq, which have a sensitivity of one in 106 cells, and one in 104 cells, respectively) in identifying LBCL patients who will relapse following front-line therapy. In a retrospective study of 93 patients who received curative first-line therapy, the Foresight assay identified 23 patients as MRD-positive at end of therapy. For the 21 MRD-positive patients with >1 year of follow-up, 86% (18/21) had progression events within three years. In contrast, 99% of patients (69/70) who were MRD-negative at end of therapy remained alive without progression after three years of follow-up.

The ALPHA3 pivotal trial will evaluate cema-cel as consolidation therapy for patients who

respond to front-line therapy (with either a complete response or a partial response) but are MRD-positive. Trial enrollment is expected to initiate in mid-2024 and will compare cema-cel to observation. Part one of the trial will evaluate two different lymphodepletion regimens (FCA versus FC), and an interim analysis will evaluate MRD conversion and safety. Once a regimen has been selected, part two of the study is expected to commence in mid-2025. The primary endpoint for part two will be event-free survival (EFS), with key secondary endpoints being PFS and OS. The study is expected to accrue 110 patients, and the median EFS for the observation arm is expected to be eight months. Allogene estimates that the addressable US market opportunity is ~7,700 patients/year, which could translate to a revenue opportunity of >$3bn.

For the CLL opportunity, a Phase Ib trial (ALPHA2) will evaluate cema-cel in second-line patients who progressed on a BTK inhibitor and third-line patients previously treated with both a BTK inhibitor and a BCL2 inhibitor. ALPHA2 is expected to begin enrolling patients in Q1 2024, with a transition to a potentially pivotal Phase II trial planned by year-end 2024/H1 2025. Allogene estimates the addressable population as ~2,500 second-line patients/year and ~5,000 third-line or later patients/year for a revenue potential of ~$3bn.

CD19-directed CAR-T cells target both tumor and normal CD19-expressing B lymphocytes, and B-cell aplasia is a known side effect of CD19 CAR-T therapy. This CAR-T-induced B-cell aplasia has been shown to be beneficial to patients with autoimmune diseases such as lupus and lupus nephritis. It is thought that this benefit may be due to CAR-T cell-mediated depletion of lymphocytes resetting the immune system. However, the risk tolerance of patients with autoimmune diseases is different than those with cancer. Furthermore, rheumatologists generally lack experience with the chemotherapy that is typically used for lymphodepletion prior to CAR-T infusion, and they also lack experience with leukapheresis procedures and cell therapies. One important differentiator of ALLO-329 is that it targets both CD19 and CD70, with the latter expressed on activated T cells. Since ALLO-329 targets both B and T cells, it may enable lymphodepletion with lower doses of chemotherapy or even chemotherapy-free lymphodepletion. The dual targeting of CD19 and CD70 may also allow for the elimination of both pathogenic B and T cells underlying autoimmunity. Finally, the allogeneic nature of ALLO-329 means there is no need for leukapheresis. ALLO-329 is currently in the IND-enabling phase, with manufacturing and analytic assays under way. Initiation of a Phase I trial is expected in H1 2025, with potential clinical proof-of-concept data in a yet-to-be-disclosed autoimmune indication expected by the end of 2025.

The RCC program has reported encouraging Phase I data for ALLO-316, with a 30% ORR and 100% disease control rate in 10 CD70-positive RCC patients. Targeting CD70 allows targeting of both tumor cells and alloreactive host lymphocytes. The lymphodepleting properties of the CD70-targeted CAR are also thought to contribute to the remarkable allogeneic CAR T-cell expansion and persistence seen in the Phase I trial. However, in some patients, this expansion and persistence was accompanied by a hyperinflammatory response. Allogene has developed a diagnostic and treatment algorithm that may mitigate the hyperinflammatory response without compromising CAR T function. This algorithm will be presented in Q2 2024 and will be incorporated into the ongoing Phase I trial in 2024. A pivotal Phase II trial is expected to initiate by the end of 2025. Longer-term plans include evaluating ALLO-316 in other CD70-positive solid tumors, as well as hematologic indications including LBCL and T-cell leukemia/lymphoma.

Almirall

Presenting on behalf of Almirall at this year's JPM conference was chairman and CEO Carlos Gallardo. Almirall is a European medical dermatology leader with a strong portfolio of 48 products in dermatology across different modalities (topical, systemic, and biologics). It has an extensive sales network covering 60% of office-based dermatologists and 90% of hospital-based dermatologists, along with a growing pipeline of internally developed and in-licensed dermatology assets, with a direct presence in the US and in the rest of world through partners.

Medical dermatology remains a very attractive market and is expected to grow at a rate of 10% YOY in the next five years. Almirall has key strategic positioning in dermatology with pipeline-in-a-product opportunities. The company has a leading commercial platform in the dermatology space and has delivered a steady stream of launches since 2017 with Skilarence and most recently with Ebglyss, which has the potential to be a best-in-class treatment for atopic dermatitis. Ebglyss was approved in Europe in November 2023 and launched in Germany late in the year. It will be rolled out in additional European countries throughout 2024.

Around 30% of Almirall's net sales are driven by its already launched portfolio of products including Ilumetri, Wynzora, Klisyri, Seysara, and Skilarence. The company is focusing on areas of multiple severe unmet needs and high prevalence in indications such as atopic dermatitis, hidradenitis suppurativa, alopecia areata, vitiligo, and psoriasis. It also has a presence in non-melanoma skin cancer, where there is a tremendous opportunity because of a lack of treatments and a growing disease prevalence due to increasing sun exposure and the aging population. There is also a focus on rare dermatology diseases including epidermolysis bullosa, ichthyosis, and bullous diseases.

Almirall is present in the two dermatology indications with the highest commercial potential. In the area of atopic dermatitis and psoriasis there is a large pool of diagnosed moderate-to-severe patients and a low penetration of advanced systemics.

Over the last year, the company has announced multiple partnerships to access the latest therapeutic modalities for long-term success. It seeks to access state-of-the-art technology platforms to create innovative best-in-class therapeutics while diversifying its pipeline in medical dermatology. Almirall is leveraging mRNA through a collaboration with etherna, accelerating the discovery of new chemical entities with Evotec and the University of Dundee, and employing best-in-class antibody discovery engines through partnerships with Absci, AlivaMab, and EpimAb.

Gallardo concluded the presentation by stating that the company's newly launched products have the potential to generate over €700m in peak sales, driving double-digit biologics growth from 2023 to 2030. Overall, Almirall is financially strong and has all the resources necessary to execute on its ambition in the coming years.

Alpine Immune Sciences

Alpine is focusing on developing immune therapies for treating autoimmune and inflammatory disease by leveraging its directed evolution platform. In this presentation, CEO Mitchell Gold

discussed the clinical progress of the in-house program known as povetacicept (ALPN-303), which is an Fc fusion protein featuring a modified TACI (transmembrane activator, calcium modulator, and cyclophilin ligand interactor) domain that has been engineered to inhibit both BAFF and APRIL. Following the publication of encouraging data at international conferences in 2023, Gold announced several upcoming clinical advancements set to begin this year.

Povetacicept, a once-monthly subcutaneous injection with a small volume, has been positioned by Gold as the leading dual blocker of BAFF/APRIL, surpassing telitacicept and atacicept. Unlike its counterparts, povetacicept is an Fc fusion protein with a modified TACI domain that has exhibited superior inhibition of both BAFF and APRIL signaling, as demonstrated in Alpine's in vitro assay. The Phase I RUBY-1 study, conducted on healthy volunteers, confirmed the significant reduction of immunoglobulins by 80mg and 240mg of povetacicept using a four-weekly dosing regimen. The ongoing RUBY-3 study focuses on dose escalation and includes patients with glomerulonephritis, including proteinuric IgA nephropathy (IgAN), lupus nephritis (LN), or primary membranous nephropathy (pMN). After six months of treatment with 80mg of povetacicept, the IgAN cohort in the RUBY-3 study revealed a 53.5% reduction in urine protein-creatinine ratio (UPCR), which serves as a predictor of renal function and an endpoint for accelerated approval in IgAN. The depth of UPCR reduction is correlated with clinical outcomes and renal benefit. Gold emphasized that this reduction in UPCR represented the most significant reported to date. Four out of five treated patients achieved clinical remission within six months, defined by UPCR less than 0.5g/g, a reduction of ≥50% in UPCR from baseline, and stable renal function with ≤25% reduction in eGFR from baseline. In this cohort, the disease-specific marker Gd-IgA1 also decreased by 60%. Patients' eGFR, an indicator of renal function, was slightly increased after six months of treatment. Additionally, povetacicept demonstrated the potential for indication expansion to IgE-mediated diseases, as it substantially reduced all immunoglobulin subtypes (IgA, IgE, and IgM) in addition to IgG. Notably, one subject with pMN experienced a 99% reduction in the pathogenic autoantibody anti-PLA2R1 after six months of treatment, highlighting the selectivity of povetacicept in inhibiting pathogenic antibodies while preserving protective IgG antibodies. Povetacicept exhibited good tolerability without any injection site reactions. Based on these promising results, the company plans to advance povetacicept to a Phase III trial for IgAN patients in the second half of 2024.

Alpine is poised for a year of significant catalysts in 2024. The company will continue advancing povetacicept in two diseases, IgAN and systemic lupus erythematosus (SLE). In the first half of the year, topline data for IgAN at 240mg of povetacicept, as well as follow-up data at 80mg, are expected. Longer-term follow-up data for IgAN will be available in the second half of the year. In the second half of 2024, Alpine will not only initiate a pivotal study for IgAN but also commence a Phase II study for SLE using a placebo-controlled, blinded, and randomized design. Additional data from the RUBY-3 basket trial, which includes LN and pMN patients, will provide further insights into the potential of povetacicept in these diseases. Moreover, the RUBY-4 cytopenia basket study, which enrolls patients with immune thrombocytopenia, warm autoimmune hemolytic anemia, or cold agglutinin disease, will shed light on the expansion of indications beyond IgAN, with initial results expected in the first half of the year. Povetacicept also holds promise for the treatment of neurological diseases such as myasthenia gravis in the future. Following a follow-on offering last November, Alpine is well positioned with $368m in cash, which will support the company through 2026.

During the Q&A session, Gold reaffirmed the key strengths of povetacicept, including its monthly injection schedule, significant reduction in UPCR within six months, and dual inhibition of BAFF and APRIL. These factors present a potential opportunity for povetacicept to expand its indications beyond IgAN. When questioned about the decision to move directly to a pivotal study for IgAN, Gold emphasized the acceptance and well-established status of UPCR as an endpoint for IgAN approval. He highlighted the correlation between the degree of UPCR reduction and clinical outcomes. Considering the robust UPCR reduction observed in the current data and the successful precedent set by other companies in IgAN studies, Gold expressed confidence in povetacicept's potential in a pivotal study in the treatment of IgAN patients.

Anavex Life Sciences

Anavex Life Sciences focuses on novel small molecule treatments for CNS disorders with a high area of unmet need such as Alzheimer's disease and Parkinson's disease, as well as rare diseases like Rett syndrome. The company's precision medicine platform, SIGMACEPTOR, has enabled the development of a number of drugs targeting the sigma-1 receptor, a protein whose activation is thought to restore homeostasis and decrease cellular stress caused by genetics, aging, and lifestyle. This approach has been validated across multiple indications through biomarker analysis of sigma-1 mRNA expression, where upregulation of this mRNA was found in patients who also experienced clinical improvements. In his presentation, Anavex CEO Christopher Missling gave an overview of recent trial results as well as outlining the path forward for continuing research and commercialization.

The company's most developed asset, blarcamesine (ANAVEX2-73), has demonstrated notable success in early Alzheimer's disease, significantly lessening decline in both structural and functional measures, as well as validated biomarkers of amyloid beta pathology. This drug elicits a response at week 48 that is faster than the recently approved Leqembi at week 72 and stronger than donanemab at week 76. Additionally, the novel mechanism leaves the potential for blarcamesine to be co-administered with anti-amyloids. Anavex has initiated a regulatory submission to the EMA for blarcamesine in early Alzheimer's disease, and hopes to do the same in the US in time for a 2025 potential launch.

Blarcamesine is also in development for Rett syndrome, where significant results were seen in the adult population but not in the pediatric population, although efficacy signals were present. However, there has been robust enrollment in both the open-label extension trials and compassionate use programs, foreshadowing the potential for success in this indication if marketing authorization can be obtained.

In Parkinson's disease, blarcamesine was found to not only improve dementia but also motor symptoms. This latter finding has sparked plans for a larger Parkinson's disease trial in addition to the pivotal trial for Parkinson's dementia that is currently being designed. Since this drug is anticipated to span multiple indications where patients have varying ages and levels of disability, both a liquid and solid oral formulation are being developed.

Outside of blarcamesine, Anavex has a number of other drug candidates, primarily in preclinical stage, although ANAVEX3-71 is in early-phase studies for schizophrenia, frontotemporal dementia, and Alzheimer's disease. This drug differs from blarcamesine in that in addition to

sigma-1 activation, it also has strong and selective M1 interaction, another receptor that has been implicated in the mechanisms of these diseases.

Anavex reported that it has at least four years of cash runway and strong support from multiple external organizations including the Michael J. Fox Foundation, International Rett Syndrome Foundation, and the Australian government.

Annexon Biosciences

Annexon Biosciences is a late-stage clinical company focusing on diseases of the body, brain, and eye that are mediated by the classical complement inflammatory pathway. All of Annexon's assets target C1q, effectively blocking this cascade before upstream and downstream processes can drive inflammation. During his presentation, CEO Doug Love outlined three key milestones that the company plans to achieve in 2024 and noted that Annexon is financially poised to support its ambitious roadmap through Q2 2026.

The flagship indication for the company is Guillain-Barré syndrome (GBS), a devastating neurodegenerative autoimmune disease that causes severe disability and has no FDA-approved treatments. The proof-of-concept study showed that, compared to placebo, ANX005 improved muscle strength, reduced a key inflammatory biomarker, NfL, and improved scores on the GBS disability scale. Specifically, 28% of patients showed a three-point improvement on this six-point scale, meaning that some patients who came in on a ventilator were able to walk with assistance by week eight of the study. A Phase III trial targeting the most severe GBS patient population is on track for a readout in Q2 2024; however, this trial is taking place entirely in Europe due to a regional difference in alternate treatment availability, although the company plans to pursue US approval as well. These topline results will be the first placebo-controlled dataset for GBS in over 40 years. If all goes well, Annexon plans to prepare a BLA submission in the second half of 2024. ANX005 is also being studied in Huntington's disease, amyotrophic lateral sclerosis, and lupus nephritis, indications where the classical complement pathway is validated as a disease driver and there exists a high degree of unmet need.

Another classical complement-mediated disease is geographic atrophy, an ophthalmic disorder resulting in loss of vision. There is one other treatment approved, Syfovre, but this drug was approved based on a surrogate endpoint of reduction in lesion and not on visual function. In a proof-of-concept study, patients were treated with ANX007 in one eye and a sham injection in the other, resulting in the drug-treated eye experiencing a 74% reduction in loss of function. In the End-of-Phase II meeting with the FDA, it was agreed that the primary endpoint for this registrational program would be improvement of visual function, not a surrogate endpoint. The program consists of two studies, ARCHER II and ARROW. The former will be initiated in mid-2024 and is similar to the initial study, where one eye receives a sham injection, and the latter is a head-to-head comparison with Syfovre. Although ANX007 was granted PRIME designation by the EU, the prospective competitor is not yet approved in that region, so unless European approval is granted, the ARROW study will be based entirely in the US.

Finally, Annexon plans to initiate a proof-of-concept study for its third asset, ANX1502, which is an oral compound targeting only the activated version of a C1q transmitter protein. In a recently completed healthy volunteers study, the drug was not only well tolerated but also reduced

elevated complement in these subjects. The upcoming trial assessing ANX1502 in cold agglutinin disease will begin in the first half of 2024, and topline results are anticipated in the second half of the year.

Apogee Therapeutics

Apogee's CEO Michael Henderson led the presentation on the company's performance during 2023, as well as outlining plans for 2024. Apogee is aiming to become a leader in the inflammatory and immune space by developing therapeutics to treat indications such as atopic dermatitis (AD), COPD, and asthma, by engineering antibodies with best-in-class profiles and differentiated dosing approaches to compounds already available on the market.

Henderson began by expressing that 2023 was a foundational year for the company in which it advanced its first compound from preclinical studies into clinical development. This was achieved by its lead antibody APG777 entering a Phase I trial, which is being developed for both AD and asthma. Key safety and pharmacokinetic data readouts from the trial are anticipated in mid-2024. Henderson described plans to potentially initiate Phase II trials for APG777 in AD during 2024, while Phase II trials are planned for asthma in 2025. The company believes the AD market is potentially a larger opportunity than the current psoriasis market, which is worth approximately $30bn, and estimates that the AD market could have a total patient population that is three times the size of the current psoriasis patient population. Other emerging pipeline therapeutics include APG808, which is in development for COPD and targets the same mechanism of action as Sanofi/Regeneron's Dupixent and is expected to enter Phase I trials during 2024. Additionally, APG990 and APG222 are two additional pipeline compounds being pursued in AD.

Arcturus Therapeutics

Joseph Payne, president and CEO of Arcturus Therapeutics, began the JPM presentation with an overview of Arcturus and its proprietary mRNA technologies currently driving therapeutic programs. Payne briefly went over the current assets that he would focus on in the presentation before moving on to discussions surrounding the company's partnerships with both CSL and Meiji. Payne then moved on to provide an update on the ARCT-154 Phase III clinical study. The study was fully funded by Meiji and achieved the primary endpoint of non-inferiority of neutralizing antibody response against SARS-CoV-2 ancestral strain compared to Comirnaty. The study also achieved the secondary endpoint of superiority of ARCT-154 in neutralizing antibody response against SARS-CoV-2 Omicron BA.4/5 variant. These results also showed that ARCT-154 was generally safe and well tolerated.

Payne highlighted that an NDA for ARCT-154 was submitted in April 2023 to Japan's Pharmaceuticals and Medical Devices Agency (PMDA) for primary immunization, and a further NDA was submitted in June 2023 to the PMDA for booster use. The Phase III study was also published in *The Lancet Infectious Diseases*. ARCT-154 was approved in Japan in November 2023.

Payne then moved on to updates regarding ARCT-810 for the treatment of ornithine

transcarbamylase (OTC) deficiency, highlighting the reasons for pursuing this indication. OTC deficiency is the most common urea cycle disorder in which the present standard of care does not effectively prevent life-threatening spikes of ammonia. LUNAR-OTC (ARCT-810) has been shown to increase OTC expression in mouse periportal hepatocytes. Payne announced that data from the ongoing Phase II clinical trial are expected to be released in the first half of 2024. This asset was granted both FDA fast track and rare pediatric disease designations in June 2023.

The third and final asset discussed in the presentation was ARCT-032 (LUNAR-CF) for the treatment of cystic fibrosis, which aims to restore CFTR function. Arcturus believes that there is an unmet medical need in this indication as current standard-of-care therapies do not prevent the chronic, progressive loss of lung function that ultimately requires lung transplantation or leads to early death. ARCT-032 is an mRNA replacement therapy that has the potential to produce wild-type CFTR into the lungs of CF patients, independent of genotype. Payne shared that there are currently two ongoing trials in this indication, and the company is on track to report Phase Ib interim data in the first half of 2024. This asset has received rare pediatric disease designation and orphan drug designation from the FDA.

To conclude the presentation, the company shared its outlook for 2024 and announced new additions to its board.

Biomea Fusion

CEO Thomas Butler of Biomea Fusion, a biopharmaceutical company dedicated to developing novel covalent small molecules, began his JPM presentation by focusing on the company's mission to not only meet significant unmet need in disease but to find cures. Outlining the company's accomplishments in 2023, Butler enthusiastically described previous initial clinical data readouts for BMF209 in both oncology and diabetes, which have laid the groundwork for a successful year ahead. Having hired diabetes expert Juan Pablo Frias as CMO in August 2023, there was a focus on Biomea Fusion's potential with its combination of experienced leadership, its differentiated Fusion System platform, and promising pipeline.

With a substantial emphasis on the growing burden of diabetes and lack of progress addressing its root cause, Butler keenly presented the company's oral small molecule drug, BMF-219, which is hoped will lead to a paradigm shift in diabetes care due to its novel mechanism of action focusing on beta cell health. BMF-219 is postulated to increase beta cell mass and restore insulin secretion, thus representing a disease-modifying treatment associated with a short treatment regimen and a potential addressable market of all diabetic patients. Butler highlighted a number of upcoming milestones for 2024, including the expected completion of Phase II enrollment from the COVALENT-111 study of BMF-219 in type 2 diabetes and presentation of COVALENT-111 data at the International Conference on Advanced Technologies and Treatments of Diabetes (ATTD) in March. The presentation explored the design of COVALENT-111, including its expansion phase focus on tailoring treatment duration and dosage based on response, before moving on to BMF-219's impressive clinical results, such as its durability of glycemic results seen at week 26 following only four weeks of treatment. Overall, the data reported, including the presentation of a compelling case study, suggest that BMF-219 has the potential to be a diabetes game-changer. Aside from diabetes, Biomea Fusion briefly discussed its progress in

oncology, touching on initial Phase I topline data that had the first complete response for BMF-219 in acute leukemia.

Butler rounded off the presentation with excitement for Biomea Fusion's plans for 2024 and beyond, stating the company's position in the driving seat for accelerated development and growth. In 2024, the company expects proof of concept to be established in type 1 diabetes in the COVALENT-112 trial, as well as the completion of dose escalation and establishment of the recommended Phase II dose for BMF-219's oncology program. Biomea Fusion's innovative approach to diabetes, coupled with its promising pipeline, clear roadmap for 2024, and experienced leadership, leave us with cautious optimism about a future where diabetes is not treated but cured.

bluebird bio

In his presentation, bluebird bio president and CEO Andrew Obenshain focused on the momentum the company has built as the only commercial gene therapy company with three FDA-approved products. The status as a gene therapy leader provides bluebird with the opportunity to address the critical unmet need of 22,000 patients.

The most recent approval came late in 2023 for Lyfgenia (lovotibeglogene autotemcel, also known as lovo-cel), a one-time, single-dose treatment for sickle cell disease (SCD). Bluebird will leverage the same commercial strategy used to launch Zynteglo (betibeglogene autotemcel), a one-time gene therapy for patients with beta-thalassemia. To date, 48 established Qualified Treatment Centers (QTCs) are in place for Zynteglo patients, with 35 of the centers ready to receive referrals for Lyfgenia for SCD patients as well. Bluebird anticipates the entire network will be ready to treat with both gene therapies by the end of Q1 2024. In addition to the optimized QTC network, bluebird has created a validated access and reimbursement strategy, driving a favorable coverage landscape for Lyfgenia and Zynteglo. Approximately 200 million beta-thalassemia patients are under contract for Zynteglo with zero ultimate denials to date across commercial and government payers. The access and reimbursement strategy designed for Lyfgenia ensures timely, equitable access for SCD patients. Bluebird shares risk with payers for both therapies with outcomes-based agreement offerings. For Lyfgenia, risk is tied to vaso-occlusive episode (VOE)-related hospitalizations as patients are followed for three years. Bluebird also continues to engage with the Center for Medicare and Medicaid Innovation on its Cell and Gene Therapy Access Model, which is anticipated to be implemented in 2025. Bluebird's third approved gene therapy is Skysona (elivaldogene autotemcel), indicated to slow the progression of neurologic dysfunction in boys 4–17 years of age with early, active cerebral adrenoleukodystrophy (CALD). There have been six patient starts since its launch, four QTCs activated, and zero ultimate denials across government and commercial payers. Obenshain indicated that the company anticipates 85–105 patient starts combined across all three of its FDA-approved therapies (Lyfgenia, Zynteglo, and Skysona) in 2024.

Overall, bluebird is entering 2024 poised to deliver shareholder value. The company ended 2023 with zero debt on the balance sheet and approximately $275m in preliminary unaudited cash, cash equivalents, and marketable securities, providing a cash runway into Q1 2025.

C4 Therapeutics

C4 Therapeutics, a leader in targeted protein degradation (TPD), started its presentation at the 42nd annual J.P. Morgan Healthcare Conference showcasing its historic 2023 through the strong continued execution of milestones. To date, the company has discovered a number of degraders and advanced four INDs against a transcription factor, a chromatin modifier, and two kinases. In addition, it has evaluated three programs in the clinic, with each demonstrating robust target degradation in patients.

Accomplishments in 2023 included the presentation of positive Phase I data on CFT7455 in relapsed/refractory multiple myeloma (MM), which demonstrated a new optimal schedule, encouraging monotherapy and combination therapy activity, as well as being well tolerated. CFT7455 is a TPD targeting IKZF1/3. Degrading IKZF1 leads to MM and non-Hodgkin's lymphoma (NHL) cell death, T-cell activation, and on-target neutropenia. The Phase I trials are expected to be completed by the end of 2024, with updated results being released in the second half of 2024. Another milestone includes the dosing of the first patient in the Phase I/II trial of CFT1946, a TPD targeting BRAF V600X. CFT1946 specifically targets BRAF V600X mutations over wildtype BRAF, giving potential for it to overcome resistance mechanisms seen with inhibition in BRAF V600X cancers. Preclinical data are expected in the first half of 2024, with Phase I data expected in the second half of the year.

C4 Therapeutics is also looking outwards to accelerate its pipeline development, securing two major partnerships in 2023, with Betta Pharmaceuticals for the development of CFT8919, a TPD targeting EGFR L858R, and with Merck to discover and develop degrader-antibody conjugates. With a promising pipeline and a great potential for future collaborations, C4 Therapeutics is in a great position for future value creation and can expect an exciting year in 2024.

Caribou Biosciences

President and CEO of Caribou Biosciences Rachel Haurwitz kicked off the company's J.P. Morgan Healthcare Conference presentation. Caribou is a clinical-stage biopharmaceutical company focused on developing next-generation CRISPR genome-edited allogenic cell therapies with an initial focus on oncology. Caribou utilizes its next-generation Cas9 and Cas12a CRISPR hybrid RNA-DNA genome editing technology to develop potential therapies.

Caribou's pipeline is split by two different technologies, with three programs under the CAR-T platform for hematologic indications, and an additional program, CB-020 targeting ROR1, under the CAR-NK platform with iPSC-derived cell therapies for solid tumor indications. In the upcoming year, Caribou expects to achieve several clinical milestones. Caribou's lead clinical-stage program, CB-010, is an allogenic anti-CD19 CAR-T cell therapy in Phase I development for relapsed/refractory (R/R) B-cell non-Hodgkin's lymphoma and R/R large B-cell lymphoma (LBCL), with a Phase III pivotal trial for LBCL expected by year-end of 2024. An additional data readout for the Phase I ANTLER study is expected in Q2 2024. Another data milestone, for the Phase I CaMMouflage trial of CB-011, an anti-BCMA allogeneic CAR-T cell therapy, in R/R multiple myeloma is expected by year-end of 2024. Initiation of the Phase I AMpLify trial for CB-012 in R/R acute myeloid leukemia is expected in the first half of 2024.

Caribou continues to be well resourced with approximately $400m with cash on hand to support catalysts through Q4 2025. Included is a $25m equity investment from Pfizer and the $134.4m net proceeds from an underwritten public offering of common stock.

Centessa

Centessa CEO Saurabh Saha opened the presentation by describing 2023 as a fantastic year for Centessa, with a strong balance sheet and momentum expected to continue through 2024 with multiple catalysts. Saha then gave a broad overview of the company's most advanced programs, the SerpinPC hemophilia program, its orexin agonist program with ORX750 being developed for narcolepsy, and its LockBody technology platform with LB101 for solid tumors. He noted that Centessa's pipeline is diverse and uncorrelated, which for them means the failure of one program will not mean the failure of all programs. Saha also gave an overview on deliverables in 2023, most notably clearing the IND for LB101 and initiating a Phase I/II study in solid tumors, receiving fast track designation for SerpinPC for hemophilia B, and initiating dosing in the SerpinPC hemophilia B registrational study. The company is expecting a readout from part one of the Phase II Present-2 study in 2024.

Saha dove into more detail on the SerpinPC hemophilia program and noted that standard-of-care treatments for hemophilia have not progressed much beyond intravenous treatments. He described Centessa's candidate as a safe, subcutaneous, and efficacious treatment that has the potential to transform care for hemophilia B patients as there is no subcutaneous treatment option for hemophilia B in the US and there are limited options for hemophilia B with inhibitors. SerpinPC has the potential to be a first-in-class subcutaneous therapy with a differentiated safety profile for people with hemophilia B. With its novel mechanism of action, a 96% reduction in median all bleeds was achieved in the Phase IIa study, with no thrombosis observed. He highlighted that if this candidate makes it through the clinic, it could be a potential multi-billion-dollar market opportunity.

Subsequently he focused on the company's potential best-in-class oral OX2R agonist for the treatment of narcolepsy and other sleep-wake disorders, ORX750, and how it closely mimics functioning of the endogenous peptide with high potency. He reported increased wakefulness and suppressed cataplexy in NT1 in preclinical studies in mice. The preclinical data support potential expansion into broader sleep-wake disorders including narcolepsy type 2 and idiopathic hypersomnia, which could be another significant market opportunity for Centessa. Clinical proof-of-concept data in healthy volunteers for ORX750 are expected in 2024.

Lastly, Saha described the company's LockBody technology platform that combines tumor enrichment with activation of effector function and designed as a single-agent systemic treatment. The first LockBody candidate is LB101, which demonstrated significant tumor regression during in vivo studies. The drug was shown to be well tolerated in non-human primates with LB101 doses of up to 50mg/kg. The company is currently dosing subjects in an ongoing Phase I/IIa first-in-human clinical trial of LB101.

Cullinan Oncology

Cullinan Oncology's CEO Nadim Ahmed presented on behalf of the company at the JPM Healthcare Conference. Cullinan ended 2023 with a strong financial position, with approximately $470m in cash to support program advancement and operations into the second half of 2026. Several updates regarding timing expectations were presented regarding the company's pipeline. The majority of Cullinan Oncology's programs are currently in Phase I development, with updates planned as data matures.

CLN-619 is an anti-MICA/B monoclonal antibody being developed for different cancer indications. An ongoing Phase I trial features CLN-619 as a monotherapy, as well as in combination with pembrolizumab in multiple tumor-specific cohorts such as endometrial and cervical cancer. To date, CLN-619 monotherapy has demonstrated a favorable safety profile and shown efficacy across multiple dose levels. Initial data from the combination dose escalation module are expected in Q2 2024, with data from the disease-specific cohorts anticipated in the first half of 2025. For zipalertinib, the selective EGFR inhibitor is the only one in Cullinan's pipeline that has advanced beyond Phase I development. Zipalertinib has received breakthrough therapy designation and is currently enrolling in pivotal Phase IIb and Phase III clinical trials for non-small cell lung cancer patients with exon20 mutations. Per Phase I/IIa data, zipalertinib demonstrated superior efficacy and safety at the 100mg dose level. For Cullinan's other products such as CLN-978, we currently await Phase I trials to further progress in other indications such as B-cell non-Hodgkin's lymphoma.

Cullinan's oncology pipeline has a high value proposition, with enough cash runway to support development well beyond the timing expectations of the current catalysts. We anticipate the topline results in 2024 for these products, which should provide further guidance on the pathway towards registration.

Cytek

CEO Wenbin Jiang led the presentation for Cytek, a cell analysis company, on the final day of the JPM conference. The presentation started with the accomplishments achieved by the company in 2023. With just under 2,000 Cytek units deployed, reaching more than 1,500 customers in over 70 countries, Cytek boasted revenue for full-year 2023 of $188m–$192m and $288m net cash available.

Jiang then focused on the applications that Cytek technology enables. These include deeper assessments of patient immune status pre- and post-treatment, allowing researchers to maximize the value of laboratory samples as they are equipped with more information in less time with fewer errors and with full standardization across experiments and laboratory sites. With this combined, Cytek technology has led to more than 1,450 peer-reviewed publications in the fields of oncology, viral infections, immunology, inflammation, autoimmunity, and drug development.

The presentation then focused on the company's current products. One such product is Cytek's ImageStream, which was recently used to validate the efficacy of treatment in sickle cell

disease. This led the FDA to approve the first gene therapy to treat patients with sickle cell disease. Another example is Cytek Cloud, which provides the user base with data analysis, panel, and experimental design optimization. Finally, in the clinical space, full spectrum profiling products such as Cytek Aurora enable comprehensive clinical applications. At a low cost, the product allows for advanced flow cytometry for disease screening, diagnosis, and monitoring capabilities. Jiang was also keen to mention the specific benefits of Cytek's technology for clinical use, which include the identification of rare populations of abnormal cells, eliminating redundant reagents, and optimizing the use of smaller samples of patient specimens. Due to these products and continued development into these areas, Cytek is hopeful that continued growth and increased revenue will occur in the coming years.

Edgewise Therapeutics

Edgewise Therapeutics' CEO Kevin Koch opened the presentation with an overview of the company's 2023 accomplishments, including detailed updates on its muscle disease development programs and related trial information. Lead candidate EDG-5506 is an orally administered, allosteric, selective, fast myofiber (type II) myosin inhibitor designed to address the root cause of dystrophinopathies, including Duchenne muscular dystrophy, where the dystrophin protein is missing and contraction-induced muscle damage is ongoing, and Becker muscular dystrophy, a mutation of dystrophin and slower progressing loss of motor function. Koch emphasized that the Becker opportunity, where there is no approved therapy, could be as large as Duchenne. During 2023, the FDA granted EDG-5506 rare pediatric disease designation in Duchenne, as well as orphan drug designation for both Duchenne and Becker.

Highlighted were the positive 12-month open-label trial data for ARCH, a single-center study, to assess the safety and pharmacokinetics of EDG-5506 over two years in adults with Becker, with 12 patients enrolled and data expected in H1 2024. Edgewise overenrolled (40 adults and 29 adolescents) and continues to advance the Phase II placebo-controlled study CANYON, the largest interventional Becker study to date, with one-year data anticipated in the second half of 2024. CANYON was amended in September 2023 to include a global pivotal cohort in individuals with Becker; GRAND CANYON (with design informed by ARCH) is a multicenter, randomized, double-blind, placebo-controlled study to evaluate the safety and efficacy of EDG-5506 in adults, with a primary endpoint of North Star Ambulatory Assessment (a more sensitive endpoint to assess function) at 18 months. The company also advanced the Phase II DUNE study to evaluate the effect of EDG-5506 on biomarkers of muscle damage following controlled exercise in adults with Becker, limb girdle muscular dystrophy, and McArdle disease; data are expected in the first half of 2024.

In October 2023, Edgewise enrolled and expanded the LYNX Phase II placebo-controlled trial in children aged 4–9 years with Duchenne to assess the effect of multiple doses of EDG-5506 over 12 weeks on safety, pharmacokinetics, and biomarkers of muscle damage. An open-label extension portion of the trial for a total of 24 months aims to gain further insights into safety and functional measures in Duchenne patients not currently treated with corticosteroids. Three-month controlled dose-ranging data are anticipated in the first half of 2024. The company also initiated FOX, a new Phase II placebo-controlled trial, to assess the effect of EDG-5506 over 12 weeks on safety, pharmacokinetics, and biomarkers of muscle damage in children and

adolescents with Duchenne previously treated with gene therapy. Participants will then continue in an open-label extension portion of the trial for a total of 12 months to gain further insights. Pending ongoing study data, the initiation of a Phase III trial in Duchenne is expected in the second half of 2024.

Edgewise's second initiative is EDG-7500, a first-in-class, oral, selective cardiac sarcomere modulator for the potential treatment of hypertrophic cardiomyopathy (HCM). In September 2023, it initiated a Phase I study of EDG-7500 in healthy adults. The company aims to address two forms of disease: HCM and obstructive HCM (oHCM). It believes EDG-7500 offers an advantage over marketed direct cardiac myosin inhibitors such as mavacamten in that its fixed-dose regimen is specifically designed to slow early contraction velocity rate, accelerate rate of relaxation, and normalize impaired cardiac relaxation, without inactivating the myosin motor head. A Phase Ib study of EDG-7500 in individuals with oHCM is planned to begin in the first half of 2024.

Its $290m in cash and zero debt will enable the company to execute the 2024 milestones and give it a runway through 2026. In his closing remarks, Koch indicated that 2025 should be a promising year for multiple milestones in its muscular dystrophy programs, and as Phase II development gets moving for EDG-7500.

Enanta Pharmaceuticals

President and CEO Jay Luly presented the roadmap for 2024 for Enanta Pharmaceuticals. The company's aim is to utilize small molecule drug discovery to develop treatments for high unmet needs, with focuses on virology and immunology. Ongoing development of several new assets has been made possible by the successful commercialization of Enanta's glecaprevir, which is a component of Mavyret, an antiviral treatment for hepatitis C marketed by AbbVie. Royalties from this partnership equated to $78.2m in 2023, with a further $200m generated from sales of approximately 50% of future royalties. As a result, the company has a balance of $370m heading into 2024.

Virology has been the main area of focus for Enanta, and this continues in 2024 with drug candidates in development for treating respiratory syncytial virus (RSV), COVID-19, and hepatitis B virus (HBV) infections. Zelicapavir (EDP-938) is a nucleoprotein inhibitor in development for RSV, a disease with no treatment options at present. Promising preclinical data indicate high potency, high barriers to resistance, and the potential for synergy with other mechanisms of action. Moreover, its once-daily dosing and initial clinical data suggest it may offer benefits over competitors from Ark Bio and Pfizer that are also in development. Two global Phase II trials, one in children and one in high-risk adults, are ongoing, with the first data expected in Q3 2024. A second RSV candidate, EDP-323, targets RNA polymerase, and it too has promising preclinical data suggesting high potency, the potential for synergies, and once-daily dosing. Results from a human challenge study are also expected in Q3 2024. With COVID-19 still an ongoing health concern, Enanta's EDP-235, which targets the 3CL protease, has robust preclinical data with high barriers to resistance and once-daily dosing. Data from the Phase II trial did not identify any safety concerns and a reduction in symptoms was observed. However, the company is looking for partners to advance this asset further. Similarly, EDP-514, an HBV

core inhibitor, has shown promising Phase I data but the company believes it will need to be combined with other mechanisms of action to achieve success.

Luly highlighted the natural expansion of Enanta's areas of focus to include immunology, based on the overlap between virology and immunology and the need for orally administered treatment alternatives for immunology indications. The company's first foray is into chronic spontaneous urticaria, a mast cell-driven immunological disorder which affects up to 1% of people worldwide at some stage in their lives and manifests as hives, erythema, and itching. Many patients are not controlled on antihistamines, with the use of biologics also limited, equating to a high unmet need for novel therapeutics. Enanta is aiming to develop a tyrosine kinase receptor (KIT) inhibitor owing to the key role KIT plays in regulating mast cell activity. Proof of concept has been demonstrated with a monoclonal antibody targeting KIT, and Enanta is evaluating prototypes looking for oral, potent, and selective KIT inhibitors to advance into clinical development. Further news on candidate selection is expected later this year.

Erasca

During the JPM presentation, Erasca provided an overview of its activities, discussing aspects such as drug development, milestones, revenue, and clinical trials. The company presented its lead program, naporafenib, a PAN-RAF inhibitor that is scheduled to enter Phase III clinical trials targeting NRAS-mutant melanoma in the first half of the year. Erasca also highlighted two other clinical-stage programs: ERAS-007 (ERK inhibitor) for BRAF-mutant colorectal cancer (CRC), and ERAS-801 (EGFR inhibitor) for EGFR-driven recurrent glioblastoma.

Erasca, with $344m in cash, outlined its strategy focusing on the MAP kinase pathway through three approaches: upstream and downstream nodes, direct targeting of RAS, and addressing orthogonal escape routes. The company showcased a modality-agnostic pipeline aimed at inhibiting the RAS/MAP kinase pathway.

The presentation detailed naporafenib's progress, a PAN-RAF inhibitor with promising preclinical synergy, dosed in over 500 patients. Erasca discussed the SEACRAFT-1 and SEACRAFT-2 trials, targeting Phase Ib and Phase III trials in NRAS-mutant melanoma. The company highlighted the lack of approved targeted therapies in the indicated space, positioning naporafenib as a potential first-in-class treatment.

The ERK inhibitor ERAS-007, targeting BRAF-mutant CRC, was introduced, demonstrating positive preclinical and clinical results. Erasca's approach involves combining ERAS-007 with the standard of care, encorafenib + cetuximab, aiming to improve response rates beyond the current 20%. Additionally, Erasca touched on its IDO-1 program for glioblastoma, emphasizing its potential in addressing EGFR alterations with superior CNS penetration compared to existing inhibitors.

The presentation concluded with Erasca's milestone projections for the year, including data readouts for SEACRAFT-1, initiation of SEACRAFT-2, and updates on ERAS-007 and the THUNDERBBOLT-1 trial.

Erasca highlighted its commitment to growth, diversification, and corporate responsibility, positioning itself as a player in the evolving landscape of cancer therapeutics.

Idorsia Pharmaceuticals

Idorsia Pharmaceuticals' CEO Jean-Paul Clozel gave a company overview and expectations for the future at the J.P. Morgan Healthcare Conference. He noted that on one side, the company has innovative product offerings, while on the other side it is restrained by limited financing. What Idorsia wants is to create a sustainable organization, which requires scientific innovation and substantial investment.

The current success of Idorsia is largely based on the company's lead product, Quviviq, approved in the US, Canada, and the UK for the treatment of insomnia. Quviviq has an optimized pharmacokinetic profile, demonstrating fast absorption and an optimal eight-hour half-life without accumulation over time or active metabolites. This results in patients sleeping through the night without experiencing next-morning somnolence. Quviviq launched in the US in 2022, and to date over 125,000 patients have been treated and over 300,000 prescriptions have been dispensed. The insomnia treatment has also been launched in Italy, Germany, Canada, Switzerland, and Spain. A commercial launch in France is anticipated in Q1 2024.

Following discussion of Quviviq, Clozel discussed the development status of aprocitentan in resistant hypertension. Approval applications for aprocitentan are currently under review by the FDA and EMA, and the drug has the potential to be the first antihypertensive therapy in over 30 years which works via a new mechanism of action and new physiological pathway. The FDA has assigned a PDUFA date of 19 March 2024 for the NDA.

Other late-stage pipeline candidates include selatogrel and cenerimod. Selatogrel is a P2Y12 inhibitor under development for the treatment of acute myocardial infarction (AMI). It is intended to be similar to an EpiPen for AMI, with patients self-administering the drug using an autoinjector at the onset of AMI symptoms, slowing or stopping the heart attack. In Phase II data, subcutaneous administration of selatogrel 8mg and 16mg significantly inhibited platelet aggregation and demonstrated a rapid onset of action, within 15 minutes, with the height of its effect extending over 4–8 hours depending on the dose. The Phase III SOS-AMI study is currently recruiting globally, with recruitment in China initiating later in 2024.

Cenerimod, an S1P1 receptor modulator, is in development for systemic lupus erythematosus (SLE). Idorsia believes that cenerimod is the ideal treatment for SLE because it prevents the migration of T cells and B cells into target organs and prevents the migration of antigen-presenting cells and priming of autoreactive lymphocytes. Two Phase III OPUS studies are currently recruiting globally.

Idorsia estimates its current cash reserves to last to early April 2024, and therefore plans to extend the cash runway through various avenues, including potential partnership and out-licensing deals. In 2024, Idorsia wants to fund the company without selling everything, while retaining shareholder value within.

IGM Biosciences

IGM Biosciences presented at the JPM Healthcare Conference providing updates on its IgM antibody platforms, collaboration agreement with Sanofi, and financial position as of 2023. The company ended the year with approximately $338m in cash and investments, with runway expected into Q2 2026. The company's worldwide research collaboration with Sanofi is expected to develop agonists using IGM's proprietary antibody technology against three oncology targets and three autoimmune and inflammation targets. Per the terms of the agreement, IGM has received an upfront payment of $150m from Sanofi, with potentially $6bn in preclinical, clinical, regulatory, and commercial milestone payments. Sanofi will be responsible for the worldwide commercialization of the IgM agonist product.

IGM's pipeline consists of three products: aplitabart, imvotamab, and IGM-2644. Aplitabart is a multimeric DR5 agonist currently being investigated in a clinical trial for second-line metastatic colorectal cancer, investigating PFS as the primary endpoint and objective response rate, OS, and safety as secondary endpoints. The company plans to enroll approximately 110 patients in the Phase I trial by Q1 2024. Imvotamab is currently being investigated in systemic lupus erythematosis (SLE), rheumatoid arthritis (RA), and idiopathic inflammatory myopathies (myositis). The trials in SLE and RA are currently enrolling and the trial in myositis is expected to initiate in Q1 2024. IGM-2644 is currently in preclinical development for the treatment of autoimmune diseases.

As 2024 progresses, we anticipate IGM's undisclosed product in collaboration with Sanofi to make a worldwide impact. We expect IGM's domestic pipeline to mature with time, with topline data once the patient cohorts have been completely enrolled.

Ironwood Pharmaceuticals

Ironwood CEO Tom McCourt began his presentation speaking of the company's vision of becoming the leading GI healthcare company focused on advancing the treatment of GI diseases and redefining the standard of care for those patients.

Linzess is the US prescription market leader for adults with irritable bowel syndrome with constipation (IBS-C) and chronic idiopathic constipation (CIC). Growth has been driven primarily by patients coming over from the OTC space. Linzess is the first and only FDA-approved prescription therapy for patients with pediatric functional constipation (PFC) for patients aged 6–17 years. This is an area with significant unmet need and opportunity. The drug became commercially available for the PFC indication in June 2023, and Ironwood has an efficient investment plan in place to realize its full opportunity.

Apraglutide is a potentially best-in-class GLP-2 analog for short bowel syndrome for intestinal failure (SBS-IF). It has the potential to establish a new standard of care with its once-weekly dosing as opposed to daily dosing for other drugs for the condition. The drug has unique pharmacological properties including a long half-life which supports the once-a-week dosing regimen. The STARS Phase III trial is the largest GLP-2 trial ever conducted for the SBS-IF population. Topline data are expected in March 2024. Apraglutide has the potential to achieve

$1bn in peak net sales.

Ironwood's CNP-104 has the potential to be the first disease-modifying therapy for primary biliary cholangitis by targeting the root cause of the disease. There are currently no therapies on the market to address the root cause of the autoimmune destruction of the bile ducts. Initial assessment provided evidence of favorable T-cell response in patients dosed with CNP-104. Ironwood maintains an option from COUR Pharmaceuticals to exclusively license US rights to CNP-104 for continued development pending proof of concept and commercial viability. Ironwood expects topline data from the Phase II study in Q3 2024. Through Linzess, apraglutide, and CNP-104, Ironwood can potentially generate revenues of over $1.5bn through the 2030s.

CEO McCourt closed out his presentation by saying that 2024 has the potential to be a transformational year for Ironwood. The company is uniquely positioned to drive value as a GI-focused biotech with multiple 2024 development catalysts and strong Linzess cash flows expected until generic entry in 2029.

Kymera Therapeutics

Kymera Therapeutics, a leader in targeted protein degradation (TPD), presented a compelling overview of the company's progress and expected milestones for the near future at the 42nd annual J.P. Morgan Healthcare Conference. CEO Nello Mainolfi started the presentation by highlighting Kymera's unique target selection strategy for developing new candidates. It is based on four pillars where the company focuses on developing first- or best-in-class opportunities where there are undrugged or inadequately drugged targets with a strong pathway validation, a clear path to clinical differentiation, and large commercial opportunities. Since its founding in 2016, this strategy has led Kymera to meet significant milestones. As of today, Kymera has advanced four first-in-class programs to the clinic, demonstrated clinical translation of degradation and safety, and achieved early clinical proof of concept in its inflammation, immunology, and oncology programs.

Between 2024 and 2025, Kymera expects to achieve significant advancements within its pipeline. KT-474, a protein degrader therapy targeting IRAK4 and being developed in partnership with Sanofi, is expecting Phase II data from trials in hidradenitis suppurativa and atopic dermatitis. Two new oral degraders are expected to enter Phase I – KT-621, a protein degrader therapy targeting STAT6, and KT-294, a protein degrader therapy targeting TYK2. Lastly, KT-333 (TPD targeting STAT3) and KT-253 (TPD targeting MDM2) are expecting initial Phase I data in 2024.

Kymera is hoping that its oral TPD treatments will lead to domination of the $250bn immune-inflammation market that is currently dominated by injectables, with over 75% of drugs administered as injections. By recently closing a financing of $750m, Kymera has extended its runway into the first half of 2027, which will allow it to continue executing its ambitious vision of harnessing novel modalities to revolutionize healthcare. It has a successful track record of delivering multiple new drug mechanisms in the clinic, and is expecting up to 10 novel INDs within the first 10 years of operation. As the company continues to unlock the potential of TPD, it offers hope for patients with currently untreatable diseases.

Lexeo Therapeutics

Lexeo Therapeutics, a genetic medicine company aiming to bring precision medicine to disease areas with little or no penetration, set out its strategy for 2024 at this year's JPM Healthcare Conference. CEO Nolan Townsend outlined the company's vision and development plans, noting that evolving regulatory environments and a shifting treatment landscape have yielded untapped potential for his well-positioned company. Lexeo Therapeutics is targeting its gene therapies at areas where it sees its non-viral AAV vector excelling, specifically cardiovascular disease and Alzheimer's disease.

Townsend highlighted the company's pipeline, mainly its Phase I/II stage assets LX2006 and LX1001 under development for Friedreich's ataxia cardiomyopathy and APOE4-associated Alzheimer's disease, respectively. The company's next most advanced program is its arrhythmogenic cardiomyopathy therapy LNX2020, which is expected to move into clinical studies shortly. With this and LX2006, Lexeo Therapeutics is hoping to be the first company with two cardiovascular gene therapy programs in clinical studies, with data readouts expected in 2024. Regarding Lexeo's Alzheimer's disease program, interim data from all cohorts of a Phase I/II trial are expected in the second half of 2024, likely at the Clinical Trials on Alzheimer's Disease Conference (CTAD). Townsend enthusiastically presented the company's plethora of non-clinical and clinical evidence supporting its cardiovascular and Alzheimer's disease pipeline in tandem with comments on aligning development plans such as study designs with regulatory precedents. Rounding off the presentation, Townsend proudly summarized the company's expected catalysts for 2024 and briefly touched on the financial runway extending into Q4 2025. In summary, Lexeo Therapeutics utilized its JPM presentation to stake its ambitious claim on underdeveloped disease areas with its unique AAV technology and strategic pipeline.

Liquidia Corporation

Liquidia has been making progress towards its mission to develop treatments for pulmonary arterial hypertension (PAH). Liquidia's main product, Yutrepia, an inhalation dry powder, achieved tentative approval in 2021 for pulmonary arterial hypertension (PAH), and an additional PDUFA for pulmonary hypertension associated with interstitial lung disease (PH-ILD) is set for January 2024 with no additional clinical trials needed for review. Due to the Hatch-Waxman Act, Yutrepia for PAH cannot be marketed in the US, but favorable regulatory standards were reached, leading to tentative approval, establishing the safety and efficacy of Yutrepia and Liquidia's PRINT technology. Additionally, final approval for PH-ILD cannot occur until the regulatory exclusivity for Tyvaso expires on 31 March 2024.

In relation to the litigation affecting Yutrepia, Liquidia stated the company has not found infringement on the claims for the '793 patent asserted by United Therapeutics. Liquidia also declared the '327 patent was not infringed upon, and additionally the patent was not submitted to the Orange Book before the original NDA was filed. In January 2024, Liquidia filed the latest response to United Therapeutics under the Hatch-Waxman Act to the District Court. Liquidia continued to prepare its sales and commercial team and is ready to launch Yutrepia when given the green light to do so.

Liquidia is also developing L606 for North America in partnership with Pharmosa, with the drug being a sustained-release treprostinil for PAH and PH-ILD. In December 2023, Liquidia held a Type C meeting with the FDA to discuss a registration pathway for L606. A Phase III global placebo-controlled study in PH-ILD is expected to initiate in 2024 to support both PAH and PH-ILD, with a safety study continuing to enroll. Liquidia reiterated that the company is in position to be well capitalized through 2024, supported by a $126m financing raised since Q3 2023 to support development goals and the launch of Yutrepia.

Lyell Immunopharma

Lyell Immunopharma CEO Lynn Seely presented this year's JPM discussion surrounding the company's T-cell therapies in development for cancer. Lyell uses its genetic and epigenetic reprogramming technologies to create CAR-T cells and tumor-infiltrating lymphocytes (TIL) that resist exhaustion and have durable stemness (the ability to self-renew).

Lead CAR-T cell candidate LYL797 is in Phase I trials for triple-negative breast cancer, non-small cell lung cancer, and other ROR1+ solid tumors. Seely reviewed preclinical data exhibiting key differentiators (tumor reduction, enhanced cytokine production, and tumor infiltration in an aggressive NSCLC syngeneic model with c-Jun CAR T cells) and noted the candidate's efficacy with c-Jun overexpressing ROR1 CAR-T cells in aggressive NSCLC. Ongoing Phase I dose escalation and dose expansion trials are under way in relapsed/refractory triple-negative breast cancer and NSCLC patients who are ROR1-positive, with initial data on about 20 patients expected during the first half of 2024.

In the TIL pipeline, Seely discussed LYL845, which has exhibited robust TIL expansion across immunologically hot and cold tumors. Developed with the company's Epi-R manufacturing protocol and Stim-R technology, LYL845 produces long-lived effector cells. Phase I trials are under way in melanoma, NSCLC, and colorectal cancer, with initial data readouts planned in the second half of 2024.

Seely closed by noting that the company has partnered with Cellares and its automated manufacturing processes that can produce up to 800 doses of LYL797 per year. For other projects, Lyell produces its Phase I clinical supply in-house at its LyFE Manufacturing Center.

MacroGenics

MacroGenics' CEO Scott Koenig began the presentation by focusing on the company's efforts in developing antibody-drug conjugates (ADCs), with which it has 20+ years of experience and engineering expertise. He also showcased MacroGenics' differentiated pipeline, with various assets being investigated in multiple solid tumor types in early-phase trials. Koenig went on to highlight how MacroGenics is expanding its capabilities through numerous partnered programs, including the marketing of Margenza for HER2+ breast cancer with Eversana, Zynyz in Merkel cell carcinoma with Incyte, and Tzield for stage 2 type 1 diabetes with Sanofi. MacroGenics is also partnering with Gilead to develop various biologics in solid and hematological tumors.

Koenig discussed three key readouts expected for MacroGenics in 2024: the Phase II TAMARACK

trial of Vobra Duo (an ADC) in metastatic castration-resistant prostate cancer (mCRPC), the Phase II LORIKEET trial of lorigerlimab in mCRPC, and the Phase II HEAT trial of enoblituzumab in neoadjuvant prostate cancer. Positive results for these trials will provide a rationale to initiate Phase III trials which could lead to approvals across markets.

The objective response rate (ORR) for patients treated with Vobra Duo (a B7-H3-targeting ADC) in a Phase I trial was 25.0%, which is relatively underwhelming compared to other agents approved in this setting, although of course these data are in an extremely small cohort and may not reflect future data in later-phase trials. Similarly, Phase I data showed that lorigerlimab-treated mCRPC patients achieved an ORR of 25.7%, which is again not particularly impressive considering the current mCRPC treatment landscape which is dominated by hormonal therapeutics which have robust data and strong physician familiarity in this setting. Lorigerlimab is a PD-1- and CTLA-4-targeting bispecific antibody – prostate cancer is an immunologically "cold" tumor type, meaning that response rates to immunotherapies are low, which has already resulted in failed trials for both Keytruda and Opdivo, two PD-1 inhibitors with approvals across various oncology indications. MacroGenics hopes to produce stronger data in the Phase II LORIKEET trial and carve out a niche in mCRPC by having lorigerlimab be the first immune checkpoint inhibitor approved for mCRPC. The initial readout for the TAMARACK Phase II trial is expected in H1 2024, and the Phase II LORIKEET trial is expected to read out in H2 2024, both of which may be able to boost expectations surrounding Vobra Duo and lorigerlimab, respectively.

Finally, Koenig examined another exciting asset for MacroGenics: the next-generation CD3xCD123 DART molecule, MGD024. Gilead is partnering with MacroGenics on a currently ongoing Phase I dose escalation study for this asset in hematological malignancies; further data will be needed to assess its chances of approval in this branch of oncology.

MacroGenics is expecting record revenues in 2023, having reported total revenues of $152m in 2022. It generated $256m in cash and investments by Q3 2023, compared to only $124m in Q3 2022. Strong late-phase data will help boost revenues and investments going forward in 2024.

Mayne Pharma Group

During the JPM conference, Mayne Pharma, led by CEO Shawn O'Brien, outlined the challenges faced in the prior 18 months, including near-bankruptcy, and highlighted the company's progress and key achievements.

Mayne Pharma reduced business complexity by divesting Metrics Contract Services and the US generics business, generating a combined total of $565m. The company strategically expanded its US women's health portfolio, acquiring exclusive commercialization rights for three branded contraceptive and menopausal products.

The dermatology business, facing pricing pressures, underwent significant restructuring. O'Brien reported a remarkable 314% increase in dermatology revenue during the second half of fiscal year 2023, turning the business back to positive contribution. The company plans to launch 10 dermatology products between October 2023 and June 2024. Mayne Pharma achieved a relaunch of its flagship product, the oral contraceptive Nextstellis, resulting in a 276% revenue

increase compared to fiscal year 2022. The women's health segment, comprising 96% of the branded product portfolio, demonstrated a 45% sequential increase in net sales. Ongoing initiatives include enforcing ACA laws to minimize patient out-of-pocket expenses for birth control.

Mayne Pharma reported positive operating cash flow of AUD14m in the second half of fiscal year 2023. Asset sales led to a net cash position of AUD173m on 30 June 2023, compared to a net debt position of AUD317m the previous year. The company initiated an on-market buyback of up to 15%. For the four-month period from 1 July to 30 October 2023, Mayne Pharma reported net sales of AUS125m, indicating a run rate of AUS375m for fiscal year 2024. Gross margin increased by 50% to AUS72m, and underlying EBITDA was AUS1m. The company achieved positive contribution margins across all three business segments.

Mayne Pharma aims to achieve positive operating cash flow by the end of the fiscal year, with a strategic focus on maintaining positive contribution margins and continued growth in key segments. The company is actively pursuing growth strategies, including product launches and adherence to ACA laws, while exploring potential new products for its dermatology and women's health portfolios.

In summary, Mayne Pharma's presentation at the JPM conference highlighted a business transformation, marked by diversification, strategic asset sales, and substantial growth in key segments. The company's focus on profitability, cost efficiency, and strategic initiatives positions it for continued success in the pharmaceutical industry.

NeuroPace

NeuroPace is concentrated on transforming the lives of people suffering from epilepsy, with a focus on drug-resistant epilepsy, a highly undertreated patient population with significant unmet need. The company’s sole product, the RNS System, is a closed-loop, brain-responsive neuromodulation implantable device which monitors brain activity continually and responds to patient-specific seizure patterns. The device then records ongoing intracranial electroencephalography (iEEG) data for physicians to review to allow for a personalized treatment. In his presentation, NeuroPace CEO Joel Becker explained how real-world, post-approval data for the RNS System have been stronger than the original FDA trial data, with an 82% median seizure reduction demonstrated at 3+ years. Additionally, approximately one in three patients have a 90% reduction in seizures.

He went on to explain how alternatives to the RNS System include resection or laser ablation, which are both irreversible, destructive surgical procedures that carry neurocognitive and loss-of-vision risks. Neuromodulation competitors include deep brain stimulation and vagus nerve stimulation, but these are not responsive to brain activity or tailored to patients’ needs (as opposed to the RNS System, which only delivers electrical stimulation when a patient needs it) and can cause side effects.

In the US, one third of epilepsy patients are drug-refractory, which equates to approximately 1.2 million people. The current population focus is on Level 4 comprehensive epilepsy centers, where approximately 50,000 refractory epilepsy patients are treated annually. Of these, approximately

6,500 patients receive treatment beyond drugs. Becker stated that significant opportunity exists to close this treatment gap by expanding access to RNS therapy through three strategies.

The first way the company is aiming to do this is by educating and supporting clinicians and patients to expand RNS therapy utilization. NeuroPace is currently working to ensure that epileptologists and functional neurosurgeons understand that, within the focal indication, there are a number of different places within the brain that the device can be effectively utilized, which allows for flexibility and could lead to increased efficacy in some patients. Becker also explained that the RNS System can be used as a hybrid therapy, for example, in conjunction with surgery.

The company also plans to increase the availability of the RNS System to healthcare systems outside of Level 4 comprehensive epilepsy centers, where 1,800 epileptologists and functional neurosurgeons are practicing. In 2023, the company received approval of a PMA supplement that allows for RNS technology to be used beyond epilepsy centers, in the community setting. Expanding into the community will allow NeuroPace to uncover more complex patients who are never referred to epilepsy centers. The pilot for this project is expected to be initiated in the first half of 2024, with expansion happening in the second half of 2024.

Finally, NeuroPace aims to expand access to RNS therapy by broadening its label to include generalized epilepsy patients. Currently, the therapy is only indicated to treat focal epilepsy patients, who make up about 60% of the drug-refractory epilepsy market. Generalized epilepsy patients often go through a shorter diagnosis process compared to focal epilepsy patients, which should allow for a quicker time from patient identification to implant. There are no other FDA-approved devices for generalized epilepsy. Enrollment was completed for the generalized epilepsy clinical trial in December 2023. In January 2024, NeuroPace announced that all the trial patients had been implanted with the RNS System and that the one-year follow-up of these patients has begun.

The company is also leveraging the RNS System’s data collection and brain monitoring capabilities to help inform other treatment strategies. It recently announced a collaboration with an early-stage biotechnology company which is running a Phase IIa clinical trial of its novel compound. The RNS System was used to monitor patient response to the delivery of the novel compound, and NeuroPace could provide data to the company to help evaluate the impact of the compound on certain biomarkers associated with focal seizures.

NeuroPace works closely with its partner company, DIXI, to provide a comprehensive solution for focal seizure location. DIXI distributes stereo EEG electrodes to comprehensive epilepsy centers to determine the starting location and transmission network of a seizure. Stereo EEG is less invasive, offers faster patient recovery, and has become the predominant approach for intracranial monitoring.

In terms of financial performance, NeuroPace ended 2023 with $66.5m on its balance sheet, including ~$7.9m in net proceeds from an ATM equity financing facility in Q4 2023. This should provide sufficient capital to fund planned operations through mid-2026.

Nevro

Nevro president and CEO Kevin Thornal kicked off his presentation talking about the company's unique value proposition. It has multiple growth drivers in the large and diversified spinal cord stimulation (SCS) market through product diversification and new indications; it is entering the fast-growing sacroiliac (SI) joint fusion market; it has a unique and differentiated 10kHz technology with superior multidimensional outcomes; and has meaningful leverage opportunities to drive long-term profitability and cash flow.

Nevro's overall mission is to free patients from the burden of chronic pain. The company is targeting four major chronic pain markets: painful diabetic neuropathy (PDN), non-surgical refractory back pain (NSRBP), post-laminectomy syndrome or failed back surgery syndrome (FBSS), and SI joint pain. Its portfolio features the most diverse and comprehensive product range in SI joint and SCS solutions. The unique 10kHz SCS therapy delivers unmatched innovation and proven superior health outcomes.

The company operates around three pillars: commercial execution, market penetration, and profit progress. To date, Nevro has enhanced its executive bench strength and completed commercial realignment, it recently completed several large new hire training sessions and implemented new professional education programs with customers, and also launched a training for SI joint products as it enters the SI joint market through its recent acquisition of Vyrsa Technologies. Nevro has demonstrated strong clinical evidence and recently published 24-month data for NSRBP and PDN to drive expanded payer coverage. It is expanding indications beyond pain, and began enrollment in a PDN sensory study and continues to accelerate rollout of and innovate its HFX iQ system. Nevro recently implemented a restructuring plan which included laying off 5% of its workforce to support long-term growth and profitability. The Vyrsa acquisition is expected to be accretive to gross and operating margins with the ability to leverage its sales force.

Nevro is a leader in the $3.5bn PDN space but is less than 1% penetrated in that market. PDN represents approximately 20% of worldwide permanent implant procedures. The company's Q4 2023 global revenues of $116m ($22.4m of which were PDN revenues) exceeded expectations.

CEO Thornal went on to talk about its HFX iQ, which is the only AI-based SCS system that gets smarter over time by learning from patient responses. The first HFX iQ-implanted patient reported 80% relief and an increase in activity as of 26 October 2023, which was one year post implant. Data on HFX iQ included patients reporting getting back to relief 75% faster. HFX iQ is the most effective SCS solution for PDN, with approximately two times the responder rate and pain relief. It has the 90% highest published responder rate, 80% highest published percentage pain relief, and is the only SCS system to demonstrate neurological improvements.

In late November 2023, Nevro acquired Vyrsa, thus expanding into the $2bn SI joint fusion market. Nevro has the most comprehensive portfolio in SI joint fusion. The Nevro V1 SI joint fusion system with integrated transfixing technology provides immediate SI joint stabilization and an opportunity for long-term fusion. NevroPRO is the first MIS allograft SI joint fusion system designed to provide comprehensive decortication of the SI joint articular surface with multiple implant sizes for variable patient anatomy. The Nevro Fix lateral SI joint transfixing

lateral screws are designed to provide maximum compression of the joint space.

Thornal concluded the presentation by discussing Nevro's strategic execution blueprint for 2024 and beyond. The company will focus on commercial execution, maximization of the HFX iQ technology, continue to scale its Costa Rica manufacturing plant and leverage business, expand the SCS indication, and penetrate the SI joint fusion market.

Novocure

Novocure is a company focused on developing tumor-treating fields technology (TTFields), which uses electric fields to disrupt cell division, causing cancer cell death. Novocure is planning on using this technology via its Optune medical device to target the most aggressive forms of cancer. Executive chairman Bill Doyle started the presentation by highlighting the three key pillars of its strategy for long-term growth: driving commercial adoption, advancing clinical trials, and delivering product innovation.

Doyle reported that Optune has generated over $500m in net revenue, with over 3,750 patients being treated with this technology. Importantly, the NCCN has given Optune its highest possible recommendation in glioblastoma, Category 1, based on excellent OS data seen in the Phase III EF-14 trial, which is vital in advancing physician trust and familiarity. This is particularly notable as glioblastoma is a notoriously difficult cancer to treat. However, Novocure has only achieved 30–40% penetration in key countries, a statistic it is aiming to improve going forward.

The TTFields technology has also had positive data in the Phase III LUNAR trial in metastatic NSCLC patients with no mutational biomarkers who have progressed on platinum chemotherapies in the first line, which is an area of huge unmet need. Novocure estimates that ~30,000 patients will seek second-line therapy in this setting, a large population which could generate significant profit. Based on this trial, Novocure hopes to launch Optune in non-small cell lung cancer (NSCLC) in 2025, with the expectation of submitting Phase III data in the US and Japan in 2024.

Novocure is also investigating Optune in patients following stereotactic radiosurgery therapy for brain metastases from NSCLC and in pancreatic cancer patients, with Phase III readouts expected in both of these indications in 2024. Positive data could allow access to large patient populations in areas of high unmet need, creating a large amount of opportunity for Novocure. In the earlier stages of development, it is looking at Optune's efficacy in glioblastoma, and in various combinations and settings in both NSCLC and pancreatic cancer.

Doyle concluded by addressing the announcement that Novocure had undertaken a structural reorganization at the start of 2023, wherein ~200 employees were laid off, stating that it needed to "remove some of the fat" in order to maximize profits and allow focused innovation. As a smaller pharma company, developing relationships with governments, securing reimbursement for Optune, upscaling production to meet demand, and educating healthcare practitioners and patients on the benefits of Optune to promote uptake will be essential factors affecting Novocure's growth.

Olema Oncology

At the J.P. Morgan Healthcare Conference, Olema Oncology, a clinical-stage biopharmaceutical company developing therapies for women's cancers, provided an update on its lead investigational product, palazestrant. With a strong 2023, Olema achieved multiple clinical milestones for palazestrant in ER+/HER2- breast cancer throughout the year. In various Phase II monotherapy studies, palazestrant has demonstrated beneficial effects and a well-tolerated safety profile, with further results presented at ESMO 2023. In late 2023, Olema initiated Phase III development with the OPERA-01 study, a pivotal second-/third-line monotherapy trial. Palazestrant is also being studied in combination studies with CDK4/6 inhibitors including palbociclib and ribociclib. A Phase Ib/II combination study of palazestrant and everolimus is also expected to initiate in 2024.

Adding to its oncology pipeline, Olema recently nominated a new candidate, OP-3136, a KAT6 inhibitor to target ER+ breast cancer and castration-resistant prostate cancer. The candidate is being developed in an exclusive collaboration and licensing agreement totaling $438m in upfront and pre- and post-sales milestone payments with Aurigene, where Olema will lead clinical, regulatory, and commercial activities for the asset. In preclinical studies, OP-3136 has demonstrated potent antitumor activity. An IND filing for OP-3136 is expected to be submitted to the FDA by the end of 2024.

In 2023, Olema completed a private placement for up to $180m, with $130m initially grossed, and an additional loan and term agreement with Silicon Valley Bank for the remaining $50m. The funds, combined with the company's cash and cash equivalents, bring Olema to a financial position of approximately $276.9m to support its current operating plan into 2027, including topline data for OPERA-01 and clinical development for OP-3136.

Pacira BioSciences

Frank Lee, who has been CEO at Pacira BioSciences for less than a month, started the presentation by explaining how he was compelled to join the company following a year of semi-retirement. He was impressed by the company's leading presence in the non-opioid pain management space via three of its assets: Exparel, Zilretta, and iovera. Exparel is an expensive injectable formulation of bupivacaine, and is the only long-acting, local and regional analgesic with a broad approval for postsurgical pain. Zilretta is the only FDA-approved extended-release intra-articular injection for osteoarthritis knee pain, and iovera is the only novel, handheld device for immediate, long-lasting, drug-free pain control using advanced cold technology.

In 2023, the FDA approved a supplemental New Drug Application for the use of Exparel in lower extremity procedures as an adductor canal block and a sciatic nerve block in the popliteal fossa, following strong clinical data versus an active comparator. With more than 3 million lower extremity procedures taking place annually, Pacira has forecasted annual sales of $100m+ within five years.

Pacira claims to have a strong financial and operational foundation to self-find growth. At the end of 2023, the company had $280m on its balance sheet, with total net product sales of

$669.9m, with $538.1m of these sales attributable to Exparel. Additionally, Pacira reported an adjusted EBITDA of at least $210m for 2023, slightly lower than the $212.7m reported for 2022.

Pacira will directly benefit from the Non-Opioids Prevent Addiction in the Nation (or NOPAIN) Act, which was signed into law in the US in December 2022 and takes effect in January 2025. The NOPAIN Act directs the Centers for Medicare and Medicaid Services to reimburse non-opioid and opioid treatments separately across all outpatient settings, in hopes of reducing or replacing opioid consumption. This should help to reduce the pressure on providers to prescribe opioids by ensuring that approved non-opioid options are more widely available to individuals as a post-surgical treatment option. There are currently six branded pharmaceuticals with FDA approvals for post-surgical pain that will benefit from the NOPAIN legislation. Pacira expects the NOPAIN Act to drive Exparel sales to over $1bn. Lee emphasized the importance of educating customers and stakeholders about the Act and how it will impact them.

Currently, Pacira is focusing on growth and expanding its contract base with group purchasing organizations (GPOs). New GPO partnerships are expected to be launched in 2024. This should expand access and make non-opioid pain management more broadly accessible in inpatient settings, where ~25% of Exparel-relevant market procedures take place.

Pharvaris

Berndt Modig, CEO at Pharvaris, focused on the company's plans for its lead asset deucrictibant, a novel, orally bioavailable, bradykinin B2 receptor antagonist in development for bradykinin-mediated hereditary angioedema (HAE), a rare genetic disorder characterized by unpredictable episodes of painful swelling that can require hospitalization and be life-threatening. Current treatment options for attacks all require injections. Deucrictibant is being developed in two formulations, the first is an immediate-release (IR) preparation for on-demand treatment, and the second is an extended-release (XR) version for prophylaxis.

A desirable on-demand treatment for HAE would have a rapid onset of action, durable effect from a single dose, and be orally administered, according to Pharvaris, and the company believes its candidate can meet these needs. Data from the Phase II RAPIDe-1 trial demonstrated rapid onset of action leading to symptom relief and resolution of HAE attacks with a reduction in rescue medication use. Importantly, there were no safety concerns raised and the drug candidate was well tolerated. The success of this trial has led to plans for a Phase III trial in the on-demand setting, to be initiated in H1 2024.

Deucrictibant also has the potential for use as a preventive agent. Ideally, such an agent would have the efficacy of the injectable agents but without the pain that can be associated with injections, said Modig. The CHAPTER-1 Phase II trial showed that deucrictibant reduced HAE occurrences by more than 90%, was well tolerated, and improved quality of life for recipients. Importantly pharmacokinetic analysis of the XR formulation supports once-daily dosing to be taken into Phase III.

A clinical hold was placed on development by the FDA in August 2022 due to concerns over safety. A rodent toxicity study was conducted to address the concerns, and as a result the hold on development of the IR formulation has been lifted, but it remains in place for the XR

formulation, although the company stated that the FDA is still evaluating the relevant new data; development outside the US was not interrupted.

Pharvaris believes it is well positioned for 2024 with €140m in cash plus a $300m underwritten offering. With the company estimating the HAE market to be worth in excess of $2bn and annual growth of 15% predicted, Pharvaris is hoping that deucrictibant can secure significant market share based on its short- and long-acting formulations, promising efficacy, and convenient administration.

Pliant Therapeutics

Pliant Therapeutics continues to make strides in its development pipeline, highlighting key upcoming milestones for 2024. The presentation's opening remarks focused on its most advanced Phase II asset, bexotegrast, in both idiopathic pulmonary fibrosis (IPF) and primary sclerosing cholangitis (PSC). This small molecule is designed to prevent toxicities linked to systemic transforming growth factor (TGF) blocking reported with the present standard of care by inhibiting the activation of αvβ6 and αvβ1 integrins, which induce activation of TGF (particularly in fibrotic tissues).

Results for the Phase IIa INTEGRIS-IPF study were discussed (previously seen in mid-2022 at a lower dosage), showing clear improvements across physiologic (forced vital capacity [FVC]), radiographic (quantitative lung fibrosis), and symptomatic (cough) assessments versus placebo at a higher dosage. Additionally, the safety and tolerability profile of bexotegrast was noteworthy, as it appears to be an improvement over the current standard of care, particularly in terms of gastrointestinal side effects. Pliant is currently enrolling for its Phase IIb study (BEACON-IPF), assessing the change from baseline absolute FVC after 52 weeks, with the speaker indicating during questioning that this could be a pivotal trial. Furthermore, the presenter took time to elaborate on the current unmet needs in IPF for a treatment that shows improvements in tolerability, quality of life, or survival benefit. In addition to this, bexotegrast's ongoing Phase IIa trial's preliminary results were elaborated on in the untapped primary sclerosing cholangitis (PSC) indication. Bexotegrast was well tolerated in PSC participants, with all doses (statistically significant at 160mg) reducing enhanced liver fibrosis scores and collagen synthesis (PRO-C3) relative to placebo. Furthermore, the potential of bexotegrast was emphasized based on its localized TGF-β inhibition, giving the drug the potential to expand into multiple indications across pulmonary and liver fibrosis.

Meanwhile, Pliant's early-stage antifibrotic pipeline is progressing well, with a first-in-class dual selective αVβ8/αVβ1 integrin inhibitor, PLN-101095, in Phase I development. The company stressed the novel approach of dual inhibition to address immune checkpoint inhibitor resistance by disrupting the solid tumor microenvironment and restoring CD8 T-cell secretion. In addition to this, an IND application for PLN-101325, an α7β1 integrin activating antibody that serves to stabilize muscle fibers in patients with Duchenne muscular dystrophy and other kinds of muscular dystrophy, is scheduled to be submitted in Q1 2024.

Protagonist Therapeutics

Protagonist Therapeutics' key areas of focus are peptide-based medicines. CEO Dinesh Patel set out the 2024 prospects for the company, focusing on the development of two late-stage clinical assets, rusfertide, a hepcidin mimetic for polycythemia vera (PV), and JNJ-2113 (PN-235), an oral IL-23 receptor antagonist for psoriasis and ulcerative colitis (UC).

PV is a rare disease characterized by an increase in blood cells, particularly red blood cells (RBCs), leading to an increased hematocrit (HCT) and consequently an increased risk for cardiovascular and thrombotic events. Current treatment options are limited to phlebotomy or chemotherapy to reduce RBC levels, but there are no pharmaceutical options with an RBC-specific mechanism of action that can reduce HCT. Promising data from the Phase II REVIVIE study showed that rusfertide was associated with a significantly higher response rate than placebo (70% versus 19%; response was defined as no phlebotomy treatment for 12 weeks and HCT control); of the 26 rusfertide recipients, 92% did not need phlebotomy. Importantly no serious safety signals were identified from more than two years of mean drug exposure. Enrollment of the ongoing Phase III VERIFY trial, aiming for a total of 250 patients, is on track. Should the Phase II results be repeated in Phase III, Protagonist Therapeutics is targeting PV patients with moderate treatment burden, estimated by the company to be 60% of the treatable population.

The second key asset is JNJ-2113, an oral IL-23 receptor antagonist peptide being developed for psoriasis treatment that could potentially be a first-in-class product. The company highlighted the highly potent but stable nature of its candidate, with Phase I proof-of-concept data translating into positive results for PASI75, PASI90, and PASI100 scores in the Phase IIb FRONTIER-1 trial. A consistent dose-response pattern was observed from doses up to 100mg twice daily, and once-daily dosing appeared to offer better efficacy than twice-daily dosing, leading Janssen to put a 200mg once-daily dose forward for Phase III development. Four trials are planned for psoriasis, and investigations for UC are also under way. Cross-trial comparisons of Phase II data for oral and injectable competitors were encouraging. Progress thus far has led to milestone payments of $172.5m, with $795m in future payments possible plus royalties on revenues that are estimated to reach $4bn.

Looking to the future, Patel highlighted the potential of the company's oral IL-17 peptide antagonist program. This target has the scope for treating a variety of diseases including inflammatory bowel disease, psoriasis, and spondyloarthritis, and it was estimated that the total market could reach $50bn if similar or better efficacy were to be demonstrated compared with approved monoclonal antibodies.

Protagonist Therapeutics is moving into 2024 with $322.7m in cash and securities with a secure runway into 2026. Data readouts and new trials are the key catalysts for 2024 and 2025, with commercialization of rusfertide being targeted for 2026.

RAPT Therapeutics

Pipeline-stage RAPT Therapeutics dedicated its platform at the JPM conference to detailing results from two oral small molecule drugs, zelnecirnon and tivumecirnon, being developed in inflammation and oncology, respectively. As these represent very different areas, the company plans to focus on zelnecirnon and is in active discussion with several parties about the potential to partner on the oncology asset, tivumecirnon.

The company's lead inflammation asset, zelnecirnon, is a once-daily oral agent that targets inflammatory Th2 cells. Framing this as a potential pipeline-in-a-product, CEO Brian Wong compared the asset to anti-IL-4 antibody Dupixent, which is approved in several inflammatory indications, and touted the drug as having disease-modifying potential due to its upstream mechanism of action. In a Phase Ib atopic dermatitis study, the novel CCR4 antagonist showed safety consistent with a lack of need for laboratory monitoring or black box warning, similar to oral Otezla. At day 29, zelnecirnon achieved a 33% placebo-adjusted rate of EASI 50 which increased to a 42% difference two weeks after patients stopped the one-month treatment. Wong used the OX40 class as an analog for the potential for disease-altering success, as zelnecirnon blocks the binding of CCL17 and CCL22 to CCR4, thereby inhibiting the trafficking of Th2 cell migration into lesional skin and reducing inflammatory cytokines like IL-4. However, data on the primary endpoint for an oral drug in atopic dermatitis were lower, with 14% of treated patients achieving an IGA of clear or almost clear, though this still compared to no patients on placebo. The primary endpoint for the Phase IIb study is EASI, but the placebo difference in IGA, measured as a secondary outcome in this ongoing study, will be of interest. Regardless, with potential for better efficacy than Otezla, CEO Wong highlighted that zelnecirnon could be positioned as the first choice after an inadequate response to topical cortical steroids, prior to injectables or oral JAK inhibitors. A Phase IIb study is enrolling, with data expected in mid-2024, which could set up Phase III studies to start in 2025, if successful.

Additionally, the company has started a Phase IIa proof-of-concept study in asthma, with a design that initially evaluates the drug as an add-on to inhaled medications but, after a just over a month, follows a tapering to monotherapy use for the last three weeks. The company is also looking to explore the use of zelnecirnon in type 2 COPD.

Rapt is evaluating CCR4 antagonist tivumecirnon in oncology by selectively inhibiting regulatory T-cell trafficking, specifically into the tumor but not into healthy tissues. The drug has been evaluated in proof-of-concept studies as a monotherapy, but also in combination with pembrolizumab, with a 45% objective response rate in patients with checkpoint inhibitor-naïve non-small cell lung cancer. A South Korean study run by Hanmi showed a 67% response rate in EBV-positive gastric cancer.

Replimune Group

Replimune presented at the JPM Healthcare Conference focusing on updates to its oncolytic products, RP-1 and RP-2. In the past year, the company released favorable data from its Phase I/II IGNYTE trial of RP-1 in anti-PD-1-failed melanoma. Per the data, one in three patients demonstrated a durable response, supporting the greatly anticipated BLA filing planned in the

second half of 2024. The Phase II CERPASS trial of RP-1 in first-line chronic squamous cell carcinoma demonstrated clinical benefit per the topline data released in December 2023 for its dual primary endpoints of objective response rate and complete response rate. However, statistical significance was not met in either of the endpoints. The company will continue to assess duration of response, PFS, and OS with maturity. Commercial revenues are expected to deliver starting in late 2025.

The company's anti-CTLA-4 product, RP-2, is clinically validated and has demonstrated durable monotherapy responses in multiple immune insensitive tumor types. A 30% overall response rate was achieved in second-line uveal melanoma, supporting a pivotal randomized trial in the indication. In a heavily pretreated population with 29.4% patient responders, the longest ongoing response was over 24 months. While uveal melanoma is a rare cancer with only approximately 1,000 cases recorded per year in the US, RP-2 has the potential to address the unmet need in this patient population.

Both of Replimune's oncolytic products have potential in terms of the commercial market, yielding high-value propositions for the skin cancer environment with approximately 70,000 treatable patients in the US alone. The company ended 2023 with a strong balance sheet of $466m, with its cash runway expected to remain cash positive into the second half of 2026.

Sage Therapeutics

CEO Barry Greene kicked off Sage's presentation at the 42nd annual J.P. Morgan Healthcare Conference. The presentation started with updates on the commercialization of Zurzuvae, the second FDA-approved product after Zulresso for postpartum depression (PPD). Zurzuvae launched in December 2023. Alongside collaborations with pharmacy distributors, Sage will be actively pursuing discussions to provide broader access of Zurzuvae to patients with PPD throughout 2024 with the aim to establish Zurzuvae as a first-line therapeutic.

Sage continued to highlight its brain health pipeline with upcoming catalysts for dalzanemdor (SAGE-718) and SAGE-324. Dalzanemdor is a NMDA receptor positive allosteric modulator (PAM) in development for Huntington's disease (HD), Alzheimer's disease (AD), and Parkinson's disease (PD). Through various early-stage studies, dalzanemdor has demonstrated beneficial effects. Several Phase II topline data catalysts, including readouts for PRECEDENT (mild cognitive impairment [MCI] associated with PD), SURVEYOR (HD cognitive impairment), LIGHTWAVE (MCI and mild dementia due to AD), and DIMENSION (HD cognitive impairment), are expected in the upcoming year. Additionally, Sage is developing a next-generation PAM of GABAA receptors for essential tremor that has shown benefits in clinical studies. A data readout for a Phase IIb study is expected in 2024.

With the Zurzuvae launch aiming to destigmatize PPD and combat both economic challenges and the stressful impact of the COVID-19 pandemic on women with PPD, Sage aims to expand access to Zurzuvae to more patients. Sage also sees value in developing its brain health pipeline as cognitive impairment disorders continue to increase in prevalence globally, in addition to its early-stage pipeline, including SAGE-319 for neurodevelopmental and motor disorders and SAGE-421 for cognitive impairment including schizophrenia. Together with these value drivers

and a secure cash position through 2026, Sage continues to act on its mission to deliver life-changing brain medicines globally.

Vera Therapeutics

Vera Therapeutics focused its presentation at the J.P. Morgan Healthcare Conference on its lead product, atacicept, for the treatment of IgA nephropathy (IgAN). The company had a favorable year, ending 2023 with a strong financial position with $160m in cash, cash equivalents, and marketable securities. Combined with its $25m drawn from its credit facility back in December 2023, Vera will remain sufficient to fund its IgAN pipeline to 2026.

Atacicept is currently in Phase III development for IgAN, with multiple data readouts expected in 2025 and beyond. It is a dual inhibitor of BAFF and APRIL that is self-administered as a single 1mL injection. In the ORIGIN Phase IIb trial in IgAN, atacicept was tested at increasing dose levels from 25mg to 150mg, with the primary endpoint being UPCR-24h at week 24. The primary endpoint was met at the 150mg dose, with stable eGFR observed for patients on atacicept versus placebo. As such, the 150mg dose was selected for the Phase III trial in IgAN, which initiated in June 2023. Atacicept was generally well tolerated in IgAN patients, with no reported deaths, low rates of serious adverse events, and only one patient discontinuation due to an adverse event.

Vera's IgAN development represents a high-value proposition, as IgAN is a large unmet need with a potential $6bn–$10bn market opportunity in the US, Europe, and Japan. With multiple data readouts expected in 2024–25, a BLA submission is anticipated in the second half of 2025, which would be supported by the results from the Phase III trial of atacicept.

Vericel

Vericel CEO Nick Colangelo kicked off the presentation by highlighting the company's lead product, MACI – an advanced cell therapy that rebuilds damaged cartilage and function using the patient's own cells. Colangelo was keen to note that MACI has become the leading cartilage repair product in the sports medicine market, and it is the only FDA-approved product of its kind.

Moving to the burn care market – another important focus for Vericel – the presentation focused on the recent US product launch of NexoBrid. This product, which is indicated for the removal of eschar in adult patients, is the only FDA-approved permanent skin replacement treatment for burns on patients with greater than 30% total surface area burns.

There is currently no established biosimilar, generic, or 510(k) pathway for products like MACI or Epicel. This is due to the products having a biological competent that works with the patient's own cells which ultimately means these products are regulated by the FDA. Due to this regulation, it makes it difficult for a competitor to compete in these therapeutic spaces as they would have to run a full clinical development program. Additionally, the approval of NexoBrid came with an orphan designation which results in orphan market exclusivity in the US, and the product has patent protection into the 2030s. With all this combined, Colangelo was eager to

point out the high barriers to entry present for potential competitors looking to encroach on Vericel's market share.

This market exclusivity has also led the company to have a solid financial profile – delivering positive adjusted earnings and operating cash flow every quarter for the last three and a half years – with the company ending 2023 with $152m in cash and no debt.

Looking to the future, Vericel is keen to advance its pipeline with two regulatory submissions in Q4 2023: firstly, the supplemental BLA submission for NexoBrid in a pediatric indication; and secondly, the submission for MACI arthroscopic delivery. Both submissions have been accepted for review by the FDA.

With a high revenue growth profile, sustained positive operating cash flow, and around $152m in cash and investments, the company is financially very secure. With anticipated regulatory approval decisions and product launches just around the corner, the future looks bright for Vericel.

Viridian Therapeutics

During the JPM meeting, CEO Steve Mahoney provided an overview of Viridian, highlighting the company's focus on two franchise areas: IGF-1R and FcRn. In 2023, Viridian achieved significant milestones and has key catalysts planned for 2024. The company's pipeline includes VRDN-001 and VRDN-003, both anti-IGF-1R antibodies for treating thyroid eye disease (TED), and VRDN-006 and VRDN-008, part of the FcRn portfolio for treating autoimmune diseases. Notable accomplishments in 2023 included the initiation of two Phase III studies for VRDN-001 (THRIVE for active TED, and THRIVE-2 for chronic TED), positive results from VRDN-001's Phase II study in TED, and securing $185m through a private placement to support the company until 2026. Upcoming milestones include the release of topline results from the THRIVE study in mid-2024, initial readout of the THRIVE-2 trial at the end of 2024, and the initiation of a pivotal program for VRDN-003 in mid-2024.

Mahoney introduced each program briefly, starting with the leading asset, VRDN-001. This antibody targets IGF-1R, a validated target in TED. VRDN-001 is designed as an intravenous infusion with a shorter infusion time of 30 minutes and a reduced dosing regimen of five doses in comparison to Tepezza, the first approved anti-IGF-1R antibody for TED which requires 60–90 minutes of infusion and eight injections per regimen. The Phase II study results of VRDN-001, published last year, demonstrated a favorable efficacy profile in improving both proptosis and symptoms compared to Tepezza. VRDN-001 was well tolerated without any notable adverse effects. Currently, VRDN-001 is undergoing two Phase III studies: THRIVE for active TED, with topline data expected in mid-2024, and THRIVE-2 for chronic TED, with an initial readout at the end of 2024. Moving to VRDN-003, it is the next generation of VRDN-001 with three amino acid mutations in a subcutaneous formulation. The selection of this candidate was based on Phase I data which demonstrated an extended half-life and a substantial increase in IGF-1, an indicator of effective IGF-1R suppression, in healthy volunteers. VRDN-003 showed a generally acceptable tolerability profile, with no identification of anti-drug antibodies. Due to the protein structure similarity between VRDN-001 and VRDN-003, along with the clinical experience gained from the Phase II study of VRDN-001, it is predicted that VRDN-003 can be administered once every two,

four, or eight weeks. This dosing regimen offers convenience while minimizing the risk of adverse effects. The primary endpoint for VRDN-003 would be the proptosis responder rate, with secondary endpoints including proptosis mean change, clinical activity score, and diplopia. Further discussions with regulatory agencies are planned prior to mid-2024 regarding these endpoints and trial design.

The FcRn franchise holds promising potential for entering lucrative markets such as myasthenia gravis (MG). Two candidates, VRDN-006 and VRDN-008, have been selected for this franchise. VRDN-006 is the only other known Fc fragment designed to inhibit FcRn. It offers a self-injection formula and demonstrates a comparable PK/PD profile to Vyvgart, an approved FcRn inhibitor for treating MG, as observed in non-human primate studies. Additionally, VRDN-006 does not affect albumin recycling and does not increase LDL in non-human primates, providing a competitive advantage in the market. The submission of an IND application is anticipated at the end of 2024. As for VRDN-008, it has been optimized for a longer half-life and a more profound and durable suppression of IgG compared to Vyvgart, as demonstrated in a humanized mouse model. This suggests its superiority within its class. The non-human primate study for VRDN-008 is anticipated to commence in the second half of 2024.

Viridian is well funded with a $313m in cash and cash equivalents at the end of Q3 2023, supporting the development of four candidate drugs until 2026.

Voyager Therapeutics

Voyager Therapeutics is coming into 2024 with plans to become a clinical-stage company once again, with four INDs expected in 2024 into 2025, with plans to generate data by 2026. At the beginning of 2024, Voyager announced a $100m IPO along with a new partnership with Novartis for its Huntington's disease and spinal muscular atrophy therapies, whereby the company received an additional $100m upfront payment, including a $20m equity investment. As such, Voyager has a cash runway to 2027, with an estimated $8.2bn in potential milestone payments.

The investment and funding were secured based on the potential of its TRACER-derived capsids. Voyager views this as a potential replacement for current AAV9 gene therapy delivery systems, showing a 100-fold improvement over parental capsid tech of AAV9. Voyager is planning to advance VY-TAU01 for Alzheimer's disease with an IND filing in the first half of 2024, a Phase Ia single ascending dose study in 2024, and a Phase Ib multiple ascending dose study in 2025. Following this, Voyager is also continuing studies to advance its SOD1 silencing gene therapy for the treatment of amyotrophic lateral sclerosis.

Xeris Biopharma

Paul Edick, Xeris's chairman and CEO, opened the presentation by reviewing the company's three core pillars of value creation: commercialization of three innovative products, leveraging its proprietary formulation science to develop new product candidates, and partnerships with biopharma companies. Edick provided financial highlights, including Xeris's cash flow positive status as of Q4 2023. For Q3 2023, it achieved revenues of $48.3m, representing 63% growth compared to Q3 2022. The company provided revised guidance on its 2023 total revenue to the

high end of $160m–$165m; its cash utilization to the low end of the $52m–$57m range; and it expects its year-end cash position to exceed $72m.

Edick discussed marketed products, all of which showed growth in net revenues during Q3. Gvoke, a ready-to-use autoinjector of liquid-stable glucagon for severe hypoglycemia, had year-to-date revenue of $48.4m, a significant contributor to the higher-range revenue forecast. Gvoke is thought to represent an addressable US market of $5bn, with expectations to penetrate the 15 million at-risk diabetic patients, of which only about 1 million are currently receiving a prescription for a self-administered rescue pen. Cortisol synthesis inhibitor Recorlev (levoketoconazole), for the treatment of Cushing's syndrome, a rare endocrine disease, has demonstrated revenue growth every quarter since its 2022 launch, with year-to-date revenue of $19.7m. Oral carbonic anhydrase inhibitor Keveyis (dichlorphenamide), a therapy for primary periodic paralysis, a spectrum of ultra-rare neuromuscular disease, had year-to-date revenue of $42.7m, despite generic competition.

The company plans to leverage additional applications for its XeriJect and XeriSol proprietary formulation platforms for subcutaneous and intramuscular weekly dosing, including partnership opportunities. XeriJect is best suited for drugs and biologics, including large molecules such as proteins, monoclonal antibodies, and vaccines, while XeriSol, used in Gvoke, is best suited for peptides and small molecules.

Xeris's XeriSol-formulated XP-8121 (levothyroxine) is an injectable potential therapy for hypothyroidism that may enable once-weekly subcutaneous dosing versus daily oral dosing; the company views a $1bn–$2bn opportunity in the overall levothyroxine market. The XP-8121 Phase II clinical study is fully enrolled, with Phase III development expected to start in the first half of 2025.

Also discussed was the execution of a license by Amgen to the XeriJect technology, which it will apply to its Tepezza (teprotumumab), a product approved for intravenous infusion once every three weeks to treat thyroid eye disease, turning the intravenous product into a subcutaneous formulation. Xeris also has a partnership with Regeneron for two undisclosed assets, for which it is just beginning numerous cycles of formulations. Also mentioned were the contingent value rights from the company's 2021 acquisition of Strongbridge, triggered by certain performance milestones related to Keveyis and Recorlev, resulting in payments to stockholders.

In closing, Edick stressed the company's ability to execute on strategy, validated through its past six record quarters, the quarterly revenue growth of all three marketed products, the Amgen and Regeneron deals, as well as its robust patent estate.

Zymeworks

CEO Kenneth Galbraith opened Zymeworks' presentation with a moment to reflect on the company's progress since the last J.P. Morgan Healthcare Conference, at which the company was celebrating zanidatamab's topline readout from a Phase III trial in biliary tract cancer (BTC) and its closure of a licensing agreement with Jazz Pharmaceuticals. He went on to announce that the company used the momentum from those two events to propel it into a year of success in 2023, and feels confident with the position Zymeworks is now in for another strong year. Upon

its entrance into 2024, the company now has a product pipeline which focuses on building uniquely differentiated agents through antibody engineering. Lead product zanidatamab, a HER2 bispecific antibody, currently has a rolling US regulatory submission under way with breakthrough designation, and is also anticipating a pivotal Phase III topline readout for use in gastric and gastroesophageal junction cancer in the second half of 2024. Through a partnership with Jazz and BeiGene, the company is also exploring zanidatamab's expansion into other indications, with additional clinical trials planned and ongoing. Galbraith highlighted Zymeworks' R&D strategy of focusing on cancers with the highest unmet needs and slowest therapeutic progression, selecting cancers which had seen the least improvement to five-year survival between 2012 and 2018. These include stomach, esophageal, and non-small cell lung cancer (NSCLC), all of which are indications where zanidatamab is under investigation. Looking forward, Galbraith detailed progress on the company's "5x5" strategy, in which it has five new INDs planned before 2026, and expressed hopes to expand its therapeutic focus beyond oncology to autoimmune and inflammatory diseases. Zymeworks also plans to inject further innovation into its pipeline by investing research into multifunctional engineered cytokines and dual checkpoint inhibitors.

Key prospective catalysts for the first half of 2024 include US and China regulatory submissions for zanidatamab in second-line BTC, commencement of a Phase III confirmatory study for zanidatamab in first-line BTC, a Phase II study for zanidatamab zovodotin in HER2 overexpressing NSCLC, and an expected IND filing for the first of its "5x5" candidates. In the second half of 2024, key expected catalysts involve alignment with the FDA on the confirmatory trial in first-line metastatic BTC, pivotal Phase III topline data for zanidatamab in first-line gastroesophageal junction cancer, a Chinese regulatory decision for zanidatamab in second-line BTC, an IND filing for the second "5x5" candidate, and nomination of the fifth product candidate in "5x5." The company also detailed some anticipated catalysts for 2025, including potential US and China launch for zanidatamab in BTC and initial royalty revenue from partners Jazz and BeiGene, as well as expected IND filings for two more "5x5" candidates.

Galbraith feels positive for Zymeworks' cash runway to support it in the upcoming year, with cash resources of approximately $455m, including the recent private placement of $50m to EcoR1 Capital. Additional payments from legacy technology platform collaborations and upfront payments, alongside committed R&D funding from new partnerships, were among those highlighted as potential sources to extend cash runway into the second half of 2027.

Zymeworks also champions its development of a differentiated antibody-drug conjugate (ADC) portfolio, which has been designed to address areas of unmet therapeutic need. The five key players in this portfolio are ZW191, ZW220, ZW251, zanidatamab zovodotin, and XB002. ZW191 is a FRα-targeting ADC and is poised to have differentiated balance between drug-linker stability and payload potency compared to other Frα-TOPO1i ADCs on the market. An IND filing is expected for ZW191 in 2024. ZW220 is a NaPi2b-targeting ADC with potential utility in multiple cancers. Galbraith detailed the agent to have a combination of a bystander active TOPO1i payload at a drug-to-antibody-ratio of approximately 4, with potential to be a best-in-class ADC antibody. An IND filing is expected for ZW220 in 2025. ZW251 is a glypican 3-targeting ADC with the potential to offer an alternative mechanism for hepatocellular carcinoma (HCC) patients. Zymeworks feels ZW251 has the potential to improve upon the current standard of care for HCC, and an IND submission is expected in 2025. The ADC zanidatamab zovodotin is underscored for

having enhanced internalization of payload, with immunogenic cell death, antitumor activity across solid tumors including NSCLC, and a differentiated safety profile from other agents on the market. XB002 is a novel tissue factor targeting ADC which is currently under Phase I investigation in advanced solid tumors in the JEWEL-101 study.

The company also plans to drive the evolution of its multi-specific antibody therapeutic program in 2024. This involves zanidatamab, alongside bispecific and trispecific T-cell engagers. An IND filing for bispecific T-cell engager ZW171 is also expected in 2024.

In his concluding remarks, Galbraith reiterated Zymeworks' mission to improve the standard of care for difficult to treat cancers with poor prognosis, and championed the "5x5" portfolio to provide opportunity for success across a diverse and broader scope of indications. He finished by highlighting Zymeworks' aim to target first- and second-line market opportunities, pursuing products with global peak sales potential of more than $1bn, and to retain US commercial rights with collaboration in ex-US markets.

Micro Cap

Acumen Pharmaceuticals

Daniel O'Connell, Acumen's president and CEO, began the company's presentation by sharing his mission statement of pursuing a best-in-class treatment for the treatment of early Alzheimer's disease. O'Connell discussed why the early Alzheimer's disease patient population represents a significant market opportunity. Early Alzheimer's disease consists of patients who are experiencing mild cognitive impairment (MCI) or mild dementia as opposed to moderate or severe versions of these symptoms. Acumen, like many others, has been encouraged by recent advancements in the field, and believes that uptake of first-generation, disease-modifying, anti-amyloid beta treatment options is expected to increase, while the significant unmet need and room for improvement will persist.

O'Connell then went on to cover Acumen's founding science, which targets a specific amyloid in the brain (amyloid beta oligomers), and how this science could potentially cover the unmet need within the patient population. Acumen's leading asset currently is ACU193, a fully humanized IgG2 monoclonal antibody that selectively binds soluble Aß oligomers/amyloid beta-derived diffusible ligands (ADDLs). ACU193 is currently in Phase I development, with a Phase II/III trial expected to begin in the first half of 2024. O'Connell gave an update on the ACU193 program, including announcing that the company conducted a meeting with the FDA in Q4 2023 in which it received positive feedback on a timeline for progressing to the Phase II/III clinical study. O'Connell also announced that the company is currently designing a Phase I bioavailability study of ACU193 that is expected to initiate in mid-2024. O'Connell then discussed the most recent data from the Phase I INTERCEPT-AD study of ACU193, in which it saw rapid, significant plaque reduction which was comparable to the current market frontrunners at similar time points. In this trial, ACU193 demonstrated a compelling safety profile with low incidence of ARIA-E, and an absence of ARIA-E was observed in ApoE4 homozygotes. ACU193 provides a broad therapeutics index with convenient monthly dosing.

O'Connell then moved on to providing an overview of Acumen's leadership team, while highlighting the financial accomplishments of the company throughout 2023, before providing a summary of his presentation along with key takeaways and next steps for the company. In terms of next steps in 2024, O'Connell shared the timing for the initiation of both the new Phase I bioavailability and Phase II/III ALTITUDE-AD clinical studies.

Adaptimmune

In his JPM presentation, CEO Adrian Rawcliffe discussed how Adaptimmune is redefining the treatment of solid tumors with cell therapy. With the expected launches of two cell therapies within the next two years, the high-value sarcoma franchise (afami-cel and lete-cel) demonstrates the company's position as an integrated cell therapy company designed and built from the ground up. Adaptimmune projects the therapies to generate peak US sales of up to $400m, operate at ~70% gross margin at maturity, and provide multiple opportunities to expand the sarcoma franchise.

Both afami-cel and lete-cel are single-dose, autologous engineered T-cell therapies designed to target solid tumors. The BLA for afami-cel in synovial sarcoma was filed in December 2023, supported by data from Cohort 1 of the pivotal SPEARHEAD-1 trial, which met its primary endpoint for efficacy (full data to be released in Q3 2024). The FDA has granted orphan drug designation for afami-cel for the treatment of soft tissue sarcomas and Regenerative Medicine Advanced Therapy (RMAT) designation for the treatment of synovial sarcoma. Afami-cel is eligible for priority review, with approval and launch anticipated as early as Q3 2024. The approval would provide Adaptimmune the opportunity to have the first engineered T-cell therapy to address solid tumors. Lete-cel demonstrates promising efficacy in rare soft tissue sarcomas, synovial sarcoma, and myxoid/round cell liposarcoma (MRCLS). The Phase II IGNYTE-ESO pivotal trial met its primary endpoint for efficacy, and full pivotal data is set for Q3 2024. Adaptimmune anticipates US commercial launch in 2026. Because of the significant operational synergies between the cell therapies, afami-cel's footprint will accelerate the commercialization of lete-cel. Synovial sarcoma and MRCLS are treated in similar centers of excellence and share overlapping account types, so established referral and advocacy networks will be leveraged for commercial execution.

Adaptimmune is progressing additional large-opportunity cell therapies through its wholly owned development pipeline. Efficacy results for ADP-A2M4CD8 (targeting MAGE-A4) support development in ovarian, urothelial, and head and neck cancers. Two commercially significant preclinical programs comprise PRAME (clinically validated "clean" target highly expressed across a broad range of solid tumors including ovarian, endometrial, lung, and breast cancers) and TC-520, targeting CD70 (hematological malignancies including acute myeloid leukemia and renal cell carcinoma). IND filings for both programs are expected in 2024.

Adaptimmune's end-to-end capabilities from clinical development to commercial delivery of cell therapies bode well for a successful 2024 and beyond. The company is funded into early 2026 with >$300m including its existing balance sheet, projected payments from partners, and other non-dilutive capital sources.

AngioDynamics

Jim Clemmer, president and CEO of AngioDynamics, launched this year's JPM presentation with a summary of the company's ongoing efforts to transform its customer base and product portfolio. The process began in 2019 when AngioDynamics sold its NAMIC fluid management portfolio to Medline Industries Inc. for $167.5m. In 2023, the company offloaded its dialysis portfolio and BioSentry Tract Sealant System Biopsy product to Merit Medical for $100m. The divestitures have allowed the company to eliminate all debt and fully support strategic investments in its medtech platform, which is now funded by operating cash flows from its stable medical device portfolio of ablation products and accessories, diagnostic catheters, guidewires and kits, and radiation treatment stabilization balloons.

The medtech products include treatments for peripheral arterial disease (PAD), venous thromboembolism, cardiac thrombus and emboli, and prostate cancer. Thrombus management solutions include AngioVac for the removal of clots from the right and left heart, providing continuous aspiration and simultaneous reinfusion of filtered blood, and AlphaVac, a handheld device for large vessel venous thrombectomy (also in development for pulmonary embolism). The Auryon peripheral atherectomy system for PAD reached $100m in cumulative sales and has treated over 50,000 patients since its late 2020 launch.

In development for prostate cancer, AngioDynamics has been developing NanoKnife, a device that delivers short electrical pulses (rather than thermal energy) to ablate cancerous prostate tissue without causing damage to surrounding healthy areas. The company notes that over 500,000 men could be treated with the system, which is designed to treat in one session and results in an easier recovery without urinary control and erectile dysfunction risks associated with hot or cold ablation techniques. Enrollment has been completed in an IDE study.

Clemmer closed out the presentation noting that the company has plans in place for international expansion. It is preparing for CE mark and other international launches of Auryon and AlphaVac F18 in the first half of 2024.

Atara Biotherapeutics

Atara Biotherapeutics, along with its partner Pierre Fabre, was the first company to receive regulatory approval for an allogeneic T-cell immunotherapy, specifically Ebvallo (tabelecleucel) for the treatment of adult and pediatric patients two years of age and older with relapsed/refractory Epstein-Barr virus-positive post-transplant lymphoproliferative disease (EBV+ PTLD) who have received at least one prior therapy. The company is now working to submit a BLA for Ebvallo in Q2 2024. In December 2023, Atara expanded its partnership with Pierre Fabre to transfer all Ebvallo clinical, regulatory, and manufacturing activities to Pierre Fabre following the BLA transfer, receiving up to a total of $740m through milestones, royalties, and other considerations.

Off the success of Ebvallo, Atara will now focus on the development of ATA3219 and ATA3431, building on its proprietary allogeneic CAR-T platform. Preclinical data have shown that both therapies could target B-cell and autoimmune targets. ATA3219 is a CD19 CAR-T therapy that

Atara will develop for the treatment of non Hodgkin's lymphoma (NHL) and lupus. An IND has been cleared for NHL, and a Phase I study is being developed and an IND for lupus nephritis is planned for Q1 2024. Meanwhile, ATA3431 has advanced into IND-enabling studies, with further plans to release more preclinical data in 2024.

BenevolentAI

At the foundation of BenevolentAI is a platform to enable AI-augmented drug discovery to progress products through R&D. The company sees sources of revenue that stem from an established business in end-to-end discovery, preclinical and clinical development, to expansion into software-as-a-service products. Platform-generated assets enable upfront and milestone payments, as well as royalties, from collaborations.

BenevolentAI acting CEO Francois Nader admitted that the company does not have the best platform in the industry, but emphasized that it has been validated. One form of validation has come through partnerships with AstraZeneca and Merck, while another stems from the company's identification of baricitinib as a potential COVID-19 treatment. The company took this finding directly to Eli Lilly, which led to an FDA emergency use approval in 2020 and eventual full approval.

In early development, the company has deployed the Benevolent platform to generate five products in a pipeline that resembles that of a traditional biotech company. The lead asset is a PDE10 inhibitor in Phase I. Dubbed BEN-8744, this peripherally restricted small molecule treatment is a potential first-in-class option for ulcerative colitis. The company also has a CHK1 inhibitor, BEN-28010, a CNS-penetrant that could be used in a combination setting to treat glioblastoma multiforme patients who are resistant to the current standard of care. This drug is IND-ready and BenevolentAI is actively seeking a partner. Also a CNS-penetrant, BEN-34712 is a RAR-alpha-beta agonist to be evaluated in amyotrophic lateral sclerosis. The company believes this drug will be IND-ready by Q2 2024. Two other products will be targeted to treat Parkinson's disease and fibrosis.

As of June 2023, the company had £84.3m in cash, with a cash burn in the first half of 2023 of about £38m, which the company lowered by reducing headcount by roughly 30%. Currently, there are about 265 employees, and BenevolentAI has a cash runway to extend to mid-2025. If all goes well, the Merck partnership will start generating revenue for the company in 2026.

With AI a hot topic of the year in 2023, extending into this year's J.P. Morgan Healthcare Conference, it is no surprise that one of the first questions for BenevolentAI involved its use of generative AI. Nader responded by acknowledging that the industry is becoming more sophisticated, with AI being integrated directly into pharmaceutical companies, and that about 25% of BenevolentAI's technology group, about 25 people, are devoted to such upstream investments to try to keep up with this evolving trend. Indeed, it was released during JPM that Amgen will build models trained to analyze human datasets on Nvidia's AI data center infrastructure platform, DGX SuperPOD, which is to be installed at Amgen's deCODE genetics' headquarters.

Carisma Therapeutics

Carisma Therapeutics' president and CEO Steve Kelly gave an overview of the company and pipeline developments at the J.P. Morgan Healthcare Conference. Carisma is a cell therapy company focused on macrophages that has pioneered the space. The company believes it is in position to take the power of the macrophage, an innate immune cell that has broad applicability and orchestrates an adaptive immune response, and apply it to a range of different diseases. Kelly spoke about the unmet need in oncology and his belief that macrophages are well suited to address the challenges of solid tumors. In addition to oncology, Carisma believes macrophages can be used to address unmet needs in other areas, such as liver fibrosis.

Carisma holds the world's leading platform that combines macrophage cell biology with engineering tools in a variety of modalities (allogeneic, autologous, and in vivo) to build out therapeutics. From that, the company has built out a diverse pipeline that includes a HER2 program in an ex vivo fashion, a mesothelin program in an ex vivo fashion, and an in vivo oncology program partnered with Moderna that is currently in discovery.

The company's lead program targeting HER2 consists of two candidates, CT-0508 and CT-0525. HER2 is a validated target with significant unmet need. CT-0508 is the first CAR-macrophage to be tested in human clinical trials. Initial safety, tolerability, and clinical evidence of mechanism was achieved in monotherapy arms of a Phase I dose escalation study of CT-0508 in patients with HER2-overexpressing solid tumors. CT-0508 has a very clean safety profile, with no serious adverse events. The study also demonstrated that CT-0508 is clinically active, with data showing up to 20% lesion shrinkage, stable disease, and antigen-dependent cell shrinkage. Stable disease was correlated with CT-0508-induced TME remodeling and T-cell activation. Patients in the study showed a high baseline T-cell exhaustion, and to address this Carisma has initiated a combination arm with T-cell checkpoint inhibitor pembrolizumab. Data from this combination arm are expected in the first half of 2024.

CT-0525 is a HER2-targeted CAR-monocyte that has manufacturing advantages over CAR-macrophages and potential biological advantages. Preclinical models of CT-0525 demonstrate multiple improvements over CT-0508, including a ~5x increase in cell number production, increased cytokine release and killing, and increased trafficking and persistence. A planned Phase I study of CT-0525 will assess the safety, tolerability, and manufacturing feasibility of CT-0525 with additional analyses on TME impact. Carisma expects to treat the first patient in the study in the first half of 2024.

CT-1119 is an early-stage CAR-monocyte in Carisma's pipeline targeting mesothelin-expressing solid tumors. There is currently no approved anti-mesothelin therapy. Carisma anticipates an IND submission for CT-1119 for the treatment of mesothelin-positive solid tumors in 2025.

Carisma went public in March 2023 following a merger between the company and Sesen Bio. The company is sufficiently funded, possessing a cash runway into Q1 2025, with 40.3 million shares outstanding and $94.1m in cash, cash equivalents, and marketable securities.

Emergent BioSolutions

Emergent Biosolutions' interim CEO Haywood Miller and CFO Rich Lindahl shared presentation duties. Miller has only been with the company since July 2023, but said he is impressed with the focus that it has on its mission, and that employees have managed to keep morale high despite challenges that have arisen from recent restructuring within the company.

Miller explained that the company's mission is to protect and enhance life and work to provide solutions for complex and urgent public health threats through vaccines and therapeutic treatments, as well as manufacturing and distributing such products to governments worldwide. He went on to describe his pride in the company's large product list, which includes compounds such as Anthrasil, Cyfendus, BioThrax, and raxibacumab injection for anthrax, ACAM2000, CNJ-016, and Tembexa for smallpox, BAT for botulism, Ebanga for Ebola, Reactive Skin Decontamination Lotion (RSDL) for chemical threats, Trobigard Auto-injector for nerve agent antidotes, and Narcan Nasal Spray for emergency opioid overdose.

During 2023, a strategic shift occurred for Emergent which has seen a deemphasis on the service contract development and manufacturing organization (CDMO) side of the business and a shift in focus to the product side. A key product milestone that occurred during 2023 was the launch of Narcan as an over-the-counter opioid reversal treatment. The opioid crisis is a major healthcare issue, and opioid overdose is the leading cause of accidental death in the US. Demand for Narcan from federal/state programs is only expected to increase as the opioid epidemic continues. In August 2023, the company began supplying hundreds of thousands of two-dose cartons of Narcan to over-the-counter retailers, and will continue to explore other channels of exportation for the product, such as potentially supplying businesses and workplaces.

Cyfendus was another product which received FDA approval during 2023, and is a two-dose anthrax vaccine that can be used for post-exposure prophylaxis. The company has also received a 10-year contract from the Biomedical Advanced Research and Development Authority (BARDA) for the advanced development and manufacturing scale-up of Ebanga, its vaccine for Ebola.

Lindahl rounded off the presentation by describing the company's plans for 2024, which involve continued focus on core products such as Narcan, further deemphasis on the CDMO business, and restructuring to accelerate return to profitability.

Kodiak Sciences

Kodiak, a company specializing in ophthalmology medicine, had a relatively quiet H2 2023, focusing on early-phase studies and excelling in manufacturing. Focusing on breakthrough and innovation, CEO Victor Perlroth started the presentation by highlighting the commercial attractiveness of retinal medicine, with Kodiak's future focus on three main areas: 1) trailblazing science with a creative foundation; 2) leading in Generation 2.0 medicine; and 3) singular focuses on ophthalmology. With a balance sheet of $346m in cash (Q3 2023), Kodiak aims to address multiple unmet needs in this therapy area with investments into its diversified pipeline in the next 2–3 years. These include tarcocimab tedromer, an anti-VEGF therapy already in

positive Phase III studies for nonproliferative diabetic retinopathy (NPDR), retinal vein occlusion (RVO), and wet AMD; KSI-501, a first-in-class anti-IL-6 and anti-VEGF bispecific therapy designed to treat intraocular inflammation and retinal vascular disease; and finally, an unconjugated bispecific version of KSI-501 developed for retinal inflammatory diseases.

Driving initial focus on tarcocimab tedromer, Perlroth highlighted that across the entire clinical program and ABC platform, the drug demonstrated consistent and differentiated durability and favorable safety. Successful pivotal data were observed in NPDR, whereby the drug continued to establish superior efficacy when dosed every six months, observing 90% reduction in risk of developing sight-threating complications with a 29x increased response rate within 48 weeks. In RVO, tarcocimab continued to demonstrate strong durability, with a matching efficacy and comparable safety profile with significantly fewer doses than the marketed anti-VEGF aflibercept, whereby results saw a 30% higher chance of patients not requiring additional doses and 46% of patients required no additional injection in the second six months. Kodiak is planning to initiate an additional pivotal study in H1 2024 (24 months) to support the single BLA application for all three indications, with the belief that tarcocimab's breadth of indications and signature durability, combined with an appropriate commercial strategy, could support physicians' adoption and translation of the product into the growing anti-VEGF market.

Entering a novel category of retinal medicine, Perlroth continued to draw attention to KSI-501p and uncoupled KSI-501ABC, an anti-VEGF and anti-IL-6 inhibitor to address inflation and its underlying inflammatory cascade. With substantial patient-to-patient variability observed with the anti-VEGF monotherapy, the need for an additional mechanism of action has initiated Kodiak to innovate this dual-inhibition therapy which has shown significant preclinical results including inhibition of angiogenesis and normalization of inner and outer blood retinal barriers. Kodiak is currently exploring initiation of dual Phase II/III pivotal studies on KSI-501ABC in high prevalence retinal vascular diseases after a recent Phase I study in diabetic macular edema patients in 2023. Plans are also ongoing for the unconjugated KSI-501p, with Phase I/II expansion studies under way in H1 2024 and topline data expected in the next two years.

Omega Therapeutics

CEO Mahesh Karande provided an overview of the Omega platform and then shared some preliminary data from a Phase I trial of OTX-2002 for heavily pretreated hepatocellular carcinoma (HCC). OTX-2002 was designed to lower MYC gene expression in the liver by altering the methylation of MYC regulatory regions.

The OMEGA platform allows for epigenomic modulation of gene expression and is capable of both up- or down-regulation for therapeutic benefit. The regulation can be fine-tuned and is not just an on or off switch. The platform uses mRNA encoding a fusion protein consisting of a proprietary DNA-binding domain for site-specific targeting and an epigenomic effector. The epigenomic effector may control DNA methylation/demethylation or may control the state of chromatin through histone modification, acetylation, and so on. An epigenomic controller's therapeutic response can be tailored to potentially last days, weeks, or months to allow for broad flexibility in dosing intervals. The mRNA is currently being delivered by lipid nanoparticles (LNP), but the platform is amenable to other vectors such as viruses.

Omega's first and only clinical asset is OTX-2002, which was designed to lower MYC expression by 90%. Lowered MYC protein primes "MYC-addicted" HCC cells to undergo apoptosis. MYCHELANGELO I is a Phase I/II clinical trial that is currently in the dose escalation stage and is enrolling advanced HCC patients. Part I of the study will evaluate monotherapy, while Part II will look at combinations of OTX-2002 with standards of care such as tyrosine kinase inhibitors and checkpoint inhibitors. OTX-2002 is administered intravenously and dosed once every two weeks. Preclinical work showed that OTX-2002 resulted in a large increase in DNA methylation within 1–2kb of the DNA binding site and the increase was dose-dependent. After treatment with OTX-2002, circulating exosomes were collected from patient blood samples and showed that, compared to baseline levels, OTX-2002 reduced MYC mRNA in all eight patients treated to date (four patients at dose level 1, and four patients at dose level 2). MYC expression levels were reduced by 50% at dose level 1 and slightly more than 50% at dose level 2. Since the microsomes originate from both transfected and non-transfected cells and across multiple tissues, Karande explained that the reduction in MYC may be greater in the targeted tissue. In terms of next steps for this program, the dose level 3 cohort has completed enrollment, and enrollment in the dose level 4 cohort is expected to initiate in January 2024, with additional data from these monotherapy cohorts expected in H1 2024. Dose escalation for the monotherapy and combination cohorts is expected to start in mid-2024.

Apart from OTX-2002, Omega expects to bring another MYC-targeting asset to the clinic, OTX-2101 for non-small cell lung cancer. IND-enabling work is ongoing for OTX-2101 which will include a novel lung-targeting LNP formulation, with Karande stating that the company is working on both systemic and inhalable formulations. Other preclinical programs mentioned at the conference included assets targeting HNF4A for liver regeneration and CXCL 1-8 for inflammation/immunology.

With the Omega platform suitable for so many targets, the company is actively looking for partnerships. In January 2024, it announced a research partnership with Novo Nordisk. Karande explained that the partnership will seek to reprogram white fat cells into brown fat cells, which are more metabolically active. Under the terms of the agreement, Novo Nordisk will reimburse R&D costs and has the right to select one target to advance for clinical development. Omega and Flagship Pioneering Medicines are eligible to receive up to $532m in upfront, development, and commercial milestone payments, as well as tiered royalties on annual net sales of a licensed product. Karande finished by noting that Omega has enough cash to last into Q3 2024.

Rallybio Corporation

Rallybio CEO Stephen Uden began the presentation with an overview of the company and its development history. Uden shared that Rallybio is a portfolio company looking for therapeutics that will be revolutionary in rare disease R&D. The company believes it is currently in a strong financial position and is consistently building upon its global business development expertise.

Uden then went on to share the company's current pipeline, which includes four therapeutic areas: maternal fetal blood disorders, complement dysregulation, hematology, and metabolic disorders. The company currently has two clinical programs – RLYB212 and RLYB116 – both of which are poised to enter Phase II.

Next, Uden gave an overview of RLYB212, the company's potential preventive treatment for fetal and neonatal alloimmune thrombocytopenia (FNAIT). RLYB212 is a fully human monoclonal anti-HPA-1a IgG derived from a plasma cell. RLYB212 is currently in Phase I development, and Rallybio expects to provide an update on Phase II discussions with the EMA in the first half of 2024. Assuming these discussions go well, the company plans to initiate a Phase II dose confirmation study in the second half of 2024. This study is designed to confirm the RLYB212 dose regimen in pregnant women at higher risk of FNAIT prior to initiation of a larger Phase III registrational study. Uden also gave an overview of results from the ongoing single-arm, open-label study to assess the pharmacokinetics and safety of subcutaneously administered RLYB212 in pregnant women at higher risk for HPA-1a alloimmunization. These data showed that RLYB212 was well tolerated, with no reports of serious or severe adverse events. RLYB212 produced dose-dependent, rapid, and complete elimination of transfused HPA-1a-positive platelets, achieving over 90% reduction in mean platelet elimination half-life in both dose groups versus placebo.

Uden continued the pipeline updates with discussions on RLYB116 and RLYB114, both of which are advanced inhibitors of C5 that offer high potency, less frequent dosing, and ease of use. RLYB116 is currently in Phase I trials in Australia in healthy participants for the treatment of complement deficiencies/abnormalities. RLBY114 is still in the preclinical phase, and we can expect an update on when this asset will enter the clinical space during Rallybio's next portfolio update, which will take place in the second half of 2024.

Uden finished the pipeline section of the presentation by briefly highlighting RLYB331, a monoclonal antibody that selectively targets matriptase-2 (MTP-2) serine protease that plays a role in hepcidin formation, and the company's ENPP1 inhibitor which is a joint venture with Exscientia to discover/develop a small molecule therapy to treat hypophosphatasia. For RLYB331, preclinical activities are currently under way, and the company expects to report additional animal data in the first half of 2024.

Finishing the presentation, Uden again mentioned upcoming milestones for the year ahead, as well as a few success drivers that the company believes it possesses that will allow it to succeed in these planned ventures. These success drivers include its diversified portfolio, proven innovation thus far in R&D, its current robust financial position, and its pursuit of global business development expertise.

Rigel Pharmaceuticals

Raul Rodriguez, CEO of Rigel, opened the presentation by sharing two parts of the company's story. The first part was commercial execution, with two products on the market at present, Tavalisse and Rezlidhia, and importantly the second part of their story, which was Rigel's development and expansion plans for the future.

In regard to commercial execution, the company has experienced record sales, achieving $104m in 2023, representing 36% growth versus 2022. Tavalisse alone generated $93.7m, while the more recently launched Rezlidhia generated $10.6m in sales. Rodriguez described 2023 as a year of outstanding performance for both therapeutics and of significant growth that will continue to accelerate in the coming year. The company plans to do this through continued

growth of its commercial execution strategy, expanding its currently approved therapies to wider patient populations, and strategic partnerships.

Outside of the sales achievements for Tavalisse, Rodriguez gave an outline of the immune thrombocytopenia market, noting that Tavalisse is now preferred on key commercial national formularies. Rigel's goal is to continue to move this approved therapy up to second-line patients, as that is where most patients are in their treatment, and Tavalisse has shown the best efficacy in that patient population. Doctors are primarily prescribing the treatment at third and fourth line currently, but the company is optimistic that as doctors are gaining more knowledge and becoming more comfortable about Tavalisse, they will be more inclined to prescribe it in second-line patients, as this has already begun to happen. Overall, the company believes it is making tremendous progress with this product, giving doctors the confidence to prescribe with the positive efficacy levels seen in third-, fourth-, and especially second-line patients. Post-pandemic, there has been consistent quarterly progress since Q2 2021.

Regarding its approved in-licensed product from Forma, Rezlidhia, which is indicated for adult patients with relapsed/refractory acute myeloid leukemia (AML) with a susceptible IDH1 mutation as detected by an FDA-approved test, Rodriguez gave a general overview on why they were attracted to this product in the first place. Phase II data showed a CR+CRh rate of 35%, with a median duration of response of 25.9 months, and 92% of CR+CRh responders were complete responders, with a median duration of response of 28.1 months, and transfusion independence was achieved in all subgroups with a well-characterized safety profile with no cardiac events leading to discontinuation. Rigel's ambition is for this product to be a key growth driver of its pipeline going forward. The company has already set in motion a strategic alliance with MD Anderson to advance this drug in AML and other cancers such as higher-risk myelodysplastic syndrome (MDS) and advanced myeloproliferative neoplasms, as well as a collaboration with CONNECT for a Phase II trial in glioma.

Going forward this year, Rigel is looking to in-license more successful products, with a focus on late-stage opportunities with either registrational data in hand or an NDA that has already been filed or approved. It believes that its infrastructure of marketing and sales representatives is something it can leverage and use as an asset for partnerships. It is aiming to in-license differentiated assets in hematology, oncology, or related indications. The presentation briefly touched on R289's development in lower-risk MDS and the company's RIPK1 inhibitor program partnership with Eli Lilly for CNS and immune diseases. Rodriguez then closed the presentation with an overview of financial highlights from Q4 2023 and sales metrics of its products.

Solid Biosciences

Solid Biosciences, a life sciences company developing a portfolio of gene therapy candidates and neuromuscular and cardiac programs, took the stage at the JPM Healthcare Conference having raised $109m in a private placement the previous week. CEO Bo Cumbo kicked off the presentation by painting an encouraging picture of the company's transformative 2023, including its diversified and strategic pipeline, new management team, and strong balance sheet.

Featuring an optimized transgene and next-generation capsid, Solid's lead asset SGT-003 is a gene therapy for Duchenne muscular dystrophy that is based on its first-generation candidate

SGT-001. SGT-003 is currently in a Phase I/II trial which is expected to start dosing in Q1 2024 and expects safety and microdystrophin expression data in Q3–Q4 2024. Cumbo went into significant detail with respect to the Duchenne program, including the scientific rationale behind its capsid and transgene, as well as the wealth of promising preclinical data that the company believes will give it a competitive edge.

Beyond Duchenne, Solid's pipeline is targeting areas with few or no available therapies and high unmet need, for example its assets SGT-501 for catecholaminergic polymorphic ventricular tachycardia (CPVT) and AVB-401 for BAG3-mediated dilated cardiomyopathy. Cumbo remarked on the clear mechanistic rationale behind these programs, aiming to address the underlying cause of disease using its AAV-delivered transgenes with cardiac-specific and -selective promoters. SGT-501, which has received orphan drug designations, is the most advanced of these two assets, and the company anticipates submitting an IND for its first clinical trial in Q1 2025. Other notable mentions included Solid's capsid manufacturing platform, which it stated has the potential to challenge industry yields.

Cumbo rounded off his presentation with excitement for the busy year ahead, principally the dosing of its lead asset SGT-003 in the coming months and a subsequent safety readout in the middle of the year. By applying its patient-centric approach to diseases with few available therapies, Solid has significant potential to succeed in its mission to revolutionize the lives of patients battling rare neuromuscular and cardiac diseases.

Vanda Pharmaceuticals

Vanda Pharmaceuticals' senior vice president and CFO Kevin Moran provided a concise update on the company's many ongoing programs, starting with its recent $100m acquisition of Ponvory, a highly selective S1P1 receptor modulator that showed superiority to teriflunomide in head-to-head trials for relapsing multiple sclerosis. Additionally, the drug has the potential to be useful in other inflammatory and autoimmune diseases such as psoriasis and ulcerative colitis, which the company has some time to explore since Ponvory is under patent protection until December 2035.

As of Q3 2023, prior to the Ponvory acquisition, the company reported $490m in cash, with no debt, putting it in a favorable position to continue supporting the multiple late- and early-phase programs currently ongoing. Net product sales in Q3 2023 were $39m, with over half of that coming from Fanapt, Vanda's schizophrenia asset. Fanapt also showed positive results in bipolar type I, and the FDA has accepted Vanda's sNDA with a PDUFA date set for April 2024.

Vanda has had two other applications recently accepted by the FDA: an sNDA for Hetlioz in insomnia, and an NDA for tradipitant in gastroparesis. Decisions are expected in March 2024 and September 2024, respectively. Currently approved for non-24-hour sleep-wake disorder and sleep disturbances in Smith-Magenis syndrome, Hetlioz has lost exclusivity in the adult population, so the company is leaning on patient engagement and pediatric usage to drive uptake. While the NDA for tradipitant represents the first gastroparesis drug application to be accepted by the FDA in over 30 years, highlighting the degree of unmet need in this disease area, Phase II and Phase III trials produced mixed results, with the Phase III trial failing the primary endpoint of change in nausea severity at week 12. In addition to the gastroparesis

submission, tradipitant is also in trials for motion sickness. A second Phase III trial is currently under way, and there are plans for an sNDA submission following the data readout.

Lastly, the company has received orphan drug designation for VCA-894A in Charcot-Marie-Tooth disease and for VPO-227 for the treatment of cholera. Although much of Vanda's efforts are going towards the support of late-phase drug programs and the commercialization of its marketed assets, the company is also running Phase II trials in hematologic malignancy and social/performance anxiety, as well as developing its two orphan drugs.

Vigil Neuroscience

Vigil Neuroscience reaffirmed its commitment to be the frontrunner in microglia-targeted therapeutics for rare and common neurodegenerative diseases. Microglia are the sentinel immune cells of the CNS, responsible for maintaining homeostasis and responding to damage caused by disease. Vigil's most advanced therapeutic programs focus on the development of activators of TREM2, a transmembrane receptor that is specific to microglia. These activators stimulate the migration of cells in response to injury and inflammation, aiming to counteract neural degeneration observed in inherited neurodegenerative diseases where there is a common deficiency or loss of function in TREM2.

Time was taken to reflect on the milestones achieved in 2023 for the two most advanced assets, iluzanebart (VGL101) and VG-3927. These included the release of data from the first phase of a study for iluzanebart (VGL101), a monoclonal antibody candidate that works by activating the TREM2 receptor to treat colony-stimulating factor 1 receptor (CSF1R)-related leukoencephalopathy, which includes amyotrophic lateral sclerosis-parkinsonism dementia complex (ALS/PDC). ALS/PDC is a degenerative disease that progresses quickly and is often misdiagnosed. It primarily affects adults and typically leads to severe disability within 3–4 years. Unfortunately, the mortality rates are substantial, with most patients not surviving beyond 6–8 years. The current standard of care for this rare neurodegenerative disorder, which impacts over 25,000 patients in the US, EU, and UK, involves addressing symptoms (such as anti-epileptic medications for seizures) rather than directly treating the underlying disease pathology. The aptly named ILLUMINATE study was discussed in relation to identifying clinical measures of disease progression in ALS/PDC with MRI and CSF biomarkers. In relation to this, positive interim results from the Phase II IGNITE study for iluzanebart in ALS/PDC were discussed, with clear CNS target engagement with downstream pharmacological activity on crucial MRI and NfL biomarkers suggesting stabilization or slowing disease progression. Furthermore, there were no safety or tolerability concerns during the trial, with no patient discontinuations due to treatment-related adverse events.

Additionally, progress is under way on a Phase I clinical trial for VG-3927, a highly active, selective, small molecule TREM2 agonist for the potential treatment of Alzheimer's disease. Discussion focused on the encouraging preclinical and animal trial findings, which demonstrated a decrease in the accumulation of plaque when observed using MRI in rats. No comment was made about VG-3927 being currently subject to an FDA-imposed partial clinical hold with a maximum dose exposure concern. In the latest press release from Vigil, it stated confidence that the maximum exposure limit would exceed the predicted optimum dose of VG-3927.

Vigil has confirmed its position to fund the current iluzanebart and VG-3927 clinical development programs, with a projected cash runway into H2 2025. Upcoming catalysts for the company in 2024 include reporting interim data for the ongoing Phase I clinical trial of VG-3927 in mid-2024, and Phase II results from its IGNITE trial evaluating iluzanebart in ALS/PDC from all patients at six months at both 20mg/kg and 40mg/kg doses in Q3 2024.

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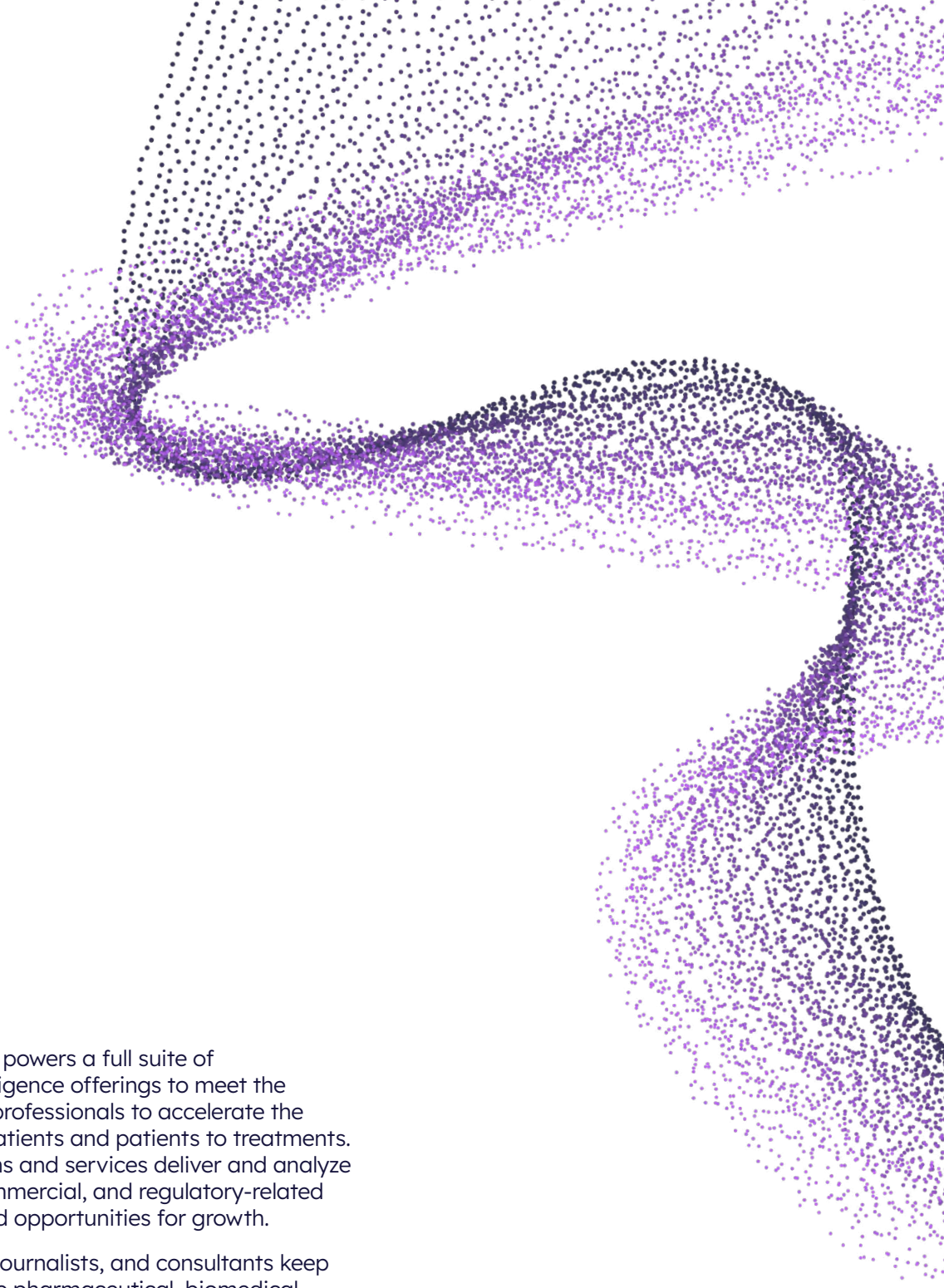

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