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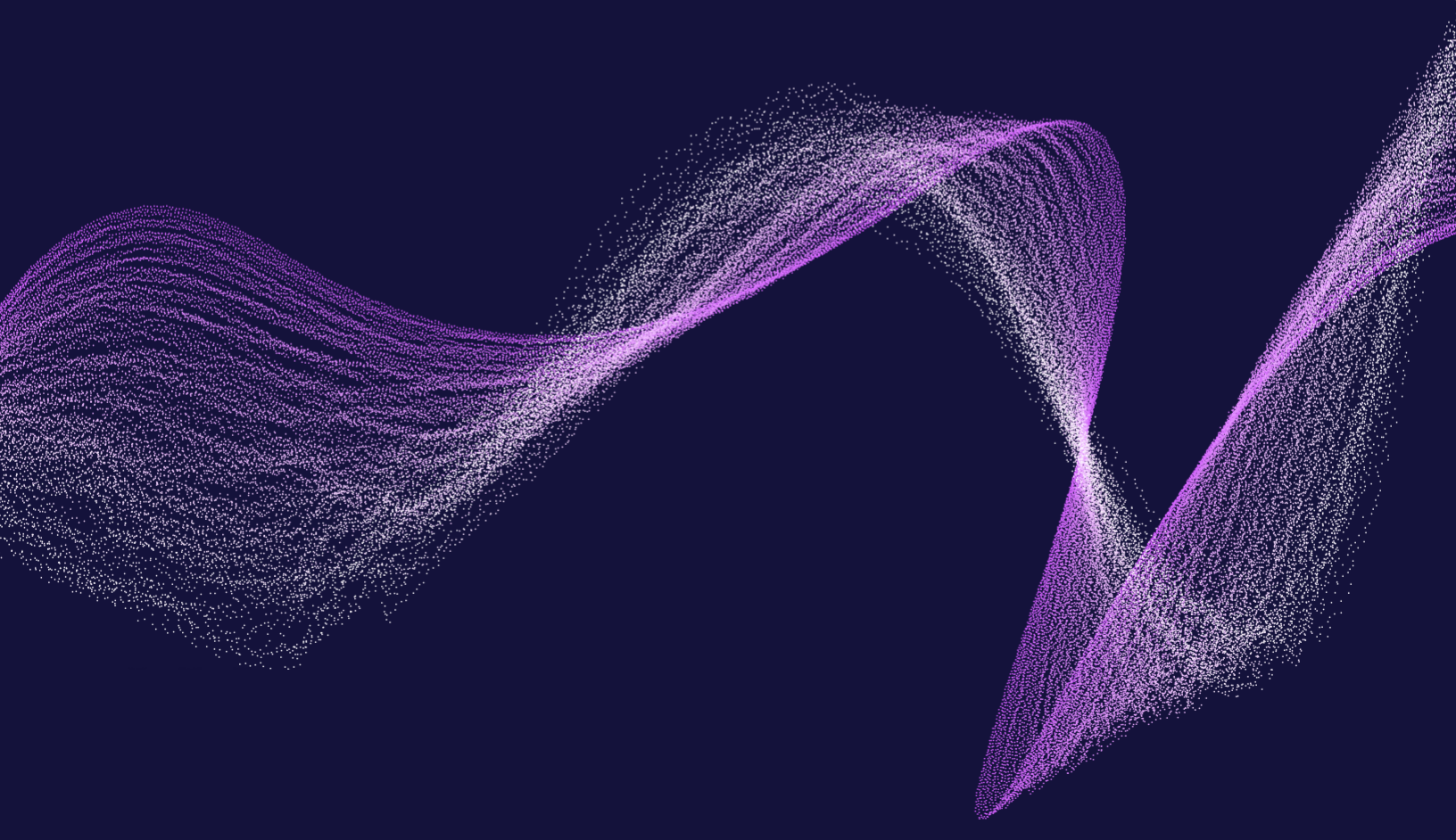
Day 1



Summary

The 42nd annual J.P. Morgan Healthcare Conference (JPM) is being held in San Francisco, CA over 8–11 January 2024. This report contains presentation highlights from a selection of companies from Day 1 of the conference. A complete list of events and catalysts that were announced or updated today 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

Novartis

Novartis CEO, Vas Narasimhan, presented how Novartis has become a pure-play 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. They have upgraded their expected CAGR from 2022 to 2027 from +4% to +5% based on the success seen with currently approved brands (with Entresto being the most successful with $5.9bn reported sales) and the forecast success of various pipeline assets. They have also executed over 15 successful strategic deals in 2023 alone, with the goal of enhancing their pipeline across core therapy areas and technology platforms.

Narasimhan began with a victory lap, highlighting the 10 positive Phase 3 readouts Novartis has 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 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. Whilst 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 overall survival 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 their intention to strengthen their presence in rare diseases, and their 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 are expecting to submit at least 15 key submissions to the FDA for approval between 2024 and 2027, with 6 of these expected in 2024, and 3 of these 6 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 for Novartis across their four core therapy areas. The company is establishing themselves 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 their current blockbuster brands, are forecast to generate further billions for Novartis as access to larger and newer patient populations is granted. Overall, Novartis' 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.

Large Cap

Alnylam Pharmaceuticals

Alnylam Pharmaceuticals began their presentation by focusing on their past and present achievements in both commercial and clinical aspects, highlighting their strong financial position with an annual rise of 39% in combined net product revenues, and emphasizing their 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 $2.4 billion. These results were funded by the success of its RNAi (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 (PH1), Givlaari [givosiran] for the treatment of acute intermittent porphyria (AIP), 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: cardio-metabolic disease, infectious disease, and central nervous system (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 cardiovascular outcomes trial. If these trial data are positive, this could lead to an expected 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 is 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 (CAA) 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 their Phase I studies in early 2024 in Type II diabetes mellitus 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 underway, 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 their pipeline, with the biosimilars business being integrated into each of these four main disease area pillars.

Being a hot area in general medicine, MariTide (maridebart cafragultide) 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 comorbidities. 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 throughout the end of the decade.

Demonstrate 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 frontline 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 June 12, 2024, priority review of tarlatamab is underway 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 heralds 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 PRMT 5 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 underway. Tezspire is additionally being evaluated in chronic rhinosinusitis, eosinophilic esophagitis, and COPD. Amgen also highlighted their 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 version of infliximab, Aveloa, and adalimumab, Amjevita, are available while the company is 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, Uplinza 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 also pursues a subcutaneous formulation of that medicine. Phase III data for Uplinza is 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 touched on investments in harnessing artificial intelligence and a brief summary of their efforts towards good corporate responsibility.

Argenx

During the JPM 2024 presentation, Argenx outlined the company's current achievements and future objectives. Beginning with the VYVGART Horizon, it emphasized the success of the two commercial products, VYVGART and VYVGART Hytrulo, generating $1.2 billion 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 highlighted.

The presentation stressed the importance of real-world impact, showcasing the transformation in the lives of patients like Mike, diagnosed with MG, who experienced significant improvements with VYVGART. The commitment to expanding innovation access through programs like My VYVGART path and positive evaluations by Health Technology Assessment bodies outside the U.S. 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 ENHANZE technology aimed to enhance the patient treatment experience. Innovation Horizon 2 introduced empasiprubart for MMN, showcasing a 91% risk reduction for IV/IG rescue. The preclinical model for ARGX-119 targeting MuSK in congenital myasthenic syndrome displayed promising results.

The third innovation horizon unveiled four new pipeline assets: ARGX-213, targeting FcRN; ARGX-109, an ultra-potent IL6 blocker; 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 2 data readouts, and progress on the four new pipeline assets. The company maintained strong financials, with a cash position of $3.2 billion and a planned cash burn of around $0.5 billion, 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 '23 sales of $3.7 billion), healthcare systems and technologies (YTD '23 sales $2.2 billion), and pharmaceuticals (YTD '23 sales $1.7 billion). Baxter's products serve over 350 million patients annually and over 100 countries. Its portfolio includes infusion systems, IV therapies, hemostats and sealants, positioning devices and ancillaries, and specialty injectables, just to name a few. 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 '23 sales of $2.7 billion) and acute therapies (YTD '23 sales of $0.6 billion). 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.

Mr. Almeida said the company seeks 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.

BeiGene

John Oyler, BeiGene's co-founder and Chief Executive Officer, began the presentation with an

overview of the company's history, highlighting the complexity of the company and the major differences between BeiGene and their 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 5-year survival rates for most cancers in the United States and how the modalities being used at BeiGene have contributed to this effect. Oyler also touched on the fact that almost 1 in 4 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 total cost of medicine. 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 $1.8 billion in revenue, a 76% increase over the previous year. In 2024, the company will be opening a new facility in Princeton, New Jersey and they currently have over 50 potential medicines in their pipeline which they intend 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 $4 billion 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 progression free survival (PFS) up to approximately 9 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 NSCLC, a European supplemental filing in both gastric cancer and esophageal cancer indications, as well as PDUFA decisions in esophageal cancer for both 1st and 2nd line treatment. As of the end of 2023, Tevimbra has treated more than 750,000 patients globally and brought in $144 million in third quarter revenue.

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

Oyler concluded the presentation with a discussion including the clarification of misperceptions 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 the company believes they are rapidly transitioning into a leading oncology company in the industry and they look 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 the transition period, and on driving growth in the late 2020s.

BMS 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 BMS 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.

BMS plans to build on their leader status in oncology by extending the durability in immunooncology through the launch and further expansion of subcutaneously-delivered Opdivo and Opdualag. Following its acquisition of Mirati Therapeutics, planned to close by 1H 2024, BMS will also add targeted agent Augtyro (repotrectinib) to their list of brands. Additionally, licensing agreements and collaborations (e.g., SystImmune, Tubulis, and RayzeBio) will deepen BMS' platform capabilities, introducing ADCs, cell therapies, and radiopharmaceuticals to their 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 CLL/SLL, and its FDA priority review and March 2024 PDUFA date boost BMS' hopes for a significant increase in the treatment's target population, and with a significant increase in manufacturing capacity planned for 2024, their 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 much-needed therapies, Chris Boerner reiterated his company's plans to ramp up manufacturing capacity for CAR Ts in 2024.

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

BMS will also grow their presence in immunology, through maximizing the existing core indications for Sotyktu, Zeposia, and Orenzia, 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 leader 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. Chris Boerner highlighted their plans to broaden the formulary access for Sotyktu, focusing on growing the drug's volume, and presented the drug's significant expansion opportunities in psoriatic arthritis, SLE, Sjogren's syndrome, and alopecia areata, which are not only characterised by significant unmet need, but would also boost the drug's target population beyond its current label.

With their acquisition of Karuna Therapeutics, announced in December 2023, BMS will also strengthen their 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 BMS' pipeline and widening their existing footprint in this therapy area.

With blockbuster drugs Revlimid, Eliquis, and Opdivo significantly impacted by patent expirations and the Inflation Reduction Act (IRA), BMS enters a "significant period of transition", as acknowledged by Boerner during his presentation, but the company's focus on a renewed and reinforced pipeline— done through licensing opportunities, partnerships, and bold-on opportunities, may offer a much-needed momentum for growth.

Cytokinetics

Robert Blum, the chief executive officer 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 top line 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 the SEQUOIA-HCM trial which will be presented in Q2 2024. 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 trial, 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 HCM. Blum also mentioned plans to continue to pursue approval of omecamtiv mecarbil in reduced ejection fraction heart failure (HFrEF), 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.

Gilead

CEO Daniel O'Day started the presentation highlighting Gilead 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. Although seen flat development in the pandemic years, the last 4 years has seen Gilead's portfolio doubled in size with a strong margin for expansion at an accelerated growth of 8% YOY. This would be a catalyst rigged year

for Gilead with over 12 clinical trials in progress, 5 or more will be seeing phase 2 results. He was proud to announce that their core and legacy portfolio are continuing to perform well, and there has been a tremendous increase in portfolio diversification having 88% growth in pipeline since 2019, enjoying a season of durable growth output with no significant patent expirations. He continues to mention the company's position to deliver over 10 new transformative therapies by the end of 2023 and most importantly, oncology is on track to contribute to a third of sales by the end of 2023.

Initially focusing on the oncology, O'Day stated that this therapeutic area of the business was currently annualizing over $2 bn in revenues, performing at double digit growth and promising clinical momentum due to a solid team and strong network partnerships. Trodelvy is leading the way here with 30 trails underway 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 on Yescarta and Tercartus, O'Day proceeded to shed focus on Gileads 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 manufacturing, the company now draws focus on accelerating manufacturing time of these products to see improvements of less than a 16-day turnaround in the US by the end of 2024. Additionally, Gilead are also underway with 4 phase 1 studies and a comprehensive pipeline of novel CAR -T agents in the pre-clinical 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 significantly maintain position as global leader in treatment, annualizing $12 bn and maintaining >47% US market share in Q3 2023 whilst still holding exclusivity to 2033. Innovation also heavily continues with Lenacapavir, a biannually injection for prevention which has made significant headway to enter clinics in 2024 and 5 new launches to be seen in combination with daily oral therapy by the end of 2025.

With five phase 3 updates, as well as over 8 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.

H. Lundbeck

H. Lundbeck's new CEO Charl van Zyl really doubled down on Lundbeck'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. First, the deriving growth from existing assets. The current commercial portfolio focuses on Rexulti and Vyepti while the emerging pipeline is more weighted to early stage, so Lundbeck will look to external innovation to bolster the late-stage pipeline and build a more sustainable pipeline for the long term. Charl van Zyl confirmed 30-32% adjusted EBITDA target long term, excluding potential business development activities.

To grow Rexulti in its new indication, 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 salesforce, 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 mergers and acquisitions 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 presentation reviewing where the company is today as well as what it plans to achieve over the next seven years into 2030. He cited his expectation that Incyte's commercial expertise in oncology and inflammation and autoimmunity (IAI) 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 $1.9 billion, and Opzelura (ruxolitinib cream), with sales of $229 million 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, between 2020-2021, which is now a commercialization 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 (AD) and vitiligo two years ago and 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 (PN) met its primary endpoint across all three treatment dose groups, with Phase III studies in HS and vitiligo enrolling.

Also announced were key pipeline updates that could support significant future launches anticipated by 2030, including both indication expansion 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 axatilimib (for which a BLA was submitted in 3L + cGVHD); mCALR (a mAb for which Phase I 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 closing remarks, Hoppenot re-stated 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 $3 billion in revenues by 2028, particularly looking to PV, an underpenetrated indication; Opzelura adoption in existing and new indications; and the possibility of broadening through potential partnerships, using its $3.5 billion of cash on its balance sheet to bring in assets complementary to its three core therapy areas that leverage its expertise.

Regeneron

Looking back at 2023, Regeneron CEO Dr 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 chronic obstructive pulmonary disease (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 $1.46 bn for Q4 2023 with Eylea HD sales accounting for $123 million for its first full quarter after the August 2023 launch. With >750,000 patients on therapy globally, Dupixent global sales grew 34% and reached nearly $8.4 bn for the first three quarters of 2023. Potential new indications for Dupixent provide an opportunity to add up to one million additional eligible patients in the US. Dr. 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 $1 bn in sales in 2024.

The CSO, Dr George Yancopoulos, spoke next and began by discussing the combination of fianlimab (an anti-LAG-3 antibody) and Libtayo. Following results in 1L metastatic melanoma that compared well to historic 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.

Dr 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, Dr 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 results 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.

Dr 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 ± garestomab (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) siRNA in collaboration with Alnylam; (ii) 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 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.

Dr 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.

Teva

In his first year as CEO, 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 centring on debt repayment and settlement of litigation. However, at the 42nd Annual J.P. Morgan Healthcare Conference, Richard Francis exhibited the company's feats in delivering across all pillars of the implemented growth strategy. The four pillars supporting the strategy are to deliver on growth engines, step up innovation, sustain generics powerhouse, and focus their business.

Francis outlined three key assets which have helped deliver on the growth engines, namely Austedo, Uzedy, Ajovy. Some of the 2023 milestones for these assests which helped deliver on growth include 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 a 32% and 24% increase in US revenue for Austedo and Ajovy, respectively. Long-term goals for delivering on growth engines were also presented, predominantly focussing on continued growth through geographic and market share expansion. For Austedo a sizeable goal was set of more than $2.5B revenue by 2027 cross tardive dyskinesia and chorea associated with Huntington's disease, but the company expressed their confidence in achieving this goal and reaffirmed that Austedo was on track to reach the $1.2B 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 $1B 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 state 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 enrolment and is anticipating a Phase III read out in the second half of 2024, with Francis championing the product's potential to change the treatment landscape for schizophrenia if the drug is able to deliver on the product portfolio and safety measurements. TEV-'248 is a combination therapy of ICS and SABA, the two most widely used molecules in respiratory conditions, and the company estimates at least 30% of the ten million potential patients to use this combination regimen, generating a market potential of $2.5B. Teva also partnered with Sanofi in 2023 for the anti-TL1A agent TEV-'574, which is under Phase II investigation currently. Sanofi's adept experience in immunology is highlighted as a core strength in the development of this product, and a market potential of $28B is proposed for this agent. The company is also building upon its early-stage pipeline to strengthen its leading position in neuroscience and immunology.

Whilst the generics space has been an area Teva is experienced with, Teva's 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 the 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 $10B 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 underway, with a new CEO and management team now dedicated to the business. The company anticipates an expected growth of approximately 6-7% in the upcoming year.

In closing remarks, the CEO commends the efforts of all Teva's team in their willingness for change and their drive the company back into growth. Francis reiterates the financial targets of 2027, confidently affirming the company to be on track to achieve 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 advance 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 of 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, an interim analysis of the study is planned at 48 weeks, with a potential path to file for accelerated approval in the United States. A final analysis will be conducted at 2 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 I diabetes, has been fully enrolled. Efficacy from the trial continues to show curative potential. Safety data is 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

Apellis Pharmaceuticals

Apellis Pharmaceuticals' CEO Cedric Francois provided an overview of the 2024 plans for the company, which are centered around novel treatments targeting the complement cascade, including their 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 for Syfovre in the US; 2) expand Syfovre's geographic footprint beyond the US; 3) maximise 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 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, a high unmet need. However, the CEO noted that the company expects a negative opinion from the EMA's committee for medicinal products for human use (CHMP), 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 regulators.

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, the 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 2 NOBLE trial evaluating the drug in patients with C3G or IM-MPGN and kidney transplants. The ensuing Phase 3 VALIANT trial is expected to have top-line 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, PhD, 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 the 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 and hypertriglyceridemia, and zodasiran (ARO-ANG3) for homozygous familial hypercholesterolemia and ASCVD (atherosclerotic cardiovascular disease). Phase III for plozasiran in FCS should wrap up in Q2 while Phase III 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 (fazisiran 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 notes that Arrowhead has seen almost $1 billion 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 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 Mikkelsen, President & Chief Executive Officer highlighted the company's recent activities, pipeline developments and plans for 2024. The presentation kicked off with mentions of the US (United States) approved Skytrofa for paediatric Growth Hormone Deficiency (GHD) and the EU (Europe) approved Yorvipath for adult chronic hypoparathyroidism.

Mikkelsen noted that Skytrofa, which had previously received Orphan Drug Designation both in the US and EU, has accumulated around €64 million in revenue by the fourth quarter of 2023 and Ascendis anticipates the drug will eventually bring in around €320 - €340 million 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 paediatric population with GHD which showed that of the treatment completers, 59% met or exceeded their average parental height SDS (Standard Deviation Score), with mean Skytrofa treatment duration of 3.2 years. Treatment completers 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 (Food and Drug Administration) for the adult GHD indication in the second quarter of 2024. Furthermore, Ascendis announced the CTA (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 the fourth quarter of 2024.

The presentation also highlighted Ascendis' commercial organisation 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 PDFUA date of May 14, 2024, for Yorvipath and if approved, Ascendis expects a US product launch in the third quarter of 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' commercial presence in the rest of the world. These 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 ended by highlighting the fact that Ascendis has expanded their 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. This vision 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.

BridgeBio Pharma

BridgeBio Pharma CEO, Neel 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. CEO Neel 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 their presentation that they expect to submit marketing authorization to the European Medicines Agency (EMA) before long. An outline of previous data from the Phase III ATTRibute 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 magnetic resonance imaging preliminary showed Acoramidis may lead to actual disease regression in some patients, as evidenced by a decrease in extracellular volume (ECV) of the heart. The presentation then moved onto 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. 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.

Insmed

Insmed's CEO, William Lewis began the presentation with confidence surrounding the upcoming year for Insmed and the company's upcoming 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, TPIP, and their early-stage research, all of which was touched on during the presentation.

Arikayce experienced 24% year over year 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 their revenue guidance expectations falling between $340M-$360M. Lewis touched on the Phase IIIb ENCORE frontline study that is currently ongoing for Arikayce for newly diagnosed MAC disease, with enrollment completion expected in 2024 and top-line 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 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 $1 Billion peak sales product.

Lewis described the upcoming Phase III ASPEN top-line 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 current 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, and the interest surrounding the DPP-I pathway is expected to grow in the industry. Lewis mentioned Insmed competitor, Boehringer Ingelheim, has already started pursuing development of their DPP-I drug for Bronchiectasis following the success of Insmed's Phase II Brensocatib Willow study. The company also plans to expand this once-a-day convenient chronic oral treatment landscape 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 PAH and PH-ILD was the last major update out of the four pillars. Lewis reminded listeners that highly encouraging blended blinded data generated from their Phase II TPIP program was released in October 2023. A Key Opinion Leader described the hemodynamic changes as stunning. In the upcoming months, a top-line readout for the Phase II PH-ILD study is expected before the end of the second quarter of 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 if it moves forward, it would be the only inhaled prostanoid that only needs to be administered once a day with a slow release of

TPIP for continuous treatment day and night.

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

Jazz Pharmaceuticals

Jazz Pharmaceuticals' chairman and chief executive officer 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 their third quarter earnings announcements. Total revenue guidance for the year ending 2023 remains in the $3.75 - $3.875 billion range, with 49% of revenue so far driven by oncology and Epidiolex, and the remaining attributed to sleep revenue. By 2025, they hope that revenue approaches $5 billion, with 60% of revenues driven by oncology and Epidiolex.

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

For the 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 they 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 top-line readout target based on the original enrollment total, which would maintain earliest possible time to approval based on PFS and increases the probability of success of OS with two interim and a final OS readout.

Jazz expects a Phase III top-line 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 top-line data readout from the Phase IIb suvecaltamide essential tremor study late in the first half of 2024. Top-line data are also expected for Epidiolex in the second half of 2024 from the pivotal Phase III trial for Dravet/Lennox-Gastaut/TSC in Japan. The company then noted that early programs like JZP815 and JZP898 continue to advance in their Phase I studies.

PTC Therapeutics

Matthew Klein, Chief Executive Officer at PTC Therapeutics, described an eventful 2023 for the company, with a total unaudited net product revenue of $661 million, representing a 23% year-over-year growth, largely driven by PTC's Duchenne muscular dystrophy (DMD) franchise, Translarna and Emflaza, which together generated an unaudited net product revenue of $610 million. 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 a reduction of operating expenses and headcount by approximately 25% and 30%, respectively, the focusing 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 Fredreich's ataxia.

Focusing on the sepiapterin, APHENITY met the primary endpoint by showing statistically significant reductions in blood phenylalanine (phe) levels in patients with PKU. Sepiapterin treatment enabled increased dietary phe 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, 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 (AADC) 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 Fredreich's ataxia, and CHMP supplemental filing results for Translarna in DMD. Total revenue guidance for 2024 is $600-$850, 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 JPM presentation, the CEO Chris Gibson unveiled the timeline of clinical readouts for its 5 programs, comprising 4 rare disease programs and 1 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 or 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 NVIDA for computation and ML/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 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 of 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 $390 million in cash. Their 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 their pipeline in the cardiovascular domain.

Sarepta Therapeutics

At the 42nd J.P. Morgan Health Conference, Sarepta Therapeutics, a leading developer of RNA-based gene therapies, showcased their progress over the last 7 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 6 and a revenue of $5 million. Fast forward to today, Sarepta now has 3 technology platforms (RNA, gene therapy and gene editing), a pipeline of over 40 with 4 on-market therapies, and an estimated 2023 revenue of

$1.145 billion 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 through 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 between the ages of 4 through 7 years. EMBARK achieved statistical significance on all pre-specified 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 their next-generation RNA-based therapy SRP-5051 for DMD in 2024, in addition to executing research and development 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 to improve the human condition and they will continue making significant strides in the fight against rare neuromuscular diseases.

SpringWorks

Chief Executive Officer Saqib Islam began the of SpringWorks (SWTX) 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 3 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 Authorisation Application for desmoid tumors in Europe in 1H 2024. There are advanced expansion opportunities for OGSEVIO as a monotherapy in ovarian granulosa cell tumors (OvGCT) (initial data for Phase 2 study expected in the second half of the year) and 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 2b 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 granted 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 SpingWorks' emerging pipeline include the of a Phase 1 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 a solid foundation and clear drivers are in place for long-term success: First product launch underway with 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.

Ultragenyx Pharmaceutical

Ultragenyx announced new financial guidance for 2024 of 500-530 million, a growth expectation of 16-23% over the previous year's guidance. This reflects the overall trend of the company as it has 4 products on the market for 5 indications, 6 late-stage studies ongoing, and plans to reach approvals for another 3-7 indications in the next 5 years. In 2023, growth was attributed to an increase in sales of Crysvita and Dojolvi and that is expected to continue with growth estimates increase for both (375-400 million and 75-80 million, 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 (GSDIa) 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 (MPS IIIA) by pushing for FDA approval of biomarker data for their rare diseases. Finally, the company expects to complete enrollment for its Phase III programs for DTX301 for the treatment of Ornithine Transcarbamylase Deficiency (OTCD) and the Phase III ORBIT and COSMIC studies of UX143 for osteogenesis imperfecta in 2024.

Xenon Pharmaceuticals

Xenon's President and Chief Executive Officer Ian Mortimer began with a financial overview, reporting $640 million at the end of Q3 2023, and confirmed that the company is prepared to support both their extensive epilepsy and their 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, with trials ongoing in both indications. Modeled after the notably successful Phase IIb X-TOLE trial, the registrational Phase III XTOLE 2 and 3 studies address focal onset seizures, which comprises 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 are 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 seizure 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 and the company is actively working on a pediatric formula for children under six, who may not be able to handle an oral pill.

Mr. 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 SHAPS anhedonia 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 a monotherapy in MDD. At worst, the X-NOVA results support the use of XEN1101 in epileptic patients with depression, which is a common comorbidity. 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 (EOP2) 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 EOP2 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 efforts are primarily focused on the late phase programs.

Small Cap

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 have 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). This data provided early evidence on the usage of efruxifermin in NASH patients with type 2 diabetes, which given how frequently type 2 diabetes also present 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 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.

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-PD1 failed melanoma. Per the data, 1 in 3 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 (CSCC) 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 DOR, progression free survival (PFS) and overall survival (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. 30% overall response rate was achieved in second line uveal melanoma, supporting a pivotal randomized control trial in the indication. In a heavily pre-treated 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 United States, 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 U.S. alone. The Company ended 2023 with a strong balance sheet of $466 million, with its cash runway expected to remain cash positive into the second half of 2026.

Sage Therapeutics

Chief Executive Officer Barry Greene kicked off Sage's presentation at the 42nd J.P. Morgan Healthcare Conference. The presentation started with updates on the commercialization of Zurzuvae, the second approved product after Zulresso for postpartum depression (PPD) by the FDA in August 2023. 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 goals 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. Data read out for a Phase IIb study is expected in 2024.

With the Zurzuvae launch goals to destigmatize PPD and combat both economic challenges and the stressful impact of the COVID-19 pandemic had on women with PPD faced, Sage aims to expand access of 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.

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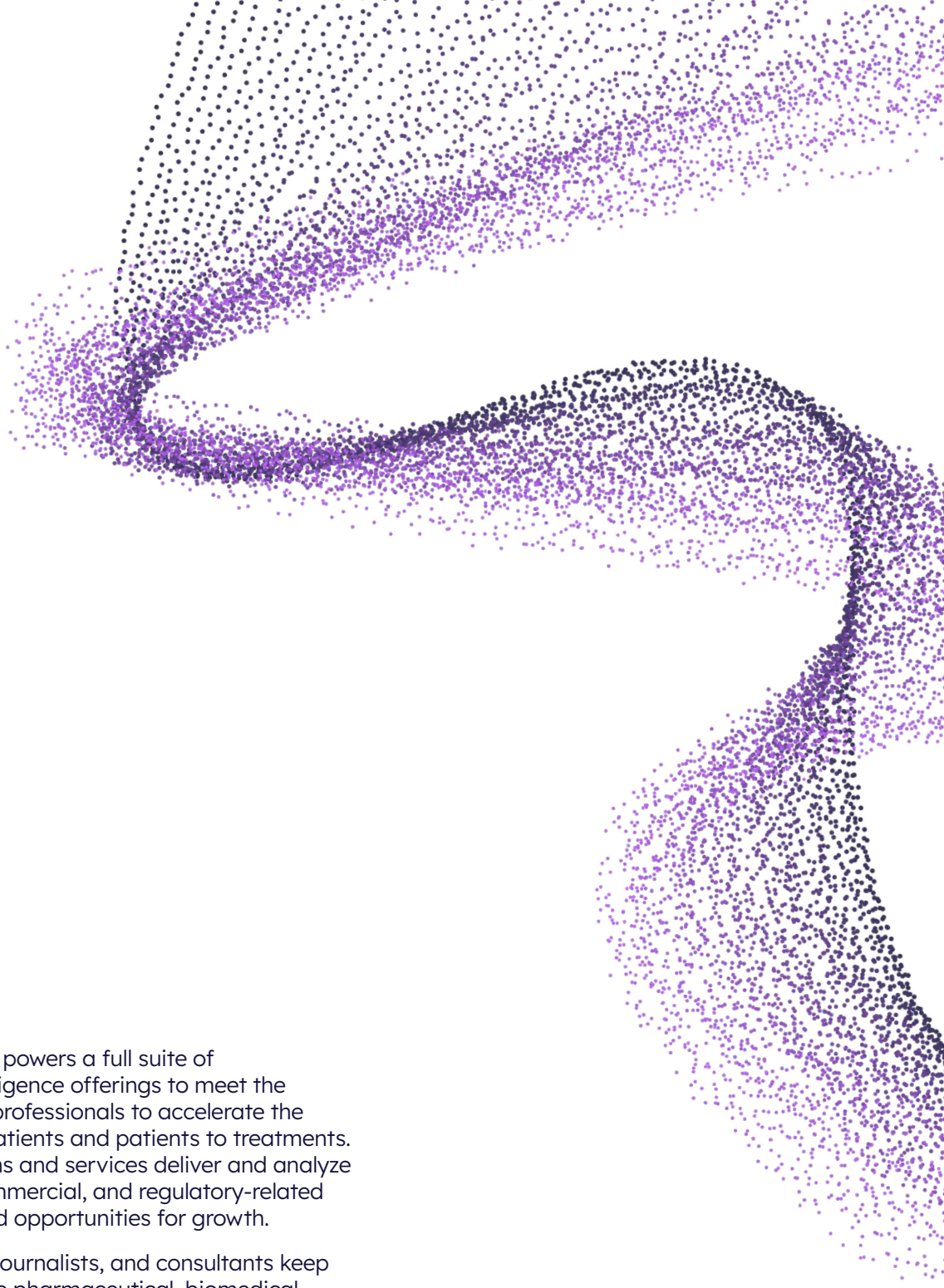

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