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#JPM24

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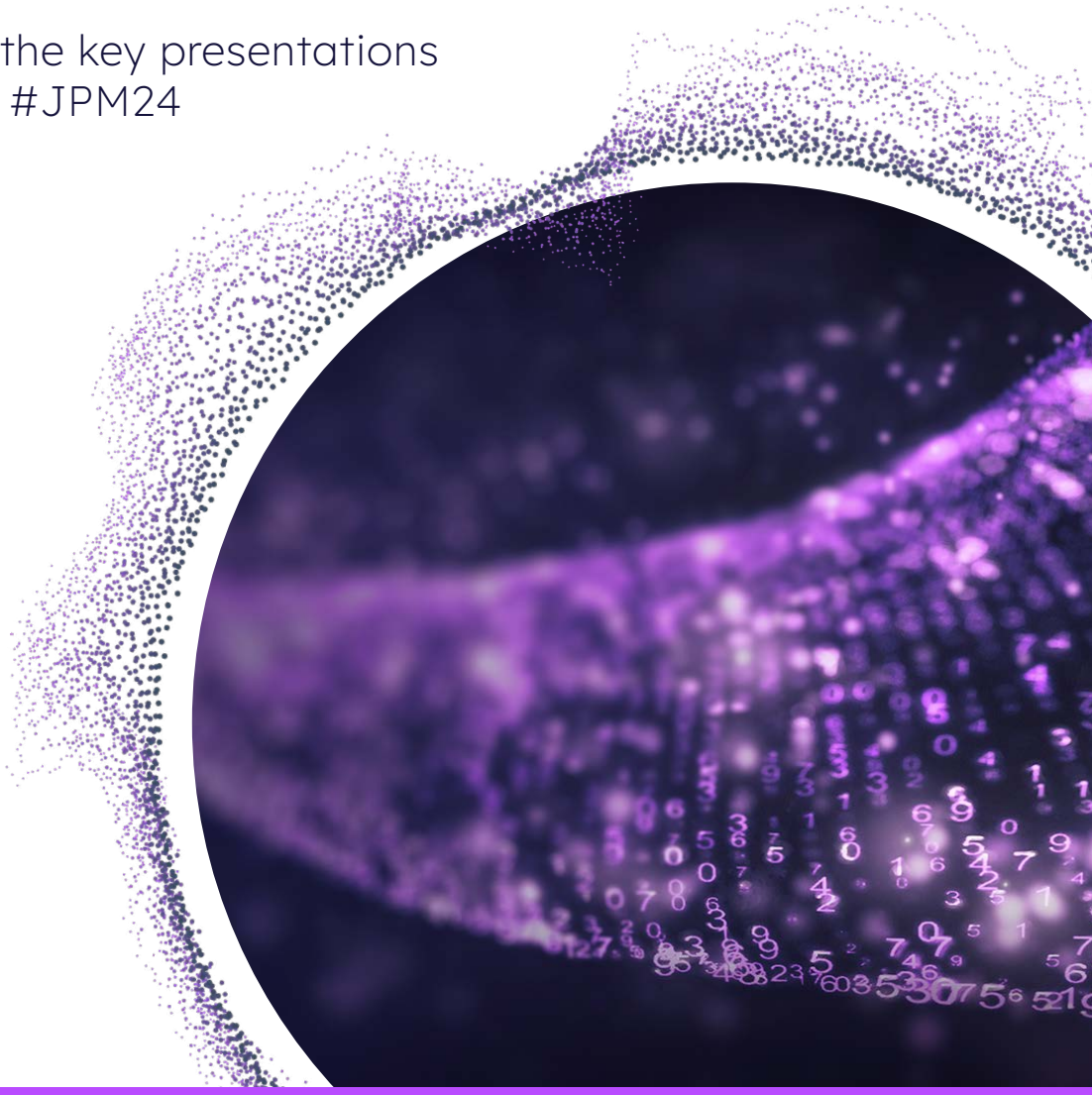
Day 4
Presentations Highlights

A detailed recap of the key presentations and highlights from #JPM24



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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 4 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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Mid Cap

Azenta Sciences

Azenta remains an established life sciences company with a unique portfolio end-to-end sample management, holding a strong track record in developing and serving an attractive high end growth market. Leading the company for over 13 years, CEO Stephen S. Schwartz addressed the crowd with confidence on their growth forecast in the next 10 years, creating value in the sample management space. The company currently (in fiscal year end Q4 2023) has performed at a 2% organic growth, outperforming the market, with positive free cashflow and 25% YOY growth aided by the completion of Ziath, Ltd. acquisition a year earlier. Azenta ended the year with £ 600mill in revenue and a balance sheet well positioned to add value. Schwartz forecasted 5-8% growth with ~300bps adjusted EBITDA margin expansion in 2024 alongside the next 6-8 quarters of strong growth pipeline. The company announced a $1,5 bill share buyback plan 14 months ago with $ 950 mill shares already purchased and the remainder to be completed in 2024. They also recently announced a governance change having nominated 3 strong additional directors to the board with operational and scientific specialities.

Watching momentum build in a $ 10 billion market size, Azenta has reached sustained growth of $700 mill ($10 mill in 2011), barely penetrating the surface with over 10 thousand customers in 150 countries. Primarily focused on growth and innovation, they have realigned the company's drive and prioritising investments into their sales organization hoping to see results in the next couple of years. With strong growth prospects and tailwinds due outsourcing ~50% of their R&D, Azenta has seen 2x growth over a 5-year period and are confident to see similar results in the next 3 years, forecasting to see long term growth in the cell and gene therapy space as well as being leaders in the cryogenic technology space.

Schwartz also discussed around the three additional segments reported by the company which are: 1) Added samples management solutions, bringing in $300mill in revenues in 2024, 2) Multiomic segment adding to scientific capabilities, generating $ 250mill with considerable scale, and 3) B medical segment, a vaccine delivery capability enabling access to remote and critical parts of the world, generating $113mill. As a growth company, Azenta is planning to reach $2bill in revenues over the next 5 years, with a 2024 forecast of 75% increase in adjusted EBITDA, adding revenue on top.

Small Cap

Akebia Therapeutics

Akebia Therapeutics, a fully integrated biopharmaceutical company in renal diseases, reaffirmed their focus on realizing profitability by reviewing their achievements from 2023 and outlining upcoming projects for 2024 and beyond. Kicking off the presentation, CEO John Butler confidently addresses the crowd on Akebia's path to profitability, relying on continued financial

discipline and meaningful near-term product growth to fund scientific innovations. The company currently expects approximately $170 million in 2023 preliminary unaudited net revenue with further growth in 2024 for Auryxia, an agent approved for hyperphosphatemia and iron deficiency anemia. While March 2025 marks the loss of exclusivity for Auryxia, Akebia highlighted a potential upside due to phosphate binders being added to the bundle, and thus are eligible for reimbursement from the Transitional Drug Add-on Payment Adjustment (TDAPA) program.

The presentation then transitioned to anemia management in dialysis patients, as it is an area with significant growth opportunities for Akebia. With the PDUFA date of March 27, 2024 approaching, Butler noted the significant $1 billion US market opportunity if vadadustat is approved. Vadadustat, a hypoxia-inducible factor prolyl hydroxylase (HIF-PH) inhibitor, was initially approved in Europe and Japan as Vafseo for the treatment of anemia associated with chronic kidney disease (CKD) in adults on dialysis. Beyond Europe and Japan, vadadustat also recently secured approvals in Australia and Taiwan in November 2023, totaling 36 countries. The potential US approval in early 2024 will initially expose vadadustat to ~558,000 CKD patients on dialysis in which the majority are reimbursed through TDAPA bundle payment. Upon FDA approval, Akebia anticipates obtaining TDAPA designation for vadadustat within 6 months of post-filing acceptance to drive adoption quickly. On launch preparation, Butler boldly underscored Akebia's commercial readiness, noting a strong embedded commercial team and supply chain readiness with adequate manufacturing and logistics setup. The CSL-Vifor partnership will be crucial to ensure access to vadadustat, as the agreement continues to provide access to up to 60% of US dialysis patients and leverages CSL-Vifor's exclusive distribution arrangements. Furthermore, international market collaborations with Medice in Europe and Mitsubishi Tanabe Pharma in Japan will provide additional upside with a potential European launch for vadadustat in the first half of 2024.

Beyond the approval of vadadustat in dialysis patients, Butler emphasized the potential of vadadustat in the non-dialysis population. The all-cause mortality risk was the discussion point, where Butler stressed the significantly higher risk in these pre-dialysis patients remain even after treatment with ESAs after dialysis. Stating that anemia may not be optimally managed in patients transition to dialysis, Butler expressed that vadadustat could offer a unique opportunity to manage risks ahead of dialysis. In addition, data from the Phase III FOCUS study was reiterated, demonstrating how vadadustat is comparable to Roche and Vifor's ESA Mircera (methoxy polyethylene glycol-epoetin beta) when used three times weekly, a pattern of administration that aligns with dialysis sessions. This adds to the convenience of vadadustat in that it could be used at the same time as dialysis, but its oral formulation also means that it could be prescribed and administered at home, adding to the opportunity for further label expansion post approval.

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

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

Anavex Life Sciences

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

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

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

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

Outside of blarcamesine, Anavex has a number of other drug candidates, primarily in preclinical stage although ANAVEX3-71 is in early phase studies for schizophrenia, frontotemporal dementia, and Alzheimer's. This drug differs from blarcamesine in that in addition to sigma-1 activation, it also has strong and selective M1 interaction, another receptor that has been implicated in the mechanisms of these diseases.

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

C4 Therapeutics

C4 Therapeutics (C4T), a leader in Targeted Protein Degradation (TPD), started their presentation at the 42nd Annual J.P. Morgan Healthcare Conference showcasing their historic 2023 through the strong continued execution of their milestones. To date, C4T has discovered a number of degraders and advanced 4 INDs against a transcription factor, a chromatin modifier, and two kinases. In addition, they have evaluated 3 programs in the clinic, with each demonstrating robust target degradation in patients.

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

C4T also looks outwards to accelerate their pipeline development, securing two major partnerships in 2023 with Betta Pharmaceuticals for the development of CFT8919, a TPD targeting EGFR L858R, and with Merck to discover and develop degrader-antibody conjugates. With a promising pipeline and a great potential for future collaborations, C4T are in a great position for future value creation and can expect an exciting year in 2024.

Caribou Biosciences

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

Caribou's pipeline is split by two different technologies with three programs under the CAR-T platform for hematologic indications, and an additional program, CB-020 targeting ROR1, under the CAR-NK platform with iPSC-derived cell therapies for solid tumor indications. In the upcoming year, Caribou expects to achieve several clinical milestones. Caribou's lead clinical-stage program, CB-010, is an allogenic anti-CD19 CAR-T cell therapy in Phase I development for r/r B-NHL and r/r LBCL with a Phase III pivotal trial for LBCL expected by the year end of 2024. Additional data readout for the Phase I ANTLER study is expected in the second quarter of 2024.

Another data milestone for the Phase I CaMMouflage trial of CB-011, an anti-BCMA allogeneic CAR-T cell therapy, in r/r multiple myeloma is expected by year end of 2024. Initiation of the Phase I AMpLify trial for CB-012 in r/r AML is also expected in the first half of 2024.

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

Cullinan Oncology

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

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

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

Cytek

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

Dr Jiang then focused on the applications that Cytek technology enables. This includes deeper assessment of patient immune status pre and post treatment, allowing researchers to maximize

the value of lab samples as they are equipped with more information in less time with fewer errors and full standardisation across experiments and laboratory sites. With this combined, Cytek technology has led to more than 1,450 peer-reviews publications in the fields of oncology, viral infections, immunology, inflammation, autoimmunity, and drug development.

The presentation then focused on the company's current products. One such product is Cytek's ImageStream which was recently used to validate the efficacy of treatment in Sickle Cell disease. This led the FDA (Food and Drug Administration) to approve the first gene therapy to treat patients with Sickle Cell disease. Another example is Cytek Cloud which provides the user base with data analysis, panel, and experimental design optimisation. Finally, in the clinical space, full spectrum profiling products such as the Cytek Aurora enables comprehensive clinical applications. At a low cost, the product allows for advanced flow cytometry for disease screening, diagnosis, and monitoring capabilities. Dr Jiang was also keen to mention the specific benefits of Cytek's technology for clinical use which include the identification of rare populations of abnormal cells, eliminating redundant reagents and optimising the use of smaller samples of patient specimens. Due to these products and continued development into these areas, Cytek is hopeful that continued growth and increased revenue will occur in the coming years.

MacroGenics

MacroGenics' executive officer, Scott Koenig, began the presentation by focusing on the company's efforts in developing antibody-drug conjugates (ADCs), of which they have 20+ years of experience engineering expertise. He also showcased MacroGenics' differentiated pipeline, with various assets being investigated in multiple solid tumor types in early phase trials. Koenig went on to highlight how MacroGenics are expanding their capabilities through their numerous partnered programs, which include the marketing of Margenza for HER2+ breast cancer with Eversana, Zynz in merkel cell carcinoma with Incyte, and Tzied for stage 2 type 1 diabetes with Sanofi. MacroGenics are also partnering with Gilead to develop various biologics in solid and haematological tumors.

Koenig discussed three key readouts expected for MacroGenics in 2024: the Phase 2 TAMARACK trial of Vobra Duo (an ADC) in metastatic castration-resistant prostate cancer (mCRPC), the Phase 2 LORIKEET trial of lorigerlimab in mCRPC, and the Phase 2 HEAT trial of enoblituzumab in neoadjuvant prostate cancer. Positive results for these trials will allow provide rationale to initiate Phase 3 trials which could lead to approvals across markets.

The objective response rate (ORR) for patients treated with Vobra Duo (a B7-H3-targeting ADC) in a Phase 1 trial was 25.0%, which is relatively underwhelming compared to other agents approved in this setting, although of course this data is in an extremely small cohort and may not reflect future data in later phase trials. Similarly, Phase 1 data showed lorigerlimab-treated mCRPC patients achieved an ORR of 25.7%, which is again not particularly impressive considering the current mCRPC treatment landscape, which is dominated by hormonal therapeutics which have robust data and strong physician familiarity in this setting. Lorigerlimab is a PD-1 and CTA-4 targeting bispecific antibody - prostate cancer is an immunologically "cold" tumor type, meaning response rates to immunotherapies are low, which has already resulted in failed trials for both Keytruda and Opdivo, two PD-1 inhibitors with approvals across various

oncology indications. MacroGenics hope to produce stronger data in the Phase 2 LORIKEET trial and carve out a niche in mCRPC for themselves by having lorigelimab being the first immune checkpoint inhibitor approved for mCRPC. The initial readout for the TAMARACK Phase 2 trial is expected in H1 2024, and the Phase 2 LORIKEET trial is expected to readout in H2 2024, both of which may be able to boost expectations surrounding Vobra Duo and lorigerlimab, respectively.

Finally, Koenig examined another exciting asset for MacroGenics; the next generation CD3 x CD123 DART molecule, MGD024. Gilead are partnering with MacroGenics on a currently ongoing Phase 1 dose escalation study for this asset in haematological malignancies; further data will be needed to assess its chances of approval in this branch of oncology.

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

Mayne Pharma Group

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

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

The dermatology business, facing pricing pressures, underwent significant restructuring. O'Brien reported a remarkable 314% increase in dermatology revenue during the second half of fiscal year 23, turning the business back to positive contribution. The company plans to launch ten dermatology products between October 2023 and June 2024. Mayne Pharma achieved a relaunch of its flagship product, the oral contraceptive NEXSTELLIS, resulting in a 276% revenue increase compared to fiscal year 22. The women's health segment, comprising 96% of the branded product portfolio, demonstrated a 45% sequential increase in net sales. Ongoing initiatives include enforcing ACA laws to minimize patient out-of-pocket expenses for birth control.

Mayne Pharma reported positive operating cash flow of AUD 14 million in the second half of fiscal year 23. Asset sales led to a net cash position of AUD 173 million on June 30th, 2023, compared to a net debt position of AUD 317 million the previous year. The company initiated an on-market buyback of up to 15%. For the four-month period from July 1st to October 30th, 2023, Mayne Pharma reported net sales of $125 million, indicating a run rate of $375 million for fiscal year 24. Gross margin increased by 50% to $72 million, and underlying EBITDA was $1 million. The company achieved positive contribution margins across all three business segments.

Mayne Pharma aims to achieve positive operating cash flow by the end of the fiscal year, with a strategic focus on maintaining positive contribution margins and continued growth in key

segments. The company is actively pursuing growth strategies, including product launches and adherence to ACA laws, while exploring potential new products for its dermatology and women's health portfolios.

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

NeuroPace

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

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

In the US, one third of epilepsy patients are drug refractory, which equates to approximately 1.2 million people. The current population focus is on Level 4 comprehensive epilepsy centers, whereby approximately 50,000 refractory epilepsy patients are treated annually. Of these, approximately 6,500 patients receive treatment beyond drugs. Becker stated that significant opportunity exists to close this treatment gap by expanding access to RNS therapy through three strategies.

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

The company also plans to increase the availability of the RNS system to healthcare systems outside of Level 4 comprehensive epilepsy centers, where 1,800 epileptologists and functional neurosurgeons are practicing. In 2023, the company received approval of a PMA supplement that allows for RNS technology to be used beyond epilepsy centers, in the community setting. Expanding into the community will allow NeuroPace to uncover more complex patients who were

never referred to epilepsy centers. The pilot for this project is expected to be initiated in the first half of 2024, with the expansion happening in the second half of 2024.

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

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

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

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

Nevro

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

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

The company operates around three pillars: commercial execution, market penetration, and

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

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

CEO Thornal went on to talk about its HFX iQ which is the only artificial intelligence based SCS system that gets smarter over time by learning from patient responses. The first HFX iQ implanted patient reported 80% relief and an increase in activity as of Oct. 26, 2023, which was 1-year post implant. Data on HFX iQ included patients reporting getting back to relief 75% faster. HFX iQ is the most effective SCS solution for PDN with approximately two times the responder rate and pain relief. It has the 90% highest published responder rate, 80% highest published percentage pain relief, and is the only SCS system to demonstrate neurological improvements.

In late November 2023, Nevro acquired Vyrsa thus expanding into the $2 billion SI joint fusion market. Nevro has the most comprehensive portfolio in SI joint fusion. The NevroV1 SI joint fusion system with integrated transfixing technology provides immediate SI joint stabilization and an opportunity for long-term fusion. NevroPRO is the first MIS allograft SI joint fusion system designed to provide comprehensive decortication of the SI joint articular surface with multiple implant sizes for variable patient anatomy. The NevroFIX lateral SI joint transfixing lateral screws are designed to provide maximum compression of the joint space.

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

Pharvaris

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

demand treatment, and the second an extended-release (XR) version for prophylaxis.

A desirable on-demand treatment for HAE would have rapid onset of action, durable effect from a single dose, and be orally administered, according to Pharvaris, and the company believes their candidate can meet these needs. Data from the Phase 2 RAPIDe-1 trial demonstrated rapid onset of action leading to symptom relief and resolution of the HAE attacks with reduction in rescue medication needed. Importantly, there were no safety concerns raised and the drug candidate was well tolerated. The success of this trial has led to plans for a Phase 3 trial in the on-demand setting to be initiated in H1 2024.

Deucrictibant also has the potential for use as a preventive agent. Ideally such an agent would have the efficacy of the injectable agents but without the pain that can be associated with injections, said Modig. The CHAPTER-1 Phase 2 trial showed that deucrictibant reduced HAE occurrences by more than 90%, was well tolerated, and improved quality of life for recipients. Importantly the pharmacokinetic analysis of the XR formulation supports once-daily dosing to be taken into Phase 3.

A clinical hold was placed on development by the FDA in August 2022 due to concerns over safety. A rodent toxicity study was conducted to address the concern and as a result the hold on development of the IR formulation has been lifted but it remains in place for the XR formulation although the company stated that the FDA is still evaluating the relevant new data; development outside the US was not interrupted.

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

Viridian Therapeutics

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

Mahoney introduced each program briefly, starting with the leading asset, VRDN-001. This antibody targets IGF-1R, a validated target in TED. VRDN-001 is designed as an intravenous infusion with a shorter infusion time of 30 minutes and a reduced dosing regimen of five doses, in comparison to Tepezza, the first approved anti-IGF-1R antibody for TED which requires 60-90

minutes of infusion and eight injections per regimen. The Phase II study results of VRDN-001, published last year, demonstrated a favorable efficacy profile in improving both proptosis and symptoms compared to Tepezza. VRDN-001 was well tolerated without any notable adverse effects. Currently, VRDN-001 is undergoing two Phase III studies: THRIVE for active TED, with topline data expected in mid-2024, and THRIVE-2 for chronic TED, with an initial readout at the end of 2024. Moving on to VRDN-003, it is the next generation of VRDN-001 with three amino acid mutations in a subcutaneous formulation. The selection of this candidate was based on Phase I data from last December, which demonstrated an extended half-life and a substantial increase in IGF-1, an indicator of effective IGF-1R suppression, in healthy volunteers. VRDN-003 showed a generally acceptable tolerability profile, with no identification of anti-drug antibodies. Due to the protein structure similarity between VRDN-001 and VRDN-003, along with the clinical experience gained from the Phase II study of VRDN-001, it is predicted that VRDN-003 can be administered once every 2, 4, or 8 weeks. This dosing regimen offers convenience while minimizing the risk of adverse effects. The primary endpoint for VRDN-003 would be the proptosis responder rate, with secondary endpoints including proptosis mean change, clinical activity score, and diplopia. Further discussions with regulatory agencies are planned prior to mid-2024 regarding these endpoints and trial design.

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

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

Xeris Biopharma

Paul R. Edick, Xeris' chairman and CEO, opened the presentation reviewing the company's three core pillars of value creation: commercialization of three innovative products, leveraging its proprietary formulation science to develop new product candidates, and partnerships with biopharma companies. Edick provided financial highlights, including Xeris' cash-flow positive status as of Q4 2023. For Q3 2023, it achieved revenues of $48.3 million, a 63% growth compared to Q3 2022. The company provided revised guidance on its 2023 total revenue to the high end of $160-$165 million; its cash utilization to the low end of the $52-57 million range; and expects its year-end cash position to exceed $72 million.

Edick discussed marketed products, all of which showed growth in net revenues during Q3. Gvoke, a ready-to -use autoinjector of liquid stable glucagon for severe hypoglycemia, had year-

to-date revenue of $48.4 million, a significant contributor to the higher-range revenue forecast. Gvoke is thought to represent an addressable US market of $5 billion, with expectations to penetrate the 15 million at-risk diabetic patients of which only about one million are currently receiving a prescription for a self-administered rescue pen. Cortisol synthesis inhibitor Recorlev (levoketoconazole), for the treatment of Cushing's syndrome, a rare endocrine disease, demonstrated revenue growth every quarter since its 2022 launch, with year-to-date revenue of $19.7 million. Oral carbonic anhydrase inhibitor Keveyis (dichlorphenamide), a therapy for primary periodic paralysis (PPP), a spectrum of ultra-rare neuromuscular disease, had year-to-date revenue of $42.7 million, despite generic competition.

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

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

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

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

Zymeworks

CEO Kenneth Galbraith opens Zymeworks presentation with a moment to reflect on the company's progress since the last J.P. Morgan Healthcare conference in 2022, in which the company were celebrating zanidatamab's top-line readout from a Phase III trial in biliary tract cancer (BTC) and their closure of a licensing agreement with Jazz Pharmaceuticals. He goes on to announce that the company used the momentum from those two events to propel them into a year of success in 2023 and feels confident with the position Zymeworks is now in to head another strong year. Upon their entrance into 2024, the company now has a product pipeline which focuses on building uniquely differentiated agents through antibody engineering. Their lead product zanidatamab, a HER2 bispecific antibody, currently has a rolling USA regulatory submission underway with breakthrough designation and also anticipates a pivotal Phase III top-line readout for use in gastric and gastroesophageal junction cancer (GEA) in the second half of 2024. Through their partnership with Jazz and Beigene, the company is also exploring

zanidatamab's expansion into other indications with additional clinical trials planned and ongoing. Galbraith highlights Zymeworks R&D strategy of focusing on cancers with the highest unmet needs and slowest therapeutic progression, selecting cancers which have seen the least improvement to five-year survival between 2012 and 2018. These include stomach, esophageal, and non-small cell lung cancer (NSCLC), all of which are indications zanidatamab is under investigation for. Looking forward, Galbraith details their progress on their '5x5' strategy in which they have five new INDS planned before 2026, and expresses hopes to expand their therapeutic focus beyond oncology to autoimmune and inflammatory disease. Zymeworks also plans to inject further innovation into their pipeline by investing research into multifunctional engineered cytokines and dual checkpoint inhibitors.

Key prospective catalysts for the first half of 2024 include US and China regulatory submission for zanidatamab in second line BTC, commencement of Phase III confirmatory study for zanidatamab in first line BTC, a Phase II study for zanidatamab zovodotin in HER2 over-expressing NSCLC and an expected IND filing for the first of their '5x5' candidate. In the second half of 2024, key expected catalysts involve alignment with FDA on the confirmatory trial in first-line metastatic BTC, pivotal Phase III top-line data for zanidatamab in first-line GEA, Chinese regulatory decisions for zanidatamab in second line BTC, an IND filing for the second 5x5 candidate and nomination of the 5th product candidate in 5x5. The company also details some anticipated catalysts for 2025 including potential USA and China launch for zanidatamab in BTC and initial royalty revenue from partners Jazz and Beigene, an expected IND filing for two more 5x5 candidates.

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

Zymeworks also champions its development of a differentiated antibody-drug conjugate (ADC) portfolio, which has been designed to address areas of unmet therapeutic need. The five key players in this portfolio are ZW191, ZW220, ZW251, zanidatamab zovodotin, and XB002. ZW191 is a FRα-targeting ADC and is poised to have differentiated balance between drug-linker stability and payload potency compared to other Frα-TOPO1i ADCs on the market. An IND filing is expected for ZW191 in 2024. ZW220 is a NaPi2b targeting ADC with potential utility in multiple cancers. Galbraith details the agent to have a combination of a bystander active TOPO1i payload at a drug-antibody-ratio of approximately 4 with a potential best-in-class ADC antibody. An IND filing is expected for ZW220 in 2025. ZW251 is a glypican 3-targetting ADC with the potential to other an alternative mechanism for hepatocellular carcinoma cancer (HCC) patient. Zymeworks feels ZW251 has the potential to improve upon the current standard of care for HCC patients, and an IND submission is expected in 2025. The ADC zanidatamab zovodotin is underscored for having enhanced internalisation of payload, with immunogenic cell death, antitumor activity across solid tumors, including NSCLC, and a differentiated safety profile from other agents on the market. XB002 is a novel tissue factor targeting ADC which is currently under Phase I investigation in advanced solid tumors in the JEWEL-101 study.

The company also plans to drive the evolution of their multispecific antibody therapeutic

program in 2024. This involves zanidatamab, alongside bispecific and trispecific T-cell engagers. An IND filing for their bispecific T-cell engager ZW171 is also expected in 2024.

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

Micro Cap

Acumen Pharmaceuticals

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

O'Connell then went on to cover Acumen's founding science which targets a specific amyloid in the brain (amyloid beta oligomers) and how this science could potentially cover that unmet need previously discussed within the patient population. Acumen's leading asset currently is ACU193, a fully humanized IgG2 monoclonal antibody that selectively binds soluble Aß oligomers / ADDLs (amyloid beta derived diffusible ligands). ACU193 is currently in Phase 1 development with a Phase 2/3 trial expected to begin in the first half of 2024. O'Connell gave an update on the ACU193 program including announcing that the company conducted a meeting with the FDA in the fourth quarter of 2023 in which they received positive feedback on their timeline for progressing to the Phase 2/3 clinical study. O'Connell also announced that the company is currently designing a Phase 1 bioavailability study in ACU193 that they expect to initiate in mid-2024. O'Connell then discussed the most recent data from the Phase 1 INTERCEPT-AD study of ACU193 in which they saw rapid, significant plaque reduction which was comparable to the current market front-runners at similar timepoints. In this trial, ACU193 demonstrated a compelling safety profile with low incidence of ARIA-E and an absence of ARIA_E was observed in ApoE4 homozygotes. ACU193 provides a broad therapeutics index with convenient monthly dosing for patients.

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

1 bioavailability and Phase 2/3 ALTITUDE-AD clinical studies.

Adaptimmune

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

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

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

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

AngioDynamics

Jim Clemmer, president and CEO of AngioDynamics (ANGO), launched this year's JPM presentation with a summary of the company's ongoing efforts to transform its customer base

and product portfolio. The process began in 2019 when AngioDynamics sold its NAMIC fluid management portfolio to Medline Industries Inc. for $167.5 million. Last year, the company off-loaded its dialysis portfolio and BioSentry Tract Sealant System Biopsy product to Merit Medical for $100 million. The divestitures have allowed the company to eliminate all debt and fully support strategic investments in its medtech platform, which is now funded by operating cash flows from its stable medical device portfolio of ablation products and accessories, diagnostic catheters, guidewires, and kids, and radiation treatment stabilization balloons.

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

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

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

Atara Biotherapeutics

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

Off the success of Ebvallo, Atara will now focus on the development of ATA3219 and ATA3431, building on its proprietary allogeneic CAR T platform. Preclinical data has shown both therapies could target B-cell and autoimmune targets. ATA3219 is a CD19 CAR T therapy that Atara will develop for the treatment of NHL and Lupus. An IND has been cleared for NHL and a Phase I study is being developed and a planned IND for Lupus Nephritis is planned for the first quarter of 2024. For ATA3431 has advanced into IND-enabling studies with further plans to release more preclinical data in 2024.

BenevolentAI

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

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

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

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

With AI a hot topic of the year in 2023, extending into this year's JPM 2024 conference, it's no surprise that one of the first questions for BenevolentAI involved their use of generative AI. Nader responded by acknowledging that the industry is becoming more sophisticated, with AI being integrated directly into pharmaceutical companies, and that about 25% of BenevolentAI's technology group, about 25 people, are devoted to such upstream investments to try to keep up with this evolving trend. Indeed, it was released during JPM that Amgen will build models trained to analyze human datasets on NVIDIA's AI data center infrastructure platform, DGX SuperPOD, which is to be installed at Amgen's deCODE genetics' headquarters.

Carisma Therapeutics

Carisma Therapeutics' President and CEO Steve Kelly gave an overview of the company and pipeline developments at the J.P. Morgan Healthcare Conference. Carisma is a cell therapy company focused on macrophages who has pioneered the space. The company believes that

they are in position to take the power of the macrophage, an innate immune cell that has broad applicability and orchestrates an adaptive immune response, and apply it to a range of different diseases. Steve spoke about the unmet need in oncology and believes that macrophages are well suited to address the challenges of solid tumors. In addition to oncology, Carisma believes macrophages can be used to address unmet needs in other areas, such as liver fibrosis.

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

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

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

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

Carisma just recently went public in March of 2023 following a merger between the company and Sesen Bio. The company is sufficiently funded, possessing a cash runway into the first quarter of 2025, with 40.3M shares outstanding and $94.1M in cash, cash equivalents and marketable securities.

Emergent BioSolutions

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

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

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

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

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

Omega Therapeutics

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

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

Omega's first and only clinical asset is OTX-2002 which was designed to lower Myc expression by 90%. Lowered MYC protein primes "MYC-addicted" HCC cancer cells to undergo apoptosis.

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

Apart from OTX-2002, Omega expects to bring another Myc targeting asset to the clinic, OTX-2101 for NSCLC. IND-enabling work is ongoing for OTX-2101 which will include a novel lung-targeting LNP formulation with Mr Karande saying they are working on both systemic and inhalable formulations. Other preclinical programs mentioned at JPM24 were an asset targeting HNF4A for liver regeneration and CXCL 1-8 for inflammation/immunology.

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

Rigel Pharmaceuticals

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

In regard to Rigel's first half of the story, commercial execution, the company experienced record sales, achieving $104 million for entire year of 2023, a 36% growth versus 2022. Tavalisse alone generated $93.7 million and their more freshly launched product Rezlidhia generated $10.6 million in sales. Rodriguez described 2023 as a year of outstanding performance for both therapeutics and of significant growth that continues to accelerate forward in the coming year. They plan to do this through continued growth of their commercial execution strategy, exploration to expand their currently approved therapies to wider patient populations,

and strategic partnerships.

Outside of the well-performing sales achievements for Tavalisse, he gave an outline of the ITP market, noting that Tavalisse is now preferred on key commercial national formularies. Rigel's goal is to continue to move this approved therapy up to 2nd line patients, as that is where most patients are in their treatment, and Tavalisse has shown the best efficacy in that patient population. Doctors are primarily prescribing the treatment in 3rd and 4th line currently, but the company is optimistic that as doctors are gaining more knowledge and becoming more comfortable about Tavalisse, they will be more inclined to prescribe in 2nd line patients, as this has already begun happening. Overall, the company believes they are making tremendous progress with this product, giving doctors the confidence to prescribe with the positive efficacy levels seen in 3rd, 4th, and especially 2nd line patients. Post-pandemic, there has been consistent quarterly progress since the second quarter of 2021.

Regarding their approved in-licensed product from Forma, Rezlidhia, indicated for adult patients with R/R AML with susceptible IDH1 mutation as detected by an FDA-approved test, he gave a general overview on why they were attracted to this product in the first place. In Phase II, data showed CR+CRh rate of 35%, with a median duration of response of 25.9 months, and 92% of CR+CRh responders were CR, with a median duration of response of 28.1 months, and transfustion independence was achieved in all subgroups with well characterized safety profile with no cardiac events leading to discontinuation. Rigel's amibiton is for this product to be a key growth driver for their pipeline going forward. They have already set in motion a strategic alliance w MD Anderson to advance this drug in AML and other cancers such as higher-risk MDS advanced MPN, and a collaboration with CONNECT for a Phase II trial in glioma.

Going forward this year, Rigel is looking to in-license more successful products, with a focus on late-stage opportunities with either registrational data in hand or an NDA has already been filed or approved. They believe that their great infrastructure in marketing and sales representatives is something they can leverage and use as an asset for partnerships. They are aiming to in-license differentiated assets in hematology, oncology, or related indications. He briefly touched on R289 development in lower-Risk MDS and their RIPK1 inhibitor program partnership with Eli Lilly for CNS and immune diseases. Rodgriguez then closed the presentation with an overview of financial highlights from the fourth quarter of 2023 and sales metrics of their products.

Solid Biosciences

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

Featuring an optimized transgene and next generation capsid, Solid's lead asset SGT-003 is a gene therapy for Duchenne's muscular dystrophy that is based off its first-generation candidate SGT-001. SGT-003 is currently in a Phase I/II trial which is expected to start dosing this quarter and expects safety and microdystrophin expression data in Q3-Q4 2024. Cumbo went into

significant detail with respect to the Duchenne program, including the scientific rational behind its capsid and transgene, as well as the wealth of promising preclinical data that the company believes will give it a competitive edge.

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

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

Vigil Neuroscience

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

Time was taken to reflect on the milestones achieved in 2023 for the two most advanced assets, iluzanebart (VGL101) and VG-3927. This included the release of data from the first phase of a study for iluzanebart (VGL101), a monoclonal antibody candidate that works by activating the TREM2 receptor to treat colony stimulating factor 1 receptor (CSF1R)-related leukoencephalopathy, which includes ALSP. Amyotrophic Lateral Sclerosis-Parkinsonism Dementia Complex (ALSP) is a degenerative disease that progresses quickly and is often misdiagnosed. It primarily affects adults and typically leads to severe disability within 3-4 years. Unfortunately, the mortality rates are substantial, with most patients not surviving beyond 6-8 years. The current standard of care for this rare neurodegenerative disorder, which impacts over 25,000 patients in the US, EU, and UK, involves addressing symptoms (such as anti-epileptic medications for seizures) rather than directly treating the underlying disease pathology. The aptly named ILLUMINATE study was discussed in relation to identifying clinical measures of disease progression in ALSP with MRI and CSF biomarkers. In relation to this, the positive interim results from the Phase II IGNITE study for iluzanebart in ALSP were discussed with clear CNS target engagement with downstream pharmacological activity on crucial MRI and NfL

biomarkers suggesting stabilization or slowing progression of ALP. Furthermore, there were no safety or tolerability concerns during the trial, with no patient discontinuations due to treatment-related adverse events.

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

Vigil has confirmed its position to fund the current iluzanebart and VG-3927 clinical development programs, with a projected cash runway into H2 2025. Upcoming catalysts for the company in 2024 include reporting interim data for the ongoing Phase I clinical trial of VG-3927 in mid-2024 and Phase II results from its IGNITE trial evaluating iluzanebart in ALSP from all patients at 6 months at both 20 mg/kg and 40 mg/kg doses in Q3 of 2024.

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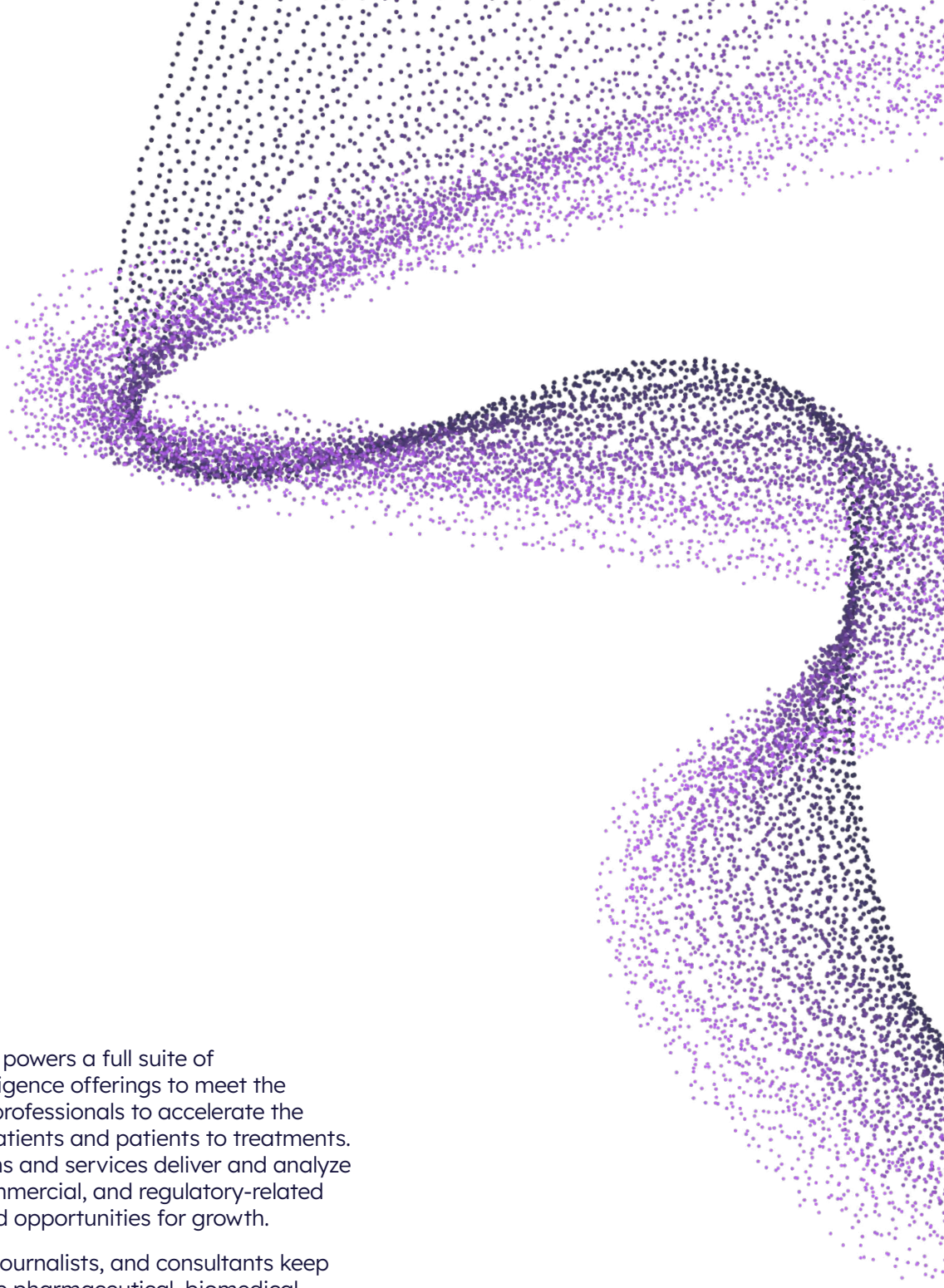

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