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2018 JP MORGAN HEALTHCARE CONFERENCE: REVIEW
Summary

The 36th annual JP Morgan Healthcare Conference was held in San Francisco, CA from January 8-11, 2018. A full list of events and catalysts that were announced or updated during the conference is included in this report. Below are our key points from the conference’s company presentations.

Key Points – Conference Review

Large/Mega Cap Companies

- The meeting was kicked off by Celgene (CELG), who followed their overnight announcement of acquiring Impact Biomedicines and its late-stage myelofibrosis asset fedratinib in a deal worth $1.1bn up-front and up to an additional $5.9bn in regulatory and sales-based milestone payments. While some question the value of the drug, which earlier had safety concerns but is now expected to be submitted mid-2018, the company hopes it will help build its leadership in myelofibrosis, addressing important unmet needs in patients intolerant or resistant to the current standard of care Jakafi. It could also be used in potential combinations with the company’s investigational luspatercept to address first-line myelofibrosis patients that co-present with anemia.

Celgene’s Q4 2017 revenue of $3.48bn was up 17% compared to the previous year, generally within expectations. Growth has been primarily driven by the continued uptake of key products Revlimid, Pomalyst and Otezla with Celgene reporting revenues in 2017 of $8.2bn (up 17.4% compared to 2016), $1.6bn (23.1%) and $1.3bn (25.7%), respectively. Revlimid in particular continued to gain uptake after earning approvals in 2017 in Europe and the US as a maintenance therapy for post-stem cell transplant multiple myeloma patients. FY 2018 guidance ($14.4-14.8bn), as well as longer term for 2020 ($19.0-20.0bn) were also within expectations. Last year, the company disappointed for more bullish investors, but it has good foundations and should continue to make progress, as long as Revlimid’s IP can be maintained in the near-term.

Celgene expects key pivotal readouts in 2018 for Abraxane as an adjuvant in pancreatic cancer, Revlimid in follicular lymphoma, luspatercept in beta-thalassemia and ringed sideroblast-positive myelodysplastic syndrome, and Pomalyst as a second-line therapy in multiple myeloma, as well as FDA regulatory decisions for Ozanimod in relapsing multiple sclerosis and a once-daily formulation of Otezla in psoriasis.

In lymphoma, management didn’t dwell on the recent failure of Revlimid in the Phase III RELEVANCE trial in follicular lymphoma, but instead focused on its collaboration with Juno for JCAR017 in relapsed/refractory DLBCL and its emerging efficacy and safety profile that after 6 months compares favorably to Gilead’s Yescarta and Novartis’s Kymriah. Also in CAR-T, Celgene did emphasis that it has accelerated its development program for bb2121 after its impressive Phase I data in heavily pre-treated relapsed/refractory multiple myeloma patients, and planned to initiate Phase III trials as a third-line therapy in 2018.
On tax reform, management said they get to maintain tax rate they have had historically, but get to access about 60% of cash that they could not previously. Finally, in the breakout session Celgene reiterated their commitment to continuing to utilize their partnership model and that pursuing additional partnerships continues to be their top priority for the coming year.

- **Incyte (INCY)** focused discussion around its main revenue driver, Jakafi, where it reiterated 2017 net product revenue guidance of $1,125-1,135mn and highlighted results in myelofibrosis and polycythemia vera, while also reviewing its potential in essential thrombocytopenia and acute/chronic graft versus host disease (GVHD). Incyte reiterated that top-line results for the pivotal Phase II REACH-1 trial in steroid-refractory GVHD are expected in the first half of 2018. These additional indications, along with robust demand and increased persistency in MPN, led to new 10-year (2027) guidance of $2.5-3bn.

The company also discussed new avenues of their JAK inhibition program, discussing novel combinations of Jakafi with PI3K-delta and PIM inhibitors, as well as the GRAVITAS-301 trial, evaluating JAK1 inhibitor itacitinib in first-line steroid-naïve treatment of acute GVHD, results for which are expected in 2019.

Incyte also reiterated their plans surrounding epacadostat in melanoma and baricitinib in rheumatoid arthritis (RA); Specifically, that progression-free survival results for ECHO-301, evaluating IDO1 inhibitor epacadostat in combination with Keytruda in melanoma, are expected in the first half of 2018, and that FDA action for a New Drug Application (NDA) for baricitinib in RA is expected in mid-2018.

Finally, Incyte announced other plans for 2018, including data release for FGFR1/2/3 inhibitor INCB54828 in cholangiocarcinoma, a potential NDA submission for capmatinib in MET-high non-small cell lung cancer, the initiation of monotherapy and combination therapy trials with licensed PD-1 inhibitor MGA012, and the emergence of three new clinical candidates (INCB81776, INCAGN2390, and INCAGN2385).

- In the context of investor concerns surrounding Gilead’s (GILD) ability to drive future growth as sales of its hepatitis C portfolio continue to decline, Gilead opened its presentation with a review of its achievements over the last five years, stressing steady non-HCV revenue growth and strong return of cash flow to shareholders. Management then focused on its HIV portfolio, which experienced strong growth in 2017 due to the launches of key tenofovir alafenamide (TAF)-based products, which have cannibalized the share of their TDF-based predecessors and recouped market share from Viiv Healthcare’s rival dolutegravir-based regimens. They touted the fact that as of September 2017, the majority (56%) of HIV patients in the US were receiving TAF-based regimens. Officials went on to outline their continued growth plan for the HIV franchise highlighting the anticipated approval and launch of bictegravir (B/F/TAF) in the first quarter of this year. We anticipate that this, as well as the continued development of novel therapeutic and preventative agents, will continue to drive significant growth in this indication, despite the fact that competition continues to intensify and widespread genericization of key products looms on the horizon.
After outlining the immediate growth prospects of the HIV business, the presentation focus shifted to Gilead’s longer-term aspirations, where management outlined 3 key growth drivers to diversify its revenue streams and compensate for continued declines in hepatitis C sales. The first was their NASH portfolio. The company communicated that enrollment in the pivotal STELLAR-3 and STELLAR-4 trials of selonsertib is progressing rapidly and that patient enrollment for both be complete in the coming months (with STELLAR-4 completing enrollment by the end of the month). Based on the 48-week treatment timeline it is likely the company will have data from these programs available early next year.

The second compound the company expects to be a growth driver is filgotinib, which the company is testing in a number of inflammatory indications. Management outlined the clinical trial program, noting that they anticipated the first Phase III trial readout from this program (FINCH-2 in rheumatoid arthritis) to occur in the second half of this year.

While we are optimistic regarding selonsertib’s potential to generate blockbuster sales in the underserved NASH population based on promising Phase II data showing rapid reduction in fibrosis scores, it is still unclear if filgotinib will display a differentiated enough clinical profile from Pfizer’s established JAK inhibitor Xeljanz (tofacitinib) and rival pipeline JAK inhibitors to achieve significant sales.

Finally, the company believes it is now a leader in the cell therapy space, following its 2017 acquisitions of Cell Design Labs and Kite Pharma, including the latter’s recently-approved CAR-T cell therapy, Yescarta (axicabtagene ciloleucel). Management provided more information on its clinical development efforts to support indication expansions for Yescarta into additional lymphoma indications, as well as the progression of novel CAR-T cell candidates for a range of leukemias. With the expertise and technology platforms of Cell Design Labs and Kite Pharma, the company believes it is well-placed to develop second-generation CAR-T cell therapies with simplified manufacturing processes and superior tolerability, addressing key drawbacks of first-generation entrants Yescarta and Kymriah (tisagenlecleucel; Novartis). When asked about potential mergers and acquisitions officials mentioned that they may see a need for cell therapy technologies targeting solid tumors.

- **Biogen’s (BIIB) presentation** emphasized the success of their launch of Spinraza for spinal muscular atrophy (SMA). Spinraza has now been approved and reimbursed across 12 countries. As such, the number of patients taking Spinraza grew by over 60% (1210 patients in Q2-17 vs 1980 patients in Q3-17). As the only FDA approved treatment for SMA, Biogen believes that there are potentially 20,000 SMA patients that could benefit from the product. The company further believes that competition for Spinraza will occur at the earliest in 2019 (notably AVSX-101). Biogen also unveiled plans to move a new gene therapy into the clinic for SMA by mid-year. Interestingly, Avexis (AVSX) announced the same day an expanded license with RegenexBio for all of its gene therapy vectors for SMA, which would complicate matters for Biogen if it sought a partnership with that company.

Another important 2018 catalyst is BAN2401’s Phase IIb trial readout in the second half of the year, one of Biogen’s most anticipated upcoming events. The drug is an anti-amyloid beta
protofibril selective antibody for Alzheimer’s disease. Initial Independent Data Monitoring Analysis indicated that BAN2401 did not cross a threshold for either success or futility at 12 months. Management also refined the timing of the initiation of the Phase III trial of Cirara, in-licensed from Remedy Pharmaceuticals last year, to mid-2018. The study will involve large hemispheric infarction.

Management noted it was also important to maximize the resilience of their core multiple sclerosis business, though this is not easy in the face of mounting competition. Their efforts include the recent in-licensing of BIIB098 from Alkermes and advancing opicinumab into Phase IIb. They acknowledged competitor Ocrevus (for which they receive up to 24% of royalties) is having some impact, but also that they are seeing a rebound in Tysabri and Tecfidera starts.

Finally, management also said that the company has the potential to leverage up to $37bn in cash if needed ($7bn on the balance sheet currently), resources the company could invest in business development. They said the focus remains on early stage deals, with an emphasis in neuroscience, where the company has built a focused pipeline.

- **Amgen’s (AMGN)** presentation provided no new surprises, and instead highlighted their successes in 2017 as a basis for a positive outlook for 2018. Several R&D efforts were discussed in Amgen’s six areas of therapeutic focus (osteoporosis, CV, oncology/hematology, neuroscience, inflammation, and biosimilars). While management did not provide any 2018 revenue guidance, the company expects double digit non-GAAP EPS growth this year, continuing on from an 11% growth through September 2017. Long term growth is expected to be driven by sales of Prolia, Repatha, Kyprolis, and biosimilars, increasing expansion into international markets, as well as the potential approvals of their innovative pipeline products such as the calcitonin gene-related peptide (CGRP) receptor antagonist, Aimovig (erenumab), Amgen’s first product in the neuroscience field expected to gain approval this year.

While there was nothing new reported in the oncology/hematology part of the presentation, Amgen stressed that the next 12-24 months would provide key data insights and “considerable visibility” to its BiTE franchise. Although Amgen’s Blincyto is currently the only approved bispecific molecule, the company also has 12 early phase BiTE programs in development for several hematological and solid tumors with multiple targets including BCMA, CD33, and EGFR. The company’s “differentiated approach” to immuno-oncology means that it will leverage its experience with Blincyto and Imlygic to pursue other potential indications and/or BiTEs, CAR-Ts, small molecules, bispecifics, or antibody drug conjugates to further develop its immuno-oncology programs.

Like many other biopharmaceutical companies presenting at the meeting, Amgen’s biggest benefit from tax reform appears to be the ability to use its cash held overseas – a stockpile of about $39bn. The legislation, management noted during the Q&A, puts Amgen on a level playing field with its competitors headquartered outside of the US. In terms of how they will use the extra money, management said their priority is to expand their portfolio, noting that the company is "very active" in business development. The company is not likely to execute a large M&A deal, because management reiterated their prior thinking about deal-making. Amgen is focused on transactions that add molecules within its six main therapeutic areas, accelerate the
company’s global build out, and improve its data skills. Management said that after allocating appropriate funds to execute deals, they will consider the most efficient way to deliver cash to investors through increased dividends or buybacks.

- **Vertex Pharmaceuticals (VRTX)** share price had doubled in 2017, and officials outlined their plan for continued growth in 2018 and beyond, though much of the presentation, while encouraging, was incremental. While they did not provide their usual revenue guidance, pending approval of tezacaftor/izacaftor in February, they expected growth drivers that will occur in 2018 to increase treated CF patients from 31,000 to 44,000, with the tezacaftor/izacaftor approval (residual function patients and those discontinuing Orkambi due to side effects – or those who never started it) and, for Orkambi, EU reimbursement and label expansions (a couple days later, for example, they announced expansion of the EU label to 6-11 year olds). There was not much new on plans for the existing triple combinations, with Phase II data expected in early 2018 for VX-152, VX-659, and VX-445 and hopes to start pivotal trials of two triple combinations in 2018 to eventually expand treatment to 68,000 CF patients. But in addition to solidifying their advantage in CF, where they will also be looking at complementary R&D for acquisitions, they would like to expand to other indications, planning in 2018 to start Phase I/II trials of gene editing CTX001 in beta-thalassemia and sickle cell disease and advance one other compound to clinical development.

- **Alnylam Pharmaceuticals (ALNY)** opened their presentation with a recap of their morning announcement of a restructuring deal with Sanofi, where Alnylam took back ex-US/EU rights to patisiran from Sanofi (SNY), which will now be the lead partner (instead of co-developer) for fitusiran in the US and EU (as well as ROW). Management said that Sanofi wanted a more global footprint, and Alnylam wanted to resolve a potentially complicated business arrangement with different stakes in ALN-TTRsc02 and patisiran. They indicated that launching globally is, of course, more complicated for them, but they are looking at learnings from other orphan drug companies. They will also not just be launching patisiran, but in terms of reputation, Alnylam itself, so they need to get things right.

Management spent the majority of the presentation highlighting the results of its APOLLO trial, the upcoming approval decision from both the FDA and EMA in 2018, and the initiation of a Phase III program for ALN-TTRsc02 in ATTR. They also highlighted how hATTR is generally underdiagnosed within the medical community, and said analyst models are too aggressive in the near term, but on the other hand, too conservative mid- and longer-term. Givosiran for porphyria is also expecting an interim analysis in mid-2018, and management said, along with pivotal reductions in ALA and safety, it will be important to show recurrence data from the Phase I/II study where patients have entered into an extension phase.

- **The biggest news from Regeneron Pharmaceuticals (REGN)** came from its press releases announcing an additional $1bn commitment from Regeneron and Sanofi toward the development of Regeneron’s only exciting late-stage investigational drug, cemiplimab (Regeneron/Sanofi), and the Regeneron Genetics Center (RGC), a human genetics consortium, currently involving Biogen, Alnylam, AstraZeneca, AbbVie, and Pfizer, to sequence 500,000 exomes, all with associated health data, by the end of 2019.
Regeneron’s presentation reemphasized the company’s focus and dependence on Dupixent (dupilumab; Regeneron/Sanofi) as a key driver of short- to long-term growth. Regeneron announced additional funding for Dupixent development, and re-outlined its plans for the drug’s expansion into severe pediatric atopic dermatitis (Phase II/III), uncontrolled, persistent asthma (supplemental Biologics License Application submitted with FDA decision expected H2 2018), nasal polyposis (Phase III), eosinophilic esophagitis (Phase II), chronic obstructive pulmonary disease (Phase I), and allergic diseases (preclinical). The company is of course also expecting the data from the Phase 3 cardiovascular OUTCOMES study of Praluent of in the first quarter of 2018. Other key update included the expanded investment for REGN3500 in atopic dermatitis, asthma and chronic obstructive pulmonary disease.

Management preannounced Eylea revenues for 2017 at $3.71bn, in line with expectations, but not that for other major products.

- **Alexion Pharmaceuticals’ (ALXN)** presentation held no real surprises, reinforcing its “complement is who we are” and switch from ultra-rare disease to rare disease refocused company strategy. Alexion is heavily relying on business development deals in 2018 to rebuild its clinical development pipeline, with no real clinical prospects apart from the second-generation Soliris (eculizumab) investigational antibody, ALXN1210.

Alexion believes that the double-digit volume and revenue growth seen for Soliris in paroxysmal nocturnal hemoglobinuria (PNH) and atypical hemolytic uremic syndrome (aHUS) in the first three quarters of 2017, 10 years after its first approval, will be sustained in the short- to medium-term, with “more opportunity ahead than already achieved.” According to Alexion, 60% of the addressable patient population for Soliris in PNH and aHUS remains untapped. While that may well be the case, the question is why, and can they really overcome it. The company also believes that aHUS presents a bigger opportunity for Soliris than PNH (currently sales are highest in PNH) in the short- to medium-term, and that the recent launch of Soliris in anti-acetylcholine receptor antibody-positive generalized myasthenia gravis will be its biggest yet.

Alexion has no real clinical pipeline prospects apart from ALXN1210, leaving the company, which is already under significant shareholder pressure, vulnerable to takeover if ALXN120 fails its pivotal Phase III trial in complement inhibitor treatment-naive PNH patients, expected to read out in Q2 2018. Even if ALXN1210 succeeds, Alexion is heavily relying on the second-generation Soliris investigational antibody to further expand the commercial market starting in H2 2019, through additional indications (e.g. immunoglobulin A nephropathy) and increased patient penetration in existing Soliris indications, rather than simply cannibalizing Soliris sales.

- **Pfizer (PFE)** briefly presented clinical timelines and an R&D overview for the company in 2018. Highlighting Pfizer’s H1 2018 milestones are planned submissions with US and EU regulatory bodies for both Xtandi in nmCRPC patients based on the PROSPER trial and PARP inhibitor talazoparib in BRCA-mutated breast cancer patients based on the EMBRACA trial. Action dates in H2 2018 are forthcoming for Xeljanz in ulcerative colitis in the US and EU markets, as well as the TKI lorlatinib in NSCLC in the US. Several early-phase data are expected over 2018, including Phase I results for the Bavencio, 4-1BB, and OX-40 triplet combination. In the Q&A session,
management reinforced Pfizer’s commitment to the combination approach as the future of immuno-oncology treatment and reiterated the company’s published stance on refocusing the business when asked about the closure of the neuroscience programs.

- **Roche Holding’s (RHHBY)** presentation began with a performance update, which highlighted the company’s sixth consecutive year of sales growth. Part of this sales growth was generated by $1.1bn in additional sales through the end of Q3 2017 stemming from new launches and approvals involving Alecensa (alectinib), Perjeta (pertuzumab), Tecentriq (atezolizumab), and Ocrevus (ocrelizumab). In addition, Roche currently has 18 breakthrough therapy designations, more than any other company.

The Company also briefly discussed plans to grow the existing business by improving standard of care in HER2-positive breast cancer and CD20-positive hematological malignancies. However, Tecentriq will clearly play an increasingly important role in Roche’s oncology portfolio.

Development efforts from 2018-2019 will look to expand populations that benefit from Tecentriq by combining the drug with currently available therapies. Beginning in 2020, Roche hopes to differentiate its cancer immunotherapy portfolio through combinations involving Tecentriq and new molecular entities. Non-small cell lung cancer (NSCLC) will be crucial to realizing this strategy, and Roche has planned a comprehensive program for the NSCLC space. From Q4 2017 to Q2 2018, the Company is also expecting readouts from Phase III trials in lung cancer, renal cancer, breast cancer, and colorectal cancer.

- The pharmaceuticals business unit of **Novartis (NVS)** enters 2018 with a priority of ensuring the success of Entresto (valsartan + sacubitril) and Cosentyx (secukinumab), and both drugs are expected to gain label expansions in 2020 for heart failure with preserved ejection fraction (HfPpEF) and non-radiographic axial spondyloarthritis (nr-axSpA), respectively. In addition, Aimovig (erenumab), the Company’s calcitonin gene-related peptide (CGRP)-targeted monoclonal antibody, is expected to gain regulatory approval from the US Food and Drug Administration (FDA) for migraine in 2018.

- **Much of Merck & Co’s (MRK) discussion centered on the company’s decision to promote overall survival (OS) as a co-primary endpoint in the Phase III KEYNOTE-189 trial, which investigates Keytruda plus chemotherapy in first-line non-squamous non-small cell lung cancer (NSCLC). Merck & Co strongly believes that KEYNOTE-189 will recapitulate KEYNOTE-021G, which demonstrated a progression free survival (PFS) advantage as well as a promising trend for OS. In addition, the Company noted that the independent data monitoring committee could in theory conduct interim analysis that reveal PFS advantage.**

Earlier in the day, the company released data from KEYNOTE054 in resected high-risk melanoma, where it showed a strong reduction in recurrence-free survival (HR 0.57). However, the study was against placebo, and in CheckMate-238, first-to-market competitor Opdivo demonstrated an RFS advantage over an active comparator, Yervoy. Merck noted that the trial would continue in order to evaluate other key points, including overall survival, and more detailed analysis to be presented at future conferences may reveal whether PD-L1 expression impacts patient outcomes.
Merck ended its presentation noting that while there are approximately 700 registered studies on ClinicalTrials.gov, with many Phase III trials expected to read out in 2018, the company has other pillars of growth that continue to innovate, to include animal health, neuroscience, and vaccines. While mergers and acquisitions may be considered, the focus of the company is on innovation rather than consolidation as a strategy.

- Much of AbbVie’s (ABBV) presentation was focused on its flagship product, Humira, and the company’s strategies to maintain leadership as competitors and biosimilars enter the immunology market. Although the company expects Humira to face biosimilar competition in the US in 2022, the drug is still expected to be its main cash generator through 2025 and beyond, with a predicted $21bn in sales globally in 2020.

Management highlighted that within the next year, AbbVie’s Immunology franchise would increase from a single product to a portfolio of products, creating a diversification of assets and further opportunities for growth. Two late-stage pipeline drugs were discussed in detail, the anti-IL-23 antibody, risankizumab, and the oral JAK1 inhibitor, upadacitinib, which the company forecasts will reach $5bn and $6.5bn, respectively, in peak sales by 2025. Management revealed in the Q&A session that two factors were behind the optimistic revenue predictions. While Humira will continue to be the “workhorse backbone” of the company, AbbVie expects that these pipeline assets will be used to treat patients who don’t respond well to Humira. Secondly, the company is aggressively advancing these assets in multiple immunology indications in addition to RA and PsA, which will increase their commercial potential. When asked about the apparent safety concerns associated with JAK inhibitors (FDA complete response letter for Eli Lilly’s baricitinib) in RA, AbbVie said they have not seen any evidence so far of increased safety risks with upadacitinib and that they were mitigating the risk by testing two doses of the drug.

AbbVie’s management re-iterated that their non-Humira business platform was “under-appreciated” and that it is expected to grow from $9.6bn in 2017 to more than $35bn in 2025 (CAGR = 17%), aided by a prediction that it will have more than twenty new launches by 2020. Short-term growth drivers included in this platform are the company’s hematological cancer assets, Venclexta and Imbruvica, which are being developed for further label expansions and oncology indications. The company believes that Imbruvica is on track to generate $7bn in revenues. Within this platform, management highlighted their acquisition of Stemcentrx and its lead asset, Rova-T, a DLL3-targeted antibody-drug conjugate comprised of a humanized anti-DLL3 monoclonal antibody conjugated to a DNA-damaging pyrrolobenzodiazepine (PBD) dimer toxin. The company expects to file for approval in third-line SCLC shortly after top-line data from the Phase II TRINITY study are announced in the 2nd quarter of this year.

In 2018, AbbVie expects an adjusted EPS of $6.37 to $6.57, representing a growth of 15% to 19%, with top-tier revenue growth and double digit EPS growth through 2020.

- Sanofi (SNY) acknowledged that their share price has languished as they have faced significant headwinds in diabetes, as well as the fact that major recent launches have been mixed, but outlined how they hope to return to growth. On the recent launches, management said they were pleased with results from Dupixent in atopic dermatitis (AD) and have seen encouraging
results from Kevzara in rheumatoid arthritis, though they recognize how competitive the latter indication is. Both drugs are partnered with Regeneron. But they admitted that expectations were not met for Praluent in dyslipidemia (whose reimbursement has been constrained by payers, though they hope CV outcomes study results will change that), Soliqua (a combination of their popular insulin Lantus and their relatively weak GLP-1 agonist Lyxumia), and Dengvaxia (a vaccine for Dengue fever).

Management noted that in the last few years, their R&D has gone a significant transformation with increased productivity and better success rates across phases, due to more rigorous prioritization and proprietary platforms. Their key R&D strategies now are to increasingly target biologics (rather than small molecules) given higher success rates, moving to multi-targeting agents (molecules that can address multiple disease mechanisms), and shifting to proprietary platforms rather than licensing.

Management pointed out that they have 9 potential submissions over the next 18 months. Among these are expanded indications for Dupixent, the CVOT results for Praluent, and two oncology assets (cemiplimab and isatuximab), which are to form the base for their rebuild in oncology, a strategy goal. While management acknowledged potential limitations with the two oncology drugs, they outlined reasons they could be more successful. Moreover, they highlighted all of the activity they expect in oncology in 2018, including 9 pivotal studies ongoing or planned, 4 potential proof-of-concept study readouts, 14 new proof-of-concept indications, and 7 preclinical programs entering the clinic.

They also highlighted 6 other drugs with potential pivotal trials to start in the next 12 months. A major goal is building leadership in specialty care, particularly with Dupixent targeting multiple indications. Management highlighted that their IL33 mAB could also be useful in combination in AD, as well as potentially asthma and COPD. As for other drugs in specialty care, they highlighted fitusiran for hemophilia (at the beginning of the conference, it was announced that Sanofi would become the lead partner for the drug in the US and EU in exchange for certain ex-US/EU rights to patisiran) and venglustat for various orphan indications.

In diabetes, where the company’s flagship Lantus product has faced increased competition and reimbursement pressures, management highlighted their novel peptide platform for diabetes, obesity, and NASH, including their GLP-1/glucagon agonist. However, we should note they will be up against Novo Nordisk, among others, who is also exploring a range of peptides against multiple targets. They also highlighted sotagliflozin, which may have SGLT-1 as well as SGLT-2 inhibition, though so far it is unclear whether that will confer much of a clinical advantage.

- **Bristol-Myers Squibb (BMY)** began their presentation by outlining the growth prospect of their two most important approved products. They started by outlining the strong uptake of their novel oral anticoagulant (NOAC), Eliquis, citing that the medication was the leading new-to-brand NOAC in 2017. The company estimates that only 56% of patients receive NOACs regimens and signaled that they expect Eliquis sales to continue to increase as NOACs continue to gain stronger uptake. Officials then outlined their growth plans for Opdivo. This plan features the advancement of the medication to the first line of therapy in non-small cell lung cancer (NSCLC), renal cell
carcinoma (RCC), hepatocellular carcinoma (HCC) and gastric cancer. In the breakout session
officials also alluded to the fact that they may investigate a triple immunotherapy combination
which would likely feature Opdivo, Yervoy, and BMS-986205.

After discussing the strategies surrounding the growth of their approved therapies, officials
shifted focus to their early pipeline. Here the presenter briefly mentioned their IDO inhibitor,
BMS-986205, prior to moving on to discuss their novel TYK-2 inhibitor. The company outlined
how they will look to potentially develop the medication in a variety of indications including,
inflammatory bowel disease (IBD), psoriasis, psoriatic arthritis, and lupus. This was the first true
unveiling of their plans for this oral agent, which they described as possessing biologic-like
efficacy. It is likely that initial trials will be conducted in psoriasis as the company has completed a
proof of concept in this indication. The company finished by outlining their various partnerships
throughout the industry and highlighting their continued commitment to work collaboratively
with their partner companies.

- **Allergan (AGN)** prefaced its presentation with its outlook for the year, cautioning of the impact
  of several loss of exclusivities. These include new or increased competition for Restasis, Estrace,
  Namenda XR, Delzicol, and Aczone, with accompanying cost-cutting initiatives. Total revenues will
  be in the range of $15.0–15.3bn, which will be a contraction from ~$15.5bn in 2017, with the
  final number being confirmed in February. 2018 looks to be a year of consolidation and returning
to the underlying core business, with key brands, constituting 80% of total revenues, growing at
mid-single digit rate. Longer-term, Allergan expects this business, anchored around its “$2.8bn
fortress Botox”, and successes in the pipeline, to contribute to 5% annualized growth over 2017–
22.

The pipeline catalysts that Allergan is looking toward in 2018 include new clinical data in migraine
and wet AMD. Specifically, Allergan is completing a Phase III trial of ubrogepant in acute migraine
and a Phase II trial of atogepant for chronic migraine. These are both oral CGRP antagonists,
following closely behind several anti-CGRP antibodies that may reach the market in 2018.
Abicipar will compete with other anti-VEGF antibodies such as Eylea and Lucentis in wet AMD
should its Phase III trial be positive. Additionally, the company is preparing for the FDA approval
of Esmya in uterine fibroids, and expects to advance several other programs, most notably
brazikumab in Crohn’s disease and ulcerative colitis.

- **The Astellas Pharma (ALPMY)** presentation began with previously announced M&A,
  licensing/collaborations, and divestiture activity to demonstrate their commitment to prioritizing
disease areas with unmet medical needs. New focus areas include muscle diseases and
ophthalmology.

Highlighted growth drivers for 2018 and beyond were Xtandi in prostate cancer and neurokinin-3
receptor antagonist fezolinetant in menopause-related vasomotor symptoms (MR-VMS). Astellas
valued the 2016 MR-VMS market potential at $1bn and expects that opportunity to increase in
subsequent years. Astellas believes synergy exits between physicians treating MR-VMS and those
treating patients in their existing over-active bladder franchise. PCPs, NP/PAs, and OB/GYNs
collectively account for 79% of OAB-treating physicians and 90% of VR-MRS-treating physicians.
The latter part of the presentation focused on their mitochondria research platform. The most advanced mitochondrial program stems from Astellas’ acquisition of mitobridge and consists of MA-0211 in Phase I for DMD.

- **Daiichi Sankyo (DSNKY)** management presented the company’s five-year business plan to 2020, to include growth plans for its current core businesses as well as its antibody-drug conjugate (ADC) technology and pipeline. Lixiana (edoxaban), marketed under the name Savaysa in the US, is currently approved for venous thromboembolism (VTE) and stroke prevention in atrial fibrillation (SPAF), and is expected to be a mainstay for the company. Daiichi Sankyo hopes to grow the brand to over $1bn in FY 2020, though we should note, it faces substantial competition. In addition, the company hopes to grow Injectafer (ferric carboxymaltose), broadly approved for iron deficiency anemia (IDA), to over $1.25bn in FY 2020.

Finally, management briefly discussed ongoing developments in ADC technology, the highlight of Daiichi Sankyo’s oncology unit. The company hopes to grow their oncology business to over 40bn JPY by FY 2020, and to over 300bn JPY by FY 2025. This growth in part will be driven by their ADC franchise. In particular, the company highlighted promising data of its pipeline ADC therapy DS-8201 in several early-phase trials with HER2-expressing cancers. The drug could be filed for approval in breast cancer and gastric cancer as early as 2019-2020. The company is also planning for trials in lung cancer, colorectal cancer, and bladder cancer, several of which involve immunotherapy combinations.

- **Merck KGaA (MKGAY)** provided a 2017 net sales guidance of €15.3–15.7bn. In comparison, reported sales in 2016 were €15.0bn, of which the healthcare segment accounted for 46% of revenues. Key drivers of future growth within healthcare highlighted by the company include the continued uptake of Mavenclad, which is approved for multiple sclerosis, and Bavencio, which is approved for Merkel cell carcinoma and urothelial carcinoma. Although the company showed that Bavencio’s patient share of the immuno-oncology segment of the US Merkel cell carcinoma market was 80% as of October 2017, such uptake is to be expected given that the drug is thus far the only immunotherapy approved for the indication. Nonetheless, Bavencio is expected to see a number of key catalysts in 2018, including Phase III trial readouts in second-line NSCLC and platinum resistant/refractory ovarian cancer.

**Mid Cap Companies**

- **Ionis Pharmaceuticals (IONS)** announced that the inotersen NDA for patients with hereditary TTR amyloidosis (hATTR) has been accepted for priority review by the FDA, with an anticipated PDUFA date of July 6, 2018. Despite the drug’s safety issues, management said they did not expect an FDA advisory committee meeting (FDA had told them this with the NDA acceptance, though plans could change). They still are in discussions to partner the drug, but did not provide a lot of details.

Management indicated they were at an inflection point, with commercial revenues starting to add substantially to R&D revenue in 2017 leading to a second year of positive operating income – trends they hope will continue with 2018 approvals of inotersen and volanesorsen, along with their burgeoning pipeline (though inotersen and volanesorsen have safety issues, and for
inotersen, potentially stiff competition from Alnylam’s patisiran). In addition to these approvals, they expect 6 Phase II readouts and 5 phase II initiations in 2018. The company also highlighted their next generation platforms and relative ease of developing new drugs (some of the clinical trial initiations involve Gen 2.5 LICA candidates, though we should note, they still need to demonstrate that the new generations meet their hopes of routinely avoiding significant safety issues).

- **Spark Therapeutics (ONCE)** announced a new gene therapy program in Pompe disease that they hope will outdo enzyme replacement therapy. The program uses a gene from Genethon with some advantages over the wild type gene. They also gave an overview of their hemophilia drugs and Luxturna, the first gene therapy approved for a genetic disorder, with some options for novel payment and distribution models that they think would be useful more broadly for such therapies (direct sales to payers or their specialty pharmacies, outcomes-based rebates, and options for payment installments, which they are currently discussing with CMS).

- **Sarepta Therapeutics (SRPT)** reported Exondys 51 Q4 2017 revenues of $57.3mn, for a full year of $154.6mn, which was on the high side of some expectations, and provided full 2018 guidance of $295-305mn, which is in line with overall expectations, but how one views it depends on estimates of European sales to start. The stock had initially been down earlier in day, perhaps reflecting nervousness about what would be reported, but subsequently recovered. Management said one driver was almost no patient dropouts, whereas they previously had expected more, and this factor is baked into 2018 guidance. At the breakout, there was a question about how the medical community viewed efficacy in the face of quite small increases in dystrophin (ie, uncertainty whether Exondys 51 even works after a controversial FDA approval), and management noted, in addition to sales and low dropouts, anecdotal evidence that physicians feel like they are getting results. Management also said 2018 was set to be a transformative year, with 8 key milestones/inflection points from Exondys 51, golodirsen, gene therapy (which should have data readouts), and their PPMO platform. They also noted that there may be a role for exon skipping therapy even if gene therapy works, as there is some evidence that exon skipping treatment may improve efficacy of gene therapy.

- **The Medicines Company (MDCO)** did not provide additional information about their pivotal Phase III ORION trial programs at the conference. Instead, the company did make repeated references to their upcoming investor day, January 23rd, and promised to share information regarding specific for enrollment and monitoring of the trials at their event. In the breakout session officials were quite reserved in their answers to the questions, though they did suggest that in the coming years they may be interested in investigating the potential for global partnerships to expand development in additionally geographic regions. Finally, while officials would not comment directly on the anticipated price of inclisiran, they did make it clear that the future price would be based on the clinical value of low-density lipoprotein cholesterol (LDL-C) reductions in shown in clinical trials, and that ultimately the cost will surely be less than $14,000 (the price of the marketed PCSK9 inhibitors, Repatha [AMGN] and Praluent [SNY/REGN]).

- **Agios Pharmaceuticals (AGIO)** announced their key milestones for 2018, many of which surround the continued development of IDH inhibitors Idhifa and ivosidenib. The company expects to
receive US approval for ivosidenib in relapsed/refractory AML in H2 2018 and also plans to file for regulatory approval in Europe for the same indication in Q4 2018. A Phase III trial testing Idhifa and ivosidenib in combination with the standard 7+3 regimen in first-line AML will initiate in Q4 2018. Interestingly, the trial will utilize event-free survival as its primary endpoint and will include a maintenance phase of treatment lasting up to two years. Details were also provided on the launch of Idhifa, with the company noting that the rate of IDH2 mutation testing in AML had reached about 50% as of October 2017, just two months following the US approval of the drug. Finally, Agios revealed two biological targets that will be the focus of early-phase programs: MAT2A (in MTAP-deleted tumors) and DHODH (in AML and DLBCL).

- **Amicus Therapeutics (FOLD)** announced they had over 310 patients on Galafold at the end of 2017 with full-year 2017 revenue for the drug at $36mn (first announced in a release yesterday). In 2018, they expect to double Galafold revenue to $75-85mn. They did not specify how much of that was from the US launch of Galafold, though that is likely not large, since if they receive a priority review (they will find out in February), approval is only expected in August. While the earnings were in line with expectations, 2018 guidance was slightly low, which may explain the stock's 6+% decline after the initial release. Additional key later stage priorities in 2018 are securing approval of Galafold in Japan and advancing ATB200/AT2221 towards regulatory submissions.

Management also presented what they said was new preclinical proof-of-concept data for a novel enzyme replacement therapy (ERT), ATB101, co-formulated with migalastat (Galafold) leading to greater substrate reduction in the heart and kidney in a Fabry knockout model than agalsidase beta (Fabrazyme). However, the amount of ERT in the Amicus combo was higher than for agalsidase beta, so the comparison may not have been a fair one, depending on enzyme activity (3mg/kg ATB101 + 10mg/kg migalastat resulted in significantly greater substrate reduction than 1mg/kg agalsidase beta). A poster presented last year appeared to have similar data, and if that was indeed from the same study, the co-formulation appeared to perform as well as 10mg/kg agalsidase beta. They are also hoping that the combination approach reduces immunogenicity of the ERT. While another key priority is to expand their preclinical pipeline, they only expect one or more new programs to enter the clinic in 2019.

Finally, in addition to reviewing their Pompe program and incremental data milestones for 2018, the Company highlighted an important manufacturing milestone announced yesterday, that the FDA had recently agreed on comparability between their clinical scale GMP production and commercial scale 1000L engineering batches, as well as agreement on the testing strategy for further showing comparability.

- **Much of the discussion from Nektar Therapeutics (NKTR)** surrounded their 2018 developmental program for NKTR-214 in several oncology indications. The PIVOT trial, evaluating NKTR-214 in combination with Opdivo in melanoma, non-small cell lung cancer (NSCLC), renal cell carcinoma, bladder cancer, and triple-negative breast cancer, demonstrated positive overall response rate and disease control results in the dose-escalation portion of the trial. This was seen in both PD-L1 negative and PD-L1 positive patients, with complete responses observed in every tumor type. Management provided a slight update since last year’s SITC presentation, noting that all
responses have now been confirmed. There were further reductions in target lesions in 2 patients with melanoma, 7 with RCC, and 1 with NSCLC. In addition, there were no grade 3 or higher immune-related side effects at the recommended Phase II dose and all patients with responses continue on therapy. Management also announced that initial data from the PIVOT expansion trial is expected to be presented at ASCO 2018 in June.

Initial data for an investigator-sponsored trial testing NKTR-214 in sarcoma will be released in the first half of 2018. Additionally, Nektar announced that data for the PROPEL trial, testing NKTR-214 with Tecentriq or Keytruda in bladder cancer and NSCLC, will be released in the second half of 2018. Finally, Nektar expects to initiate a Phase I trial evaluating NKTR-214 in combination with their small molecule toll-like receptor agonist NKTR-262 in solid tumors in early 2018, and to release data for this trial later in the year. NKTR-214 is a modified recombinant IL-2 that has biased signaling towards CD121, to avoid pitfalls of general IL-2R targeting, resulting in expansion of tumor-killing CD8+ T-cells, and an increase in PD-1 expression. These features have Nektar enthusiastic about NKTR-214’s potential as an important agent that works synergistically with other immunomodulators.

In non-oncology indications, Nektar discussed plans to submit a New Drug Application (NDA) for NKTR-181 in chronic lower back pain in Q2 2018, and to initiate a multiple dose ascending Phase I/II trial of NKTR-358 for lupus. Nektar plans to commercialize NKTR-181, an opioid whose slow rate of entry into the central nervous system gives it a lower potential for abuse, with a partner. Management noted that they have demonstrated a difference for the drug in euphoria compared to analgesia in preclinical studies, where NKTR-181 showed much less of an increase in dopamine release, which they believe causes craving. For NKTR-358, Nektar expects full data from a Phase I single ascending dose study to be presented in 2018, and to initiate a Phase I multiple dose ascending study in Q1 2018. NKTR-358 selectively expands regulatory T-cells, suppressing the immune system.

- **Alkermes (ALKS)** touted the long-term sales prospects of its two FDA-approved drugs, Vivitrol for alcohol and opioid dependence and Aristada for schizophrenia. The company highlighted their combined potential to generate over $2bn into the 2020s. While Alkermes emphasized the administrative flexibility of Aristada, with a dosing schedule up to every two months and a distinct oral NanoCrystal Dispersion formulation expected to be approved in June (for easier transition to the injected product), the drug is relatively late to market. In particular, three-monthly dosed Invega Trinza poses a significant threat to Aristada’s market share.

The company did not present any new data for its late-stage pipeline agents, instead outlining their development statuses. Alkermes anticipates ALKS 5461’s launch during 2018 for the treatment of major depressive disorder, though they expect the drug to face an FDA advisory committee. Its Phase III development program for ALKS 3831 is expected to complete with data in fall 2018, on-track for a filing in H1 2019. Approval and clinical utility will depend heavily on the drug’s metabolic side effect performance compared to olanzapine. Alkermes’s strategic partnership aims to leverage Biogen’s experience in the multiple sclerosis market to better position ALKS 8700, which is planned for submission in H2 2018. Alkermes looks to demonstrate the drug’s differentiated gastrointestinal tolerability compared to Tecfidera in H1 2018. However,
improved GI tolerability is unlikely to be sufficient for ALKS 8700 to supplant market-leader Tecfidera.

- **SAGE Therapeutics (SAGE)** presentation provided a thorough update on the Company’s development plans heading into 2018. With the anticipated NDA filing of Brexanolone for the treatment of postpartum depression (PPD) in the first half of 2018, Sage announced its aim of launching in the first half of 2019.

Important updates from SAGE-217 included results from Part C of the Phase IIa study in essential tremor where only a modest 16% decrease in tremor symptoms was seen. However, the company noted in a separate release that reductions in kinetic tremor measures of up to 21% at 40mg suggested that twice-daily dosing may be preferable for this indication, so they decided that further development in essential tremor will be moved from SAGE-217 to SAGE-324. At the conference, management said that SAGE-324 has less potential for sedation, making it more suitable for twice-daily dosing, and they plan to initiate a Phase I study for essential tremor and epileptiform disorders next year. Despite the results in essential tremor, the company still touted the benefits of SAGE-217 with plans in 2018 for expansion into bipolar depression, initiation of additional studies in Parkinson’s disease and major depressive disorder (MDD), as well as data expected from the Phase I study in insomnia in Q1 2018 and from the Phase II study in PPD in Q2 2018.

- Whether complement inhibitors can be effective in retinal diseases such as AMD has been a point of great interest. **Apellis Pharmaceuticals' (APLS)** talk focused on encouraging results seen with C3 blocking APL-2 in geographic atrophy (GA), an advanced form of AMD that can lead to blindness. There are approximately 1 million patients with GA in the US and no approved therapies. Apellis provided an update on a Phase II study, previously seen in August 2017, which showed that monthly injections with APL-2 led to a 29% reduction in lesion growth compared to sham injection (p=0.008). We now await 18-month data which will be available February 2018 and report changes in lesion size six months after the last injections which is expected to on guide whether dosing holidays are possible. A Phase III design similar to the Phase II trial has been finalized with the FDA and is expected to initiate in the 2H of 2018.

A subcutaneous formulation of APL-2 is being developed for paroxysmal nocturnal hemoglobinuria (PNH), auto-immune hemolytic anemia (AIHA) and complement-dependent nephropathies (CDN). Apellis shared early data from a Phase Ib/II trial in PNH and is expecting top line data in the 1H of 2018 with a Phase III program initiating in 2H of 2018. Phase I studies are in progress for AIHA and CDN with Phase II data expected in the 1H and 2H of 2018, respectively. Finally, a second product, APL-9, is currently in Phase I development for an undisclosed indication.

- **Bluebird Bio (BLUE)** announced for the first time that the company hopes to file for regulatory approval of three products within the next two years: LentiGlobin for transfusion-dependent β-thalassemia in the EU (2018), Lenti-D for cerebral adrenoleukodystrophy (2019), and bb2121 for multiple myeloma in the US and EU (2019). They will provide a registration strategy update for sickle cell in 2018.
• Acadia Pharmaceuticals (ACAD) provided an update on the clinical progress of Nuplazid, the first and only drug approved by the FDA for the treatment of hallucinations and delusions associated with Parkinson’s disease (PD) psychosis. Management highlighted Nuplazid’s ability to avoid off-target liabilities of typical and atypical antipsychotics. Acadia is branching Nuplazid into dementia-related psychosis, schizophrenia – negative symptoms and inadequate response, and major depressive disorder (MDD). All of these indications have high unmet need and there is currently no FDA-approved treatment for them.

Management reiterated that they had raised 2017 net sales guidance in November 2017 for Nuplazid from $105-$115M to $124-$127M. They noted there is substantial potential for the drug, since over 50% of PD patients may have psychosis but only 10-20% are actively aware or will speak to their physicians. The also said that new CMS regulatory guidelines for nursing homes recognized, for the first time, that PD psychosis is an enduring progressive condition, which will allow prescribers to continue treatment with Nuplazid as long as they are obtaining a benefit. However, they acknowledged that it can take time for a paradigm shifting drug to change physician perspectives.

The Company is anticipating top-line results from the Phase II CLARITY in MDD in the second half of 2018, Phase II ADVANCE in schizophrenia patients with predominant negative symptoms in 2019, and Phase III ENHANCE in schizophrenia patients with inadequate response to current antipsychotic treatment in 2019.

• Halozyme Therapeutics’ (HALO) presentation focused on their Phase III oncology asset, PEGPH20, in addition to 2017 financial performance and 2018 financial guidance. The Company lists 2017 FY net revenue estimated at $310-320mn, nearly double from their original guidance due to $172mn from new ENHANZE agreements during the year. Operating expenses remained flat. Year-end cash is estimated at $305-315mn. Net revenue for 2018 is projected at $115-125mn, the same as what they guided at the beginning of 2017, which does not include the potential for new ENHANZ deals. They expect continued high royalty growth of 25-30% driven by the Rituxan Hycela launch in the US, but that API orders will decline as partners have manufacturing transitions.

Regarding PEGPH20, the company expects to achieve the target number of progression-free survival (PFS) events in the HALO-301 study of PEGPH20 for the treatment of pancreatic cancer in the fourth quarter of 2018. This will trigger final data collection, cleaning, and interim analysis. Pending positive results from the -301 study, the Company plans to file BLA and MAA submissions to the U.S. Food and Drug Administration (FDA) and European Medicines Agency (EMA), respectively, in 2019.

• Clovis Oncology’s (CLVS) presentation emphasized Rubraca’s (its only clinical stage drug) forthcoming expansion into the maintenance treatment setting for platinum-sensitive ovarian cancer. Approval in this setting is of competitive importance for Clovis as its approximately 4x larger than Rubraca’s current indication in relapsed BRCAm+ patients where it managed only $38.5m in sales through Q3 2017 (an additional $9.4m was provided as free through a patient assistance program). Encouragingly, management estimates that market adoption for the
second-line maintenance setting is already at 80% despite it being a relatively novel setting. Management also made the claim that Rubraca has differentiated itself from competing PARP inhibitors by having the longest PFS benefit in the maintenance setting and for being the only PARP inhibitor to deepen patient responses by RECIST criteria.

The Rubraca sNDA for the platinum-sensitive maintenance setting has priority review with the FDA and has an action date in April 2018. The corresponding regulatory filing in the EU will be submitted either as a variation to the existing MAA application under review in BRCA-mutated relapse patients or as a new MAA depending on the opinion of the Scientific Advisory Group (SAG) and CHMP. Clovis expects approval in the EU to occur by year-end 2018 regardless of the SAG and CHMP decision. Management also announced plan to establish a new EU organization in 2018 with leadership already in place to support a potential launch of Rubraca.

Rubraca’s ongoing development in other indications with established BRCA prevalence were also discussed, including prostate, breast, and bladder cancer. Across indications, Clovis is confident that Rubraca will be efficacious outside of patients with DNA repair deficiencies. To that effect, the TRITON2 and TRITON3 prostate cancer trials, as well as the ATLAS study in bladder cancer will have stepwise analyses for BRCAm+ patients, HRD+ patients, and all-comers.

Finally, the collaboration between Clovis and Bristol-Myers Squibb has commenced with three trials underway investigating Rubraca in combination with Opdivo. Both companies share development costs, but retain global rights to their respective medicines. Clovis is sponsoring the Phase III ATHENA trial in ovarian cancer, which is set to initiate in H1 2018. BMS is sponsoring a Phase II trial in mCRPC patients that was initiated in Q4 2017 and a Phase III trial in triple-negative breast cancer that is set to start in H1 2018.

- **Juno Therapeutics’ (JUNO)** presentation highlighted the key upcoming events in development path forward for their lead assets JCAR017 (a chimeric antigen receptor T-cell [CAR-T] therapy) and JCARH125. Management reiterated plans to file a New Drug Application (NDA) for JCAR017 for the treatment of relapsed/refractory diffuse large B-cell lymphoma (DLBCL) in the second half of 2018, and mentioned that an approval could be seen within the year. They will also this year release results from pivotal cohorts of the TRANSCEND study to support the application. The company is emphasizing the ability to treat in the outpatient setting, due to the therapy’s good safety profile, which it sees as better than the competition. Juno says it will initially aim to have the product manufactured for most patients in less than 21 days at the time of Liso-cel’s launch but hopes to get this timeframe down over time to from three to six days.

Management also reviewed plans to treat more patients with JCAR017 through launching several trials in 2018 in additional diseases, including chronic and acute lymphocytic leukemia, as well as addressing earlier lines of therapy and combinations in DLBCL; Juno expects 2.5 times more patients entering clinical trials in 2018.

Juno also announced that Phase I data for their BCMA-directed CAR-T JCARH125 in relapsed/refractory multiple myeloma is expected this year, with a potential initiation of a pivotal trial for this indication. Juno plans to test JCARH125 in combination with a gamma secretase
inhibitor to augment antitumor activity and ultimately to move into earlier lines of therapy. Juno hasn’t set the pivotal trial design yet, but it will likely be similar to the plan for bluebird Bio’s bb2121 – an open label, single arm study of less than 100 heavily pretreated multiple myeloma patients. Salvage therapy is just the beginning though; bluebird is going earlier and so will Juno, management said.

Finally, Juno has multiple ongoing Phase I trials in solid tumors with novel CAR-T and T-cell receptor (TCR)-based products directed at a variety of novel targets; data for multiple trials is expected in 2018.

- **Horizon Pharma’s (HZNP)** share price has steadily grown since a drop in the second quarter of last year, though it has not reached previous highs. Management highlighted their success increasing the net sales of KRYSTEXXA for the treatment of gout since acquiring the drug from Crealta in 2016, with a 64% increase in average vials sold. They expect over 50% growth in net sales year over year in 2018, with projections for long-term peak annual sales of over $750 million. Moving into the nephrology space where a substantial portion of patients have gout is one significant growth driver. Yesterday, the company also announced an addition to its gout pipeline with licensing of HZN-003, a genetically engineered uricase derivative combined with site-specific PEGylation, from MedImmune/AstraZeneca.

Next on Horizon’s goals is the success of teprotumumab for the treatment of thyroid eye disease, which has no current FDA approved therapies and usually results in an average of 3-5 surgeries per eye with mixed results. Having Orphan, Fast-Track, Breakthrough Therapy Designations, and successful Phase II results (69% teprotumumab vs. 20% placebo achieved the primary endpoint of reduction of proptosis and CAS points at 24 weeks), the Phase III OPTIC study could potentially lead to a BLA submission in 2019, so long as positive data comes out during 2019.

- **Ultragenyx Pharmaceutical’s (RARE)** first drug, Mepsevii, was approved late last year, and the company highlighted multiple regulatory and clinical catalysts expected in 2018. Among these are important regulatory decisions, including an EU CHMP decision for Mepsevii in H1 and, for burosumab in X-Linked Hypophosphatemia, a US PDUFA in April and EC decision in H1. They reiterated that the FDA had told them that no advisory committee was planned for burosumab, which should mean that the drug will be approved without difficulty. They gave an overview of their commercial model and infrastructure designed for rare diseases including, as might be expected, patient diagnosis activities with a dedicated patient diagnosis liaison field team, a market access strategy, and in-house patient support. For burosumab, they are continuing to find patients pre-launch.

For UX007 (triheptanoin) in long-chain fatty acid oxidation disorders (LC-FAOD), the company announced just before the conference that in an end-of-Phase II meeting, the FDA had requested additional information for a possible early filing. They provided additional details at the conference, saying that the FDA wanted data showing that in the pretreatment period, patients were really receiving standard of care and that the change was the addition of UX007 and not dietary or other factors. They believe they can gather that data as patients were regularly being followed at expert centers, and the patients they enrolled were the 2-3 worse patients that the
experts could not manage well. Ultragenyx anticipates a decision on the potential NDA filing in mid-2018. The striking reduction in hypoglycemia events requiring hospitalization suggest there is a reasonably good chance the drug could be approved from the data Phase II. Nevertheless, the company is concurrently planning a Phase III randomized, controlled study, which is expected to initiate during the second half of 2018.

Also, just before the meeting, the company released preliminary data for DTX301 in ornithine transcarbamylase (OTC) deficiency. While only 1 of the 3 patients treated so far showed a dramatic response, management at the conference pointed out that Cohort 2 will have a dose more in the mid-range, with data expected in H2 2018. That patient and another did require corticosteroids for elevated liver function tests with the AAV gene therapy treatment, but that is a known side effect. Durability and long-term magnitude of the response remains to be seen as the patient with a dramatic improvement in the rate of ureagenesis started to have a decline in effect after 6 weeks.

Management also highlighted how they had numerous platforms to find the best solution for particular genetic diseases, including small molecules, traditional biologics, mRNA, and AAV gene therapy. A second AAV gene therapy, DTX401 is approaching IND submission and should have initial Phase I/II data in H2.

- **MorphoSys’ (MPSYF) presentation focused on MOR208, its late-stage, anti-CD19, Fc engineered antibody for B cell malignancies that it in-licensed from Xencor. MOR-208 received an FDA Breakthrough Therapy Designation in Oct 2017 based on preliminary data from the ongoing Phase II L-MIND trial evaluating MOR-208 combined with lenalidomide in R/R DLBCL. The latest update (n=44) was presented at ASH 2017 and showed an ORR of 52% (CR rate of 32%). Also impressive was the 11.3 month median PFS. The Company noted that historical data from a 2017 publication showed a PFS of 6.7 months for a combination of polatuzumab, rituximab and bendamustine.

In Q1 2018, MorphoSys will meet with the FDA to discuss accelerated approval of MOR208 based on data from 80 patients in the L-MIND trial. A Phase II/III study, B-MIND, is currently evaluating MOR208 with bendamustine in second line or later DLBCL. If MOR-208 receives accelerated approval, B-MIND will serve as a confirmatory trial. A Phase II trial (COSMOS) is evaluating MOR208 combined with idelalisib or venetoclax for R/R CLL with data expected mid-2019.

MorphoSys also reviewed two other proprietary antibodies: MOR202, an anti-CD38 antibody being developed for multiple myeloma (final Phase I/II data expected late 2018) and potentially solid tumor indications and MOR106, an anti-IL17C antibody being developed for atopic dermatitis (a Phase II trial is expected to initiate in Q2 2018). MOR202 combined with dex, len/dex or pom/dex showed efficacy comparable to other anti-CD38 antibodies in multiple myeloma but was more tolerable with only Grade II or lower infusion reactions which is expected to translate to higher infusion rates/shorter infusion times. MorphoSys has partnered with I-MAB Biopharma giving it exclusive development and commercialization rights to MOR202 for the greater Chinese market and further partnering decisions are ongoing for regions outside the US.
MorphoSys started as a royalty based, antibody discovery service and has 23 partnered product candidates in clinical development. One such partnered antibody, Tremfya, an IL-23 antibody developed by Janssen for psoriasis, was launched in 2017 and royalties from this antibody will be used to finance development of MorphoSys’ proprietary antibodies. With respect to other partnered antibodies, MorphoSys is expecting 12 Phase II and seven Phase III (all of them for guselkumab) readouts in 2018. MorphoSys is expecting 2017 revenues to be 63-66 million Euros, with proprietary R&D expenses of 96-100 million Euros for a loss of 66-71 million Euros. At the end of Q3 2017, MorphoSys had 319.5 million Euros in cash.

- **Prothena (PRTA)** did not have any major news, but will be an interesting company to watch in 2018, with topline results from the Phase IIb PRONTO study (in previously treated AL amyloidosis patients and persistent cardiac dysfunction) expected in Q2. The primary endpoint is cardiac best response as measured by NT-proBNP, and management reiterated the EMA has been more open than the FDA to consider an accelerated review with those results. In response to a question, management said there were no good natural history studies that could be used to see what to expect from untreated patients. They also have an enrolled Phase III study, VITAL, in treatment naïve patients expected to complete in H2 2019. The primary endpoint of VITAL is all-cause mortality/cardiac hospitalizations, but when asked if there could be some read through from the PRONTO results, management said not really, as mortality rates are higher for the treatment naïve.

In addition to an ongoing Phase II study of RG7935, which the company is partnered on with Roche, they plan to initiate a Phase I study of PRX004 in ATTR amyloidosis by mid-2018. Unlike the higher profile candidates from Alnylam and Ionis that suppress production, Prothena’s monoclonal antibody binds to misfolded TTR amyloid protein. Management believes that while suppressing production is quite helpful, a substantial amount of deposited protein will remain, so their approach can still be useful. They noted that in their Phase I/II study of NEOD001 in AL amyloidosis, a disease more aggressive than ATTR amyloidosis, an improvement in the NIS score of 30% was seen.

- **Valeant Pharmaceuticals (VRX)** had seen their share price plunge over 90% from a peak in 2015 to 2016 amidst various scandals, and management highlighted 2017-2018 as a turnaround period, with the potential for transformation of the company in 2018 and beyond. Management summarized the wide range of their successes from 2017 as well as key updates including various potential approvals for products during 2018. Throughout 2017, the company reduced its total debt by over $6.5 billion and their business from Bausch + Lomb and Salix (totalling 77% of the company) grew by 6%. The Company provided updates from the launches of Vyzulta in December 2017 and Siliq in July 2017. The Company reiterated the NDA acceptance of Duobrii for plaque psoriasis and announced the NDA acceptance by the FDA of Plenvu for bowel cleansing in preparation of colonoscopies with PDUFA dates set for June 18th and February 13th, 2018, respectively. With additional NDA submissions of Altreno (IDP-121) for acne and Jemdel (IDP-122) for psoriasis to the FDA, management highlighted the strength of their pipeline of potential approvals and launches in 2018.
• **Hanmi Pharmaceuticals (128940:KS)** provided a pipeline update on a number of compounds that are entering clinical research this year. The Company plans to initiate Phase I studies for HM15211 in non-alcoholic steatohepatitis (NASH), HM43239 for acute myelogenous leukemia (AML), HM15910 for short bowel syndrome (SBS), and HM14220 for type II diabetes mellitus in the first half of 2018. Hanmi also released data from the Phase II study of olmutinib in T790M+ NSCLC patients, showing an overall median PFS of 9.4 months. Based on the results of this study, a global Phase III trial is expected to start in the first half of 2018 to further assess the efficacy and safety in T790M+ NSCLC patients. Additionally, Hanmi reiterated that a Phase III readout for Rolontis in neutropenia is expected in the first quarter of this year, with a BLA submission anticipated in the fourth quarter of 2018.

• **Immunomedics (IMMU)** primarily discussed plans around their antibody-drug conjugate product sacituzumab govitecan, reiterating that an accelerated approval Biologics License Application for use of the drug in metastatic triple-negative breast cancer (mTNBC) will be filed in Q1 2018. A launch is expected by the end of this year if the BLA is approved (the company’s first), potentially making sacituzumab govitecan the first and only ADC in this area of high unmet need.

In partnership with Royalty Pharma, Immunomedics plans to continue enrollment in the Phase III ASCENT trial throughout 2018, and reviewed positive data from a single arm, open-label Phase I/II study in mTNBC. Phase II monotherapy studies in other solid tumors that express TROP-2 are potentially being planned in 2018. Additionally, a European filing is currently in discussion.

The company also discussed logistical details regarding the roll-out of sacituzumab govitecan, including a recent $250 million agreement with Royalty Pharma that will provide sufficient cash to fund operations until 2020, enabling Immunomedics to prepare the drug for commercialization in mTNBC, and to further development in urothelial cancer.

**Small Cap Companies**

• **Array BioPharma (ARRY)** primarily highlighted plans for encorafenib and binimetinib in 2018. The company restated that the combination of encorafenib and binimetinib has a PDUFA date of June 30, 2018 (with no FDA plans for an ODAC) for use in BRAF-mutant unresectable or metastatic melanoma, emphasizing that they would be in a position to commercialize prior to that date. Array was optimistic about the progress of the BEACON trial, where positive results for a triple combination of encorafenib, binimetinib and Erbitux in BRAF-positive colorectal cancer (CRC) were observed in the safety lead-in portion preceding the Phase III trial. Array announced that new results for BEACON will be released at ASCO-GI on January 20, 2018, with data on median PFS, tumor markers, updated overall response rate, duration of response, and safety. Array also announced that enrollment for the randomized portion of BEACON is expected to be competed in 2018.

Array also outlined their development strategy through collaborations investigating the safety and activity of binimetinib with immune checkpoint inhibitors. Trials with Bristol-Myers Squibb and Merck are active, evaluating binimetinib in combination with Opdivo +/- Yervoy in patients with RAS-mutant microsatellite stable (MSS) CRC and binimetinib with Keytruda in MSS CRC,
respectively. A collaborative trial with Pfizer evaluating binimetinib in combination with Bavencio +/- PARP inhibitor talazoparib in non-small cell lung cancer and pancreatic cancer is set to begin in Q3 2018."

- **Alder (ALDR)** presented positive first result from PROMISE 2, eptinezumab’s Phase III study in chronic migraine prevention (the full data was released in the morning before the presentation), building on PROMISE 1 data in episodic migraine. Officials highlighted the strength of the data compared to competitors in the class, as well as their case for why physicians and patients may prefer this IV option compared to subcutaneously given competitors. While their case was not definitive, and much will depend on physician perceptions of efficacy with use of the drugs, there could well be a significant portion of patients who respond particularly well and end up preferring the option. Importantly, the company also announced settlement of a European patent dispute with Teva, which resulted in a non-exclusive license to Teva’s anti-CGRP antibodies patent portfolio, as well as new $250mn ($100mn initially) preferred stock financing.

- **Ascendis Pharma (ASND)** presented interim Phase I data for TransCon PTH for hypothyroidism. This encouraging data for a different hormone/indication increases confidence in their technology. In eight patients, TransCon PTH (100 mcg injection) showed a half-life of approximately 60 hrs (compared to approximately 3 hours for Natpara injections) and a small increase in urinary Ca excretion despite elevated serum Ca. The full data set is expected in Q2 2018 and initiation of a Phase III trial in Q1 2019.

Ascendis continues to expect results from HEIGHT, a pivotal Phase III trial of TransCon Growth Hormone (GH) for pediatric GH deficiency in Q1 2019 with database lock for filing package in Q3 2019. An autoinjector that captures dose and injection time to a cloud-based central database is being developed and is expected to start use in the ENLIGHTEN safety extension trial.

Finally, top-line data from a Phase I study of TransCon CNP for achondroplasia is expected in Q4 2018.

- **Acceleron Pharma (XLRN)** announced earlier in the day preliminary results of a Phase II study of ACE-083 in facioscapulohumeral dystrophy (FSHD), with moderate increases in muscle volume relative to baseline (without any statistics given) and small numerical decreases in muscle fat. At the conference presentation, they noted this allows them to move to part 2 of the study, with bilateral injections, which should give better information on strength and function. Management also emphasized how they focused on areas of high unmet need and reviewed their pipeline, with Phase III results for luspatercept in myelodysplastic syndrome and beta-thalassemia expected in mid-2018. They also announced further Phase II results for ACE-083 in FSHD and Charcot-Marie-Tooth Disease in 2018.

- **Radius Health (RDUS)** provided a market snapshot and lifecycle management strategy for Tymlos and updated clinical strategies for its pipeline. According to Radius Health, Tymlos access in osteoporosis has risen to approximately 214mn covered lives; driven by an out of pocket benefit in Medicare Part D plans, patient experience support, and rising anabolic class volume. Commercial coverage is at 91% and Medicare/Medicaid/other at 39-40%. To protect Tymlos
sales, Radius Health has discussed a bridging study with the FDA specifically for male osteoporosis patients and is scheduled to meet with regulators to discuss a Tymlos patch formulation.

Radius Health also discussed plans for elacestrant in ER+ breast cancer following strong data from the SABCS late in 2017. Elacestrant’s demonstrated early efficacy implies potential across several lines of treatment, but Radius Health is targeting the third-line setting for the fastest potential approval. A phase 2, potentially pivotal, study of elacestrant in ER+ breast cancer is planned for early 2018. Finally, the presenters stressed that Radius Health continues to search for potential partnerships in an effort to develop combination strategies and expand geographic reach.

- **Ablynx (ABLX)** announced they had received an unsolicited acquisition proposal from Novo Nordisk for €28.00, but linked to two upcoming events, but they felt it fundamentally undervalued the company and rejected the offer. This was the second offer from Novo.

- **Dova Pharmaceutical’s (DOVA)** presentation primarily focused on the company’s upcoming PDUFA date of May 21st, 2018 for avatrombopag for the treatment of thrombocytopenia and the company’s plan for a June 2018 launch. Management spent a significant time distinguishing between avatrombopag and its current competition, lusutrombopag, which currently has initiated a rolling NDA. The key takeaway was the difference in dosing between avatrombopag and lusutrombopag. Avatrombopag is dosed for five days followed by a five-day waiting period with a scheduled procedure on days 10-13 if the patient’s platelet count is >50K/ul. Lusutrombopag, on the other hand, is dosed for five days with only a three-day waiting period. However, if the required platelet count is not met by day three, two subsequent rounds of dosing on days six and seven are potentially required before a scheduled procedure on days 9-14. Management believes that the solitary dosing regimen offered by avatrombopag presents a potential advantage over lusutrombopag specifically for patients with a slower uptake to the drug. Furthermore, the company announced plans for the expansion of avatrombopag to treat patients with thrombocytopenia undergoing invasive surgery requiring a platelet count of >100K/ul. A multi-center, open-label Phase III study is expected to initiate in the first quarter of 2018. This announcement, on top of Dova’s previous announcement last week of its planned Phase III trial in chronic immune thrombocytopenia, create a total addressable market of ~$2.5 Billion for avatrombopag.

- **Cellectis (CLLS)** began by outlining their differentiated allogeneic approach to CAR-T therapy which utilizes proprietary TALEN gene editing technology and donor cells. The company discussed the potential of the allogeneic approach, citing lower costs (at one point comparing the cost of allogeneic CAR-T to that of monoclonal antibodies), the elimination of manufacturing time, and the potential for repeat dosing as advantages the approach may provide over autologous competitors. Cellectis compared clinical results of the early phase trials of UCART19 with that of approved autologous CAR-T products, Kymriah (Novartis) and Yescarta (Gilead), citing that UCART19 has displayed similar efficacy and tolerability as compared to the autologous competitors.

Looking forward, Cellectis’ presentations set 4 key goals for the company in 2018. These goals include continuation of the ongoing clinical program of UCART19 in ALL, determination of the ideal dose of UCART123 in AML, submission of an IND for UCART22, and the completion of
manufacturing of UCART CS1 (which will support an IND of the product in early 2019). While these goals will progress the Cellectis pipeline, investors did seem a bit disappointed that the company did not include the potential initiation of pivotal trials in its presented goals. Cellectis concluded by guiding that their current cash position should be sufficient through 2020.

- **Amag Pharmaceuticals (AMAG)** is expecting generic competition starting June 2017 for its lead molecule, an intramuscular formulation of Makena, but is expecting to resume growing revenue with a multipronged strategy that includes (i) approval of a subcutaneous auto-injector formulation of Makena expected by Feb 14th 2018 (timing of this versus generics will impact how many patients they can convert); (ii) supplemental approval for Feraheme expanding the label to all adult patients with iron deficiency anemia (expected by Feb 2nd, 2018); (iii) submission of an NDA for bremelanotide for female sexual arousal disorder in Q1 2018, an FDA advisory committee meeting is expected for Q4 2018 followed by possible approval and commercial launch in early 2019; and finally, (iv) continued growth for Intrarosa by expanding the market to the 90% of women with vaginal atrophy who utilize over the counter treatments or who are not being treated.

With the loss of Makena exclusivity AMAG is forecasting 2018 revenues at $500-560mn (down from 2017 preliminary revenues of $607-614mn GAAP / $613-620mn non-GAAP), with projected 2018 non-GAAP earnings before interest, taxes, depreciation and amortization estimated at $100-130 million (reflecting a range of scenarios). With $330 million cash in hand, Amag continues to explore licensing/acquiring long-lived, durable products.

- **Lexicon Pharmaceuticals (LXRX)** highlighted their market opportunity by presenting data on their commercial product and pipeline drug candidates. Xermelo is for the treatment of carcinoid syndrome diarrhea and is Lexicon’s first and only commercially available drug. This is the only oral drug available for the indication and launched in March 2017 in the US and was approved in September 2017 in the EU. Lexicon highlighted significant market opportunity for Xermelo. Of the estimated 14,000 US patients, up to 80% of patients and 40 – 45% of physicians believe their carcinoid syndrome diarrhea is not well controlled on their current non-oral treatment. For the commercialization of Xermelo in the EU, Lexicon is collaborating with Ipsen.

If approved, sotagliflozin will be a the first SGLT1/SGLT2 inhibitor, whose mechanism functions in both the kidneys and the GI tract and functions independently of insulin. The drug is in Phase III, and regulatory filings in the US and EU are anticipated in 1H 2018. Lexicon retains the development responsibility and the lead commercialization role for sotagliflozin for type I diabetes in the US. Lexicon is also collaborating with Sanofi, who has development responsibility and worldwide commercialization rights (excluding Japan) for sotagliflozin for type II diabetes. While the company is placing high hopes for the drug and will certainly tout how it is differentiated from SGLT2 inhibitors, there are substantial questions whether it really has clinical benefits.

- **Myokardia (MYOK)** announced that data from cohort B of mavacamten’s PIONEER-HCM study, in patients with symptomatic obstructive hypertrophic cardiomyopathy (oHCM) will be presented at the American College of Cardiology (ACC) conference in March 2018. Positive results had been
seen last August for the first cohort in patients who discontinued beta-blockers. Cohort B is evaluating a lower dose and patients are not required to discontinue beta-blockers. The data will refine the company's physiologic understanding and help to set the starting dose for Phase III, which is planned to start in Q2 2018. The company also announced plans to start a Phase II study in non-obstructive HCM (MAVERICK-HCM) in Q1 2018.

For MYK-491, important milestones in 2018 include Phase I healthy volunteer data in Q1, initiation of Phase Ib in Q1, and reporting data from the Phase Ib study along with initiation of a Phase II study in H2.

- Just before the conference, Audentes Therapeutics (BOLD) presented preliminary interim data on a small number of X-Linked Myotubular Myopathy patients, with some striking signals of efficacy, albeit without sufficient controls and with safety issues to follow. At the conference, they reviewed the results, and announced they are expanding the current cohort with 3 additional patients, as this dose may be more efficacious than they had thought. They also reiterated additional interim data will be released in Q2 2018.

They will also have interim VALENS data in Q2 from their small Phase I/II study of AT342 gene therapy for Crigler-Najjar syndrome. On the latter, management said based on preclinical studies, only 5 - 8% of normal UGT1A1 expression was needed to maintain life-long low total bilirubin levels. The company also plans to bring two other AAV gene therapy candidates into the clinic in 2018, with plans to initiate Phase I/II studies in Q4 for AT307 in catecholaminergic polymorphic ventricular tachycardia (CPVT) and AT982 in Pompe disease, in hopes of improving upon enzyme replacement therapy. On the latter, management said that preclinically they have looked at both muscle and liver-directed AAV approaches.

- Rigel Pharmaceuticals (RIGL) shares have cycled between $2-4 over the past 5 years, and it is currently at the high end of that range. The company is finally at the brink of its first approval, with a PDUFA for Tavalisse (fostamatinib) in immune thrombocytopenic purpura (ITP) in April 2018. While one of the two small pivotal studies in the orphan indication was not statistically significant, there was a fairly large and consistent difference from placebo in response rate, and it is likely a good sign that, as officials noted in the presentation, the FDA told them last September that no advisory committee meeting was planned, though that could, of course, change. Management went over commercial plans, and said they were still identifying 30 potential sales reps, with offers contingent on approval of the drug. They are still looking to partner outside the US.

The first half of the year will be quite a pivotal time for the company, given other catalysts as well, with an update on a regulatory path forward for fostamatinib in autoimmune hemolytic anemia (AIHA) by April and cohort 2 data from the Phase II study of fostamatinib in IgA nephropathy in March-April. In AIHA, management gave an updated 47% response rate (higher than the 35% reported initially), and noted that patients are treated by the same doctors as ITP, so the company could use the same sales force. For IgA nephropathy, cohort 1 showed a modestly better reduction in proteinuria, though complicated by a higher baseline in the treatment group, but management said they expect that the higher dose used in cohort 2 would be the "sweet
They also have a preclinical IRAK1/4 inhibitor that they plan to start in Phase I this year. Psoriasis is likely to be the proof-of-concept indication, but they will pursue others, some of which they may partner.

Finally, management said that with $115.6mn in cash at the end of 2017, they could fund operations well into 2019, which they felt was a good position given the potential approval this year.

- **Global Blood Therapeutics (GBT)** primarily focused on the therapeutic potential of their pipeline drug, Voxelotor. The drug is in Phase III clinical trials (HOPE Study) and has recently received Breakthrough Therapy Designation by the FDA for sickle cell disease treatment. Results from the Phase II trials are promising, with 100% of sickle cell disease patients showing hematologic response to treatment with Voxelotor and no serious or severe adverse events reported. Top-line results from Part A of the Phase III HOPE study are anticipated in 1H 2018 and top-line results of Part B are expected in 1H 2019. Complete study results for the first dosage tested in the HOPE-KIDS 1 study of adolescents will be available in 1H 2018 with top-line results of a second dosage tested in HOPE-KIDS 1 study available in 2H 2018. The market opportunity for the drug is significant, with 100,000 patients in the US and 60,000 patients in the EU.

Although Global Blood Therapeutics closed their presentation by mentioning that pipeline expansion will occur through internal R&D efforts, no elaboration on products or timelines were provided.

- **Clementia Pharmaceuticals' (CMTA)** presentation focused on their lead/only drug candidate, palovarotene, which recently advanced to Phase III testing for the treatment of fibrodysplasia ossificans progressiva (FOP) via the MOVE study. The Company confirmed previous guidance that top-line data from the Phase III MOVE study are expected in early 2019, with updated results expected in late 2020. The Company also disclosed two new indications to be developed for palovarotene: dry eye disease and multiple osteochondromas (MO). A Phase II study (MO-Ped) will enroll 240 patients with symptomatic multiple osteochondromas and confirmed EXT1 or EXT2 mutations and is expected to start in 2018. Additionally, the Company is developing an eye drop formulation of palovarotene for the treatment of ocular conditions, with clinical studies in dry eye disease expected to begin in 2018.

- **Amarin (AMRN)** pre-announced 2017 Vascepa revenues of $177-180mn revenue, an increase of $48-51mn over 2016, and said they expected growth prior to the cardiovascular outcomes trial (CVOT) REDUCE-IT results to continue at a rate of about $50mn/year. They reiterated timing for the critical CVOT trial data before the end of Q3 2018, and will of course give new guidance thereafter. The study is 90% powered to show a 15% reduction in major adverse cardiovascular events (MACE), though questions about the benefits of triglyceride lowering on top of statin controlled LDL-C have been raised in recent years due to the failure of some high-profile trials. Management noted the latter has led to low usage of triglyceride lowering agents, so a positive trial could have a significant impact. They pointed to other data, including subset analysis of CVOTs with higher baseline triglycerides (as in REDUCE-IT), the JELIS trial, and genetic studies that are more supportive of a potential positive result. They also outlined their commercialization
plans if the study is positive and gains a label addition, though of course, the outcome is quite difficult to predict.

- **Esperion Therapeutics (ESPR)** began by outlining on a month by month basis when investors should anticipate key Phase III data from their bempedoic acid program. Officials highlighted the anticipated announcement of 52-week safety data from the CLEAR Harmony trial is expected in May 2018. Additionally, data from the Phase III studying investigating the fixed dose combination of bempedoic acid and generic ezetimibe are expected in August of this year. The data from Phase III trial program is expected to help support the NDA for bempedoic acid as a lipid lowering agent, which Esperion continues to plan to submit in the US in the first quarter of 2019.

When asked about their go to market strategy company officials made it clear that their intention is to secure a partner prior to the commercial launch. The presenters mentioned that they have been and will continue to actively search for partners. The officials noted that they had been in advanced discussions with a potential partner last year, however the parties were unable to agree on financial terms. Esperion guided that it is their intention to reopen these discussions as soon as they can come to the table with Phase III data in hand.

- **The Myovant Sciences (MYOV)** presentation centered around its lead clinical candidate relugolix in prostate cancer, uterine fibroids, and endometriosis, though major Phase III catalysts are not expected until 2019. In uterine fibroids and endometriosis, Myovant estimates a combined market opportunity of approximately 11m women in the US alone. The Phase III Spirit 1 and Spirit 2 trials investigating relugolix in women with endometriosis associated pain are scheduled to complete enrollment this year and have topline data in 2019. The replicate Liberty 1 and Liberty 2 trials for relugolix in women with uterine fibroids are similarly expected to enroll by 2018 and have data by 2019. Myovant plans to submit NDA filings for these indications by the end of 2019.

For prostate cancer, management noted relugolix is the only oral GNRH receptor antagonist in development, and unlike standard-of-care agonists, does not cause testosterone flares. While injectable agonist leuprolide is well established already, management feels they may be able to gain a foothold in the large market with "long hanging fruit," such as men just starting treatment (who do not want symptoms from testosterone flares), those who want a drug holiday (since the testosterone recovery is quick, which they showed in comparison to the injectable GNRH receptor antagonist Firmagon), and those who just prefer an oral drug. In addition to data showing a substantially higher percentage of patients with at least 50% reductions in PSA at week 5 from the Phase II C27002 trial, management showed new data that relugolix had a median time to PSA nadir of 16.1 and 12.3 weeks for the 80mg and 120mg daily oral doses, respectively, compared to 20.5 weeks for leuprolide injection every 12 weeks. Finally, they also noted data from other investigators showing that Firmagon prolonged the time to castration resistance compared to leuprolide, and when leuprolide patients were switched over to Firmagon, the failure curve flattened, which the investigators hypothesized to be due to more effective suppression of FSH, a possible growth factor for pancreatic cancer cells. They said to look out for their own data related to this. The Phase III HERO trial in advanced and recurrent prostate cancer patients is recruiting with topline data expected in 2019.
• **Sangamo Therapeutics (SGMO)** officials began by outlining their current pipeline. The company signaled that they anticipate preliminary data from their hemophilia A trial of SB-525, with which they are partnered with Pfizer (PFE), during the first half of 2018. However, the company seemed a bit cautious with respect to the outlook for these results, hedging their discussion of the data by mentioning that they were impressed by recently disclosed data from Spark Therapeutics and that they remain blinded to the data.

Looking ahead to 2018 and beyond Sangamo communicated that it is their intention to maintain the rights to their zinc finger nucleases technology in house in rare liver disease, while forming partnerships in other therapeutic areas. Two key areas the company mentioned as spaces they are currently seeking partners in were CNS and oncology. The company signaled that they may be close to securing a partner in oncology with the potential for an announcement of a partner in this field in early 2018. In CNS, a $12 Million upfront payment deal with Pfizer has already been made for Sangamo’s C9ORF72 gene target.

With products such as SB-318, SB-319 and SB-FIX all expecting top-line date in 2018, Sangamo will possess a mid-stage developed pipeline targeting MPS-I, MPS-II, and Hemophilia B.

Finally, the company closed by describing their recent and ongoing corporate move to San Francisco, where they announced they will be building out an internal manufacturing facility.

• **Editas Medicine (EDIT)** used JPM to announce its "EM22" (Editas Medicine 2022) five-year goals, which involved moving its first development drug into the clinic with EDIT-101 Leber Congenital Amaurosis Type 10 (LCA10) program. The company is expected to file an Investigational New Drug (IND) application with the FDA in mid-2018. Editas also announced two new programs for the treatment of recurrent ocular herpes simplex virus type 1 (HSV-1) infection and Usher syndrome type 2a. The HSV-1 program recently achieved positive preclinical results in rabbits while the Usher Syndrome program is being validated with Massachusetts Eye and Ear Hospital. With successful testing of its CRISPR/Cas9 and CRISPR/Cpf1 genome editing systems and its own internally developed drug approaching human trials, the next 5 years for Editas will be very eventful for the company.

• The presentation from **Karyopharm Therapeutics (KPTI)** primarily highlighted ongoing developments and future plans for selinexor in 2018 and 2019. In particular, the Phase IIb STORM is expected to read out in April 2018, and investigates the drug’s safety and potential efficacy in multiple myeloma patients who have failed three or more lines of therapy. If the data are positive, the Company may submit an NDA in the second-line of 2018 requesting an accelerated approval. Karyopharm Therapeutics estimates that this setting may have a $500m peak market opportunity. This will be followed by the Phase III BOSTON study in relapsed/refractory multiple myeloma patients who have had 1-3 prior lines of therapy. Top-line data for this study is expected in 2019. The Phase Ib/II STOMP trial is also expected to read out in late 2018, and investigates selinexor in combination with several backbone therapies in heavily pretreated relapsed/refractory multiple myeloma.
Selinexor is also currently under Phase IIb development for use in third-line DLBCL. The SADAL study will investigate Rituxan (rituximab) plus chemotherapy with or without selinexor, and top-line data are expected by the end of 2018. If data are positive, the Company may submit an NDA in 2019 requesting an accelerated approval.

Karyopharm Therapeutics finally noted that several trials of selinexor are currently ongoing in solid tumors as well. The Phase III SEAL study investigates single-agent selinexor in comparison with placebo in third-line advanced dedifferentiated liposarcoma, with top-line data expected by the end of 2019. In addition, a Phase III study of the drug as a maintenance therapy in patients with endometrial cancer after first- or second-line therapy is set to begin in the first-half of 2018.

• **Keryx Biopharmaceuticals (KERX)** did not release any major news, but discussed the Q4 2017 label expansion of their existing drug, Auryxia, and how this increases potential reach among the chronic kidney disease population. The label expansion allows Auryxia to be used for the treatment of iron deficiency anemia in adult patients with chronic kidney disease, not on dialysis, such that the drug can now be used at any of the five stages of chronic kidney disease. Presently, Keryx is focusing on reaching the patient population seeing nephrologists in Stages 3 and 4 of the disease, or approximately 2.2 million of the 30 million US patients, because the company can leverage existing relationships the sales force has created through the initial approved indication of Auryxia for hyperphosphatemia in dialysis patients.

Keryx envisions a growth opportunity of approximately 14 million US patients who are iron deficient and in the early stages of chronic kidney disease, when patients are not yet seeing a nephrologist. In 2018 the company aims to increase the number of patients treated with Auryxia by driving rapid awareness of the new indication and increasing prescriber breadth and depth.

**Novocure (NVCR)** highlighted the variety of indications for their lead, and only, drug in development, Optune. Their most recent developments have been in Japan, where they received a positive opinion on reimbursement from the Japanese Ministry of Health, Labour, and Welfare (MHLW) in December of 2017 for the treatment of newly diagnosed glioblastoma, which is their only US approved indication to date. Building on that recommendation, Novocure plans to start working on regulatory approval for the glioblastoma indication in China. They also reported that since the initial presentation of data from their EF-14 study of Optune for glioblastoma in November 2014, they have had 12 consecutive quarters of active patient growth and have treated over seven thousand patients to date globally, resulting in a 77% year-over-year revenue growth. They continue to advance Optune’s development in non-small cell lung cancer (NSCLC), pancreatic cancer, ovarian cancer, and mesothelioma, with the potential to move into many other cancer indications based on in-vitro evidence, such as melanoma, renal cell cancer, and cervical cancer.

• **TG Therapeutics (TGTX)**, which targets B-cell diseases, has several important catalysts in 2018, including updated multiple sclerosis (MS) Phase II data in Q1, top-line Phase III ORR results from the UNITY-CLL trial in Q2, and potential US regulatory filings for ublituximab/Imbruvica and ublituximab/umbralisib (U2) in CLL in Q3 and Q4, respectively.
In the UNITY-CLL trial, the company has estimated that the U2 combination will provide a 15% improvement of ORR over Gazyva + chlorambucil, leading to an ORR target range of 84-88% in treatment-naïve and RR patients combined. If all goes as planned, the company aims to file for an accelerated approval in front-line and RR CLL in Q4 2018, however management was uncertain of when it could provide a mature PFS endpoint for full approval, citing 2019 as a possible time point when an adequate number of PFS events would be reached. The company gave no indication what their strategy would be if the estimated endpoint targets were not met.

Also presented was an update to the Phase III GENUINE trial (ublituximab/Imbruvica), defending the company’s strategic position given recent impressive results (MURANO) from the Venclexta/Rituxan combination against the standard-of-care, bendamustine/Rituxan, in patients with RR CLL. Management compared the data side-by-side showing overlapping CR and ORR rates, but mentioned that it was perhaps an unreasonable comparison given that the GENUINE trial enrolled a patient population that was harder to treat than the MURANO trial (3 versus 1 prior lines of therapy). In reference to a potential filing for ublituximab/Imbruvica in Q3 2018, management believes (based on the FDA industry guidance) that the combination will be eligible for an expedited program because it avoids the cytokine release syndrome and tumor lysis syndrome effects of Venclexta, thereby fulfilling an unmet need.

In the Phase II/III UNITY-NHL trial cohorts, pathways for U2’s approval were outlined with the company targeting ORRs of 45-55%, 40-50%, and 40-50% in follicular lymphoma, marginal zone lymphoma, and diffuse large b-cell lymphoma (DLBCL), respectively. Top-line ORR data for all cohorts are expected in the first half of 2019 (DLBCL, follicular lymphoma, and marginal zone lymphoma). The company believes that U2 has a window of opportunity for RR DLBCL patients in the 2nd line setting who are ineligible for transplant, avoiding possible competition with Gilead’s Yescarta which was approved for the 3rd line treatment setting.

TG therapeutics released an announcement the same day that enrollment of Part 1 in its Phase II study for ublituximab in MS was complete, wherein the median B-cell depletion for all patients was 99%. Management shared in their presentation that this is their first launch into the autoimmune space and their Phase 3 programs, ULTIMATE I & II, are under SPA with enrollment expected for completion in Q1 2019.

As of 31 December 2017, TG Therapeutics had $85 million in cash.

- **Vifor Pharma (VIFN; Galenica)** discussed their growth since 1995 and highlighted three drivers for mid-term growth. The first strategic driver involves exploiting the market potential of Ferinject, their medical device that treats iron deficiency. Significant worldwide market opportunity still exists, and the company contends the product can reach blockbuster status by 2020 through geographic expansion, targeting therapeutic areas with high unmet need, and partnering with leading companies. Vifor believes that Veltassa, their drug for hyperkalemia, can also reach blockbuster status due to its broad label and large market opportunity, though details were lacking. Finally, Vifor discussed the 2010 partnership with Fresenius Medical Care to create Vifor Fresenius Medical Care Renal Pharma. The partnership is intended to build Vifor Pharma’s portfolio and enhance value.
• **NewLink Genetics (NLNK)** focused mainly on the initiation of the pivotal Phase III Indigo 301 trial, testing their indoleamine 2,3 dioxygenase (IDO) pathway inhibitor indoximod in combination with either Keytruda or Opdivo (programmed death-1 [PD-1] inhibitors) compared to Keytruda or Opdivo alone, and announced plans to enroll the majority of patients in this trial by the end of 2018. The company reviewed Phase II data outlining that indoximod + Keytruda shows similar response and progression-free survival results as Opdivo + Yervoy, and emphasized that their combination has a much more favorable side effect profile. New Phase II results from this trial are expected in 2018. NewLink looks to compete with Incyte Corporation, who will likely be first-to-market with an IDO/PD-1 combination in melanoma, through a broad set of initiatives designed to drive enrollment and expand awareness that were outlined in the presentation.

NewLink also discussed other IDO-centered development plans for 2018. Results from a Phase II study of indoximod in combination with gemcitabine and Abraxane in metastatic pancreatic cancer are expected in H1 2018. Additionally, Indigo 201, a randomized Phase II collaborative trial with AstraZeneca, comparing a combination of indoximod/durvalumab/gemcitabine/Abraxane with the combinations gemcitabine/nab-paclitaxel and durvalumumab/gemcitabine/Abraxane in metastatic pancreatic cancer, is expected to begin enrollment in H1 2018.

• **Seres Therapeutics (MCRB)**, a microbiome company, gave a brief overview of SER-109 which had disappointing results in a Phase II trial but nevertheless is now in a pivotal Phase III trial for recurrent C. difficile which initiated last June. Seres spent much of the presentation discussing updated results from a small Phase I trial of SER-287 for ulcerative colitis (UC). The Company noted a 40% remission rate (n=15) for daily SER-287 (with oral vancomycin pretreatment) compared to a 0% remission rate for placebo (n=11) and that this data compares well to historical data for other UC drugs both approved and in clinical studies. Of the 11 patients treated with SER-287 who achieved clinical remission, no patients experienced a disease flare in the 26 weeks following the end of treatment. This durability is likely due to SER-287 being a living drug. Seres identified 27 bacterial species that were correlated with remission including both SER-287 bacteria and others augmented by treatment. Seres expects to start the next UC trial mid-2018 and is evaluating opportunities in Crohn’s disease and UC combination therapy.

Importantly, while SER-109 and SER-287 are biologically sourced from fecal material, Seres is working on second-generation treatments (SER-262 and SER-301, respectively) that are prepared from bacteria grown in fermenters. A Phase Ib readout of SER-262 for primary C. difficile infection is expected early 2018. Finally, Seres discussed a collaboration with MD Anderson and Parker Institute on SER-401. A study to evaluate impact of checkpoint inhibitors combined with oral Ser-401 on clinical outcomes in patients with advanced metastatic melanoma is expected to start in 2018. The goal is to raise the response rate to checkpoint inhibitors by altering the gut microbiome. Seres finished Q3 2017 with $171.3 million in cash which should last through 2018.

• **MacroGenics (MGNX)** presented an overview of its technology platforms and highlighted 2018 milestones for several pipeline candidates. Later this month, the Phase III SOPHIA trial testing margetuximab – the company’s only late-phase drug but one which it touts as a possible best-in-class anti-HER2 monoclonal antibody – in HER2+ breast cancer will undergo a futility analysis.
Enrollment is expected to complete by year-end 2018. Phase I/II data for margetuximab in combination with Keytruda in gastric cancer will also be presented at ASCO GI next week.

Phase I data previously shown at the 2017 ASH conference was presented for flotetuzumab (CD123 x CD3 DART) in AML and MDS. Full expansion cohort data is expected in H2 2018. A combination study of flotetuzumab and MGA012 (anti-PD-1 MAb) will be initiated by the end of H1.

MacroGenics’ MGD013 (PD-1 x LAG-3 DART) is the first bispecific checkpoint molecule in clinic with Phase I dose escalation ongoing and expansion cohorts set to initiate in H2. An IND for MacroGenics’ PD-1 x CTLA-4 DART, MGD019, will be submitted in H2, as well.

MacroGenics also emphasized its B7-H3 franchise, consisting of enoblituzumab (Fc-optimized mAB), MGD009 (B7-H3 x CD3 DART), and MGC018 (B7-H3 ADC). In 2018, MacroGenics expects data from a Phase I dose expansion study of enoblituzumab and Keytruda in bladder cancer, NSCLC, SCCHN, and melanoma. MacroGenics also anticipates an update on a Phase I study of enoblituzumab in neoadjuvant prostate cancer patients prior to radical prostatectomy. MGD009 is scheduled to complete a Phase I dose escalation study and begin a dose expansion cohort in six tumor types including NSCLC, RCC, and Prostate. A similar Phase I dose escalation and expansion trial testing MGD009 and MGA012 (an Incyte collaboration) is expected to start in H1 2018. Finally, an IND for MGC018 is scheduled for H2 2018, as well.

- **AVEO Oncology (AVEO)** focused on the potential of Tivozanib, its VEGFR TKI, during its JPM presentation. Tivozanib has recently been approved for 1st line treatment of RCC in Europe based on the Phase III TIVO-1 study that showed superiority in PFS over sorafenib and low toxicity compared to other standard of care medicines. However, for approval in the US, the FDA requested an additional study to further validate the OS data from TIVO-1. Based on the data from the TIVO-3 study, AVEO will potentially seek approval for the first and third line of treatment in RCC patients. Top-line results have been pushed to the second quarter of 2018. If the data proves to be positive, AVEO will submit both the TIVO-1 and TIVO-3 results in the second half of 2018. AVEO also noted that Tivozanib is unique among TKIs because it may be able to be positively combined with PD-1s and is being tested with Nivolumab in TINIVO. The one thing to note is whether toxicity can be lessened with this combination, which has been the key trouble of combining TKIs with PD-1s.

- **Retrophin (RTRX)** elaborated on program updates and upcoming milestones that were announced earlier this week. The company provided insight on the developmental progress of fosmetpantotenate (RE-024) for the treatment of Pantothenate Kinase-associated Neurodegeneration (PKAN), a disease for which there are no available approved treatments in the United States or Europe. Retrophin is currently conducting the pivotal Phase III FORT study of RE-024 in PKAN patients and is expected to complete patient enrollment during the second half of 2018. Notably, under a Special Protocol Agreement (SPA) with the FDA, the primary endpoint for the FORT study is PKAN-ADL, a novel measure of PKAN-specific activities of daily living. Retrophin also discussed the regulatory progress of Sparsentan for focal segmental glomerulosclerosis (FSGS). Previously, in the randomized Phase II DUET study comparing multiple
doses of sparsentan and irbesartan in patients with FSGS, sparsentan was shown to reduce proteinuria levels by more than double with a comparable safety profile to that of irbesartan. Following an End of Phase II meeting with the FDA in early 2017, the company selected proteinuria, which is associated with stable estimated glomerular filtration rate (eGFR), as a surrogate endpoint for a Phase III clinical trial. Retrophin expects an interim analysis of the Phase III study to be the basis of an NDA filing for Subpart H accelerated approval of sparsentan. Both the Phase III protocol and additional analyses requested by FDA are expected to be submitted in the first quarter of 2018.

- **CymaBay (CBAY)** focused on their lead drug candidate, seladelpar, currently in Phase II development for primary biliary cholangitis (PBC) and Phase I development for non-alcoholic steatohepatitis (NASH). Pending upcoming FDA and EMA meetings to finalize a Phase III study design in the first half of 2018, the Company plans to initiate the study in PBC during the second half of this year. Additionally, CymaBay plans to release 26- and 52-week Phase II PBC data in the first and second half of 2018, respectively. In the NASH indication, seladelpar could advance into a Phase II study in the first half of this year.

- **Dynavax (DVAX)** provided updates on expected catalysts for 2018 and further reiterated information released earlier this week. With the recent launch of Heplisav-B for the prevention of hepatitis B virus in adults, the Company focused their presentation on development updates for SD-101 and DV281. In 2018, the company expects a multitude of data including updated results from the Phase I/II KEYNOTE-184 trial of SD-101 with pemrolizumab in melanoma in mid-2018, as well as top-line results from KEYNOTE-184 in head and neck cancer in the second half of 2018. Top-line results from the Phase Ib study of DV281 in non-small cell lung cancer are expected in late 2018. Dynavax also announced that it expects to advance SD-101 into Phase III studies in 2018 and DV281 into Phase II studies by 2019.

**Micro Cap Companies**

- **Axovant Sciences (AXON)** announced that it will discontinue the development of intepirdine, its 5-HT6 receptor antagonist, for the treatment of Lewy body dementia and Parkinson’s disease dementia. This comes on the heels of the drug’s failure in Alzheimer’s disease in September last year. Top-line results from its Phase IIb HEADWAY in Lewy body dementia (DLB), initially released yesterday, revealed that intepirdine did not meet its primary and secondary endpoints. In addition, the Phase II crossover pilot study of intepirdine in patients experiencing gait impairment (with Alzheimer’s disease, DLB, or Parkinson’s disease dementia) revealed that intepirdine worsened gait speed compared to placebo.

Axovant also announced mixed results for the Phase II study of nelotanserin for the treatment of Lewy body dementia in subjects experiencing visual hallucinations. Compared to placebo, nelotanserin did not result in a statistically significant change in UPDRS Part III score, a primary endpoint, in a prespecified ITT analysis, though there was a trend for improvement. However, nelotanserin demonstrated a statistically significant improvement in UPDRS Part III score in a prespecified DLB patient subset (p=0.041), albeit in only 19 subjects. Still, there were no trends in other measures, though Axovant plans to conduct further data analyses. The company will meet with the FDA about a larger confirmatory DLB motor study. In addition, they will be reviewing
their portfolio and looking for business development opportunities, and will provide an update by the end of Q1.

- **Otonomy (OTIC)** provided an updated look at their pipeline, recent developments in the Otividex program, and insight into their strategy moving forward with Otiprio. OTO-413, OTO-5XX, and OTO-6XX are three new products that Otonomy plans to progress this year. The most developed of the three is OTO-413, a brain-derived neurotrophic factor that is expected to enter Phase I/II clinical trials in the first half of 2019. Additional data from the Phase III AVERTS-2 trial of Otividex were highlighted. Otonomy announced that after a consultation with outside experts and a review of both AVERTS trials, the Company determined that the AVERTS-1 trial failed to be statistically significant compared to the placebo because of an expectation bias. Otonomy believes that after a meeting with the FDA, scheduled for this quarter, the Company will need to conduct an additional Phase III trial in order to file for approval. With a PDUFA data set for March 5, 2018, Otonomy has begun to divest Otiprio. The Company plans to use the proceeds from the divestment to further progress Otividex and the rest of their pipeline.

- **Syros (SYRS)** anticipates multiple top-line and updated data readouts this year, following their recently announced collaboration with Incyte. Syros received $20 million upfront from Incyte for the exclusive worldwide rights of seven validated targets. Incyte will be responsible for the development and commercialization of these targets, and Syros is eligible for upwards of $170 million in option exercise fees, target validation, and milestones per target. Syros intends to use the upfront funds to continue to advance their two lead compounds—SY-1365 and SY-1425 in current and new indications, and plans to release data from their ongoing trials in the second half 2018. Syros's ultimate goal for 2018 is to leverage their platform with the strategic collaboration with Incyte, leading into preparation for commercialization in 2019.

- **aTyr (LIFE)** opened its presentation with an overview of its pipeline and the tRNA synthetase technology platform. Management emphasized that aTyr has focused its internal resources on two key candidates - ATYR1923 and ORCA. aTyr anticipates topline data from its Phase I study of ATYR1923 in the second quarter of 2018, starting further clinical development of ATYR1923 based on that Phase I data and translational work, and releasing additional data on the ORCA program in 2018 in anticipation of starting an in-human clinical trial in 2019.

**Other Highlights from Pink Sheet/Scrip**

- Tax reform was a good news story for US-based drug makers, though companies seemed reticent to shine a spotlight on the legislation, maybe because it is viewed by some as a giveaway to corporations. Generally, investors were the ones that raised the topic in breakout sessions.

  Most US biopharmas appear poised for a windfall. In some cases, that will come in the form of a lower tax rate given that the legislation reduces the corporate income tax rate to 21% from 35% as of Jan. 1. In other instances, it will come from stockpiles of cash that has been held overseas and can now be repatriated at a rate of 15.5%. Drug makers said they expect to direct the savings toward share buybacks, dividends, business development and R&D.
Johnson & Johnson Chief Financial Officer Dominic Caruso said tax reform will be a positive for J&J and generally for the industry, but he insisted it will not change the company’s capital allocation strategy. “Our primary focus on allocating capital after investing in our business is to our dividend,” he said, followed by M&A and share repurchase.

Merck & Co. Inc. CEO Kenneth Frazier similarly commented that the legislation will not change the company’s capital allocation, but said the expectation is that the running tax rate will be lower. “We are going to continue to use our cash and to use our resources to do things we have been doing,” Frazier said. “With the kinds of deals we’ve been ideally targeting, we’ve had enough access to cash and we have enough power on our balance sheet to do those deals before tax reform.”

Celgene Corp. said it will maintain its historic tax rate but will be able to access 60% of its cash that has been held overseas.

Regeneron Pharmaceuticals Inc., on the other hand, has the opposite situation. The company expects to see its tax rate drop considerably in 2018 but will not repatriate any cash from overseas. “We have been in existence for 30 years, but we haven’t been overseas for a while, so we have no repatriated cash coming back,” CFO Robert Landry said. The company’s blockbuster eye drug Eylea is sold outside the US by Bayer AG. The company will benefit, however, from a tax rate that is expected to drop to 15%-19% from 26%-29% in 2017. “It’s certainly going to be for Regeneron a very positive story,” Landry said. CEO Len Schleifer said the resources will be invested mainly in R&D, as well as shoring up the company’s manufacturing infrastructure.

Pharmaceutical companies should take advantage of contacting a more flexible US FDA while they have it, experts urged during a panel at the 2018 Biotech Showcase on the impact of new leadership and new initiatives at the agency. On the first day of the Biotech Showcase, held concurrently with the J.P. Morgan meeting, presenters spoke highly of new FDA commissioner Scott Gottlieb in a number of different sessions.

During a Biotech Showcase panel, Nancy Bradish Myers, president and founder of Catalyst Healthcare Consulting, Inc., said that one of the biggest changes happening at the FDA now is that from the top there is an "encouragement to the reviewers and others to be a little bit more forward thinking about new technologies and using that flexibility in new and novel ways." The current leadership is encouraging everyone to be more creative in their approaches, as if a message has come from on high: "let's try it."

"I think it's a time for people to be more creative than they have been in the past," said Bradish Myers, an attorney and former special assistant and senior strategic advisor in FDA’s Office of the Commissioner. She warned that if companies don't try to be more creative, then FDA can't be creative in response.
"There’s a lot of 'hey come in and talk to us.' It may not be every reviewer or every division that really wants to exercise that flexibility to the max, but there are groups that are because they are focused on the patient and what the patient really needs," Bradish Myers said.

David Horowitz, partner at the Hogan Lovells law firm and formerly deputy general counsel at the US Department of Health and Human Services (HHS) and head of the office of compliance at FDA’s drug center, added that there is a lot of variability – some FDA officials are more eager to change and be more creative than others.

- Some of Johnson & Johnson (JNJ) Innovation LLC’s latest collaborations are aimed at helping predict risk for Alzheimer’s disease early and noninvasively, at a time when the field is still reeling from the latest string of failures. Johnson & Johnson Innovation is a large initiative of J&J focused on accelerating early research through a range of strategies, including incubators in major biotech hubs, like San Francisco and Boston.

On Jan. 8, Axovant Sciences Ltd. announced that its 5-HT6 receptor antagonist intepirdine failed in the Phase II HEADWAY study of dementia with Lewy’s bodies. This followed failure in 2017 of the Phase III MINDSET study of intepirdine in Alzheimer’s disease.

Merck & Co. Inc. terminated the Phase II/III EPOCH study of the BACE inhibitor verubecestat in mild-to-moderate Alzheimer’s disease in early 2017 due to lack of efficacy.

In an interview at the J.P. Morgan conference, J&J's Guy Seabrook, vice president in scientific innovation — neuroscience, said that the intepirdine failure was no surprise – performance hadn’t been that hot in Phase II – but Merck's verubecestat had looked very promising in terms of reduction in terms of reducing amyloid levels and failure was a blow.

J&J and other sponsors are not giving up on targeting amyloid, rather they are moving toward disease prevention, before symptoms have even developed.

Among a dozen new collaborations announced on Jan. 4, just before the J.P. Morgan meeting kicked off, J&J Innovation unveiled a deal with Toronto-based WinterLight Labs, Inc., which has developed artificial intelligence technology that it says can help non-invasively predict dementia and neurodegenerative diseases long before clinical symptoms are apparent. Early changes in the brain may be detected with positron emission tomography (PET) imaging scans, but this is expensive and Seabrook noted that there are not enough PET centers in the US to allow screening of everybody who is at risk, so there is a need for alternatives, such as WinterLight’s artificial intelligence algorithms, which enable testing of the ability to remember faces, names and events.

In another newly announced deal, J&J Innovation said it will be working with the Northern California Institute for Research and Education and the San Francisco Veterans Affairs Medical Center to explore the use of speech recognition technology and neuropsychological assessments for monitoring brain health in elderly people.

"I believe those types of technologies in conjunction with availability of PET will be really quite critical for us to be able identify who is at risk, so if we come up with drugs that are effective at
reducing the conversion to Alzheimer’s disease we can intervene in an appropriate way, “Seabrook said.

J&J will also be working with the University of Pennsylvania’s gene therapy program to use Adeno-associated virus vectors for delivering antibodies aimed at Alzheimer’s disease.

• While the J.P. Morgan Healthcare Conference did not have many major deal announcements, there was a flurry of announcements around discovery and development capabilities during the conference, and shortly thereafter. These include:

  o Strongbridge Biopharma PLC obtained US and Canadian rights to Macrilen (macimorelin) from AEterna Zentaris Inc. on Jan. 17, less than a month after the US FDA granted approval for the growth hormone secretagogue receptor agonist as the first approved drug therapy for adult growth hormone deficiency (AGHD). The deal represents a value turnaround for AEterna Zentaris, which saw its share price plummet 56% in November 2014 after FDA rejected macimorelin, because the pivotal trial did not meet the primary objective agreed to under a special protocol assessment. Ultimately, FDA required a new confirmatory trial in order to approve macimorelin.

  o Syndax Pharmaceuticals Inc. and Roche/Genentech Inc. are expanding their research collaboration on the combination of Syndax’s HDAC inhibitor entinostat and Roche’s PD-L1 inhibitor, Tecentriq (atezolizumab). Under the agreement announced Jan. 10, Genentech will be responsible for evaluating entinostat plus atezolizumab, as second-line therapy for patients with hormone receptor-positive (HR+), HER2-negative (HER2-) breast cancer in an open-label Phase Ib/II study. As such, the combination will become part of Roche’s adaptive clinical trial program for cancer immunotherapy combinations, MORPHEUS.

  o Context Therapeutics acquired worldwide rights Jan. 16 to Apristor (onapristone extended-release) in exchange for a one-time payment to Arno Therapeutics Inc, which is being liquidated. Context CEO Martin Lehr said his company is excited to take over the program, which becomes its first clinical candidate and could offer a novel mechanism of action for metastatic breast cancer. In theory, onapristone works by blocking progesterone receptor monomers from dimerizing, in turn preventing activation of pro-cancer survival gene transcription programs. Data indicate that as many as 70% of metastatic breast cancers are progesterone receptor-positive, the privately held biotech says.

  o Dong-A ST Co. Ltd. said on Jan. 11 on the sidelines of the J.P. Morgan Healthcare Conference in San Francisco that it has agreed with AstraZeneca to jointly research immuno-oncology drug candidates, in its effort to beef up open innovation in early stage R&D. Dong-A Pharmaceuticals and AstraZeneca will jointly explore lead compounds and drug candidates from three of AstraZeneca’s immuno-oncology drug targets. The two will jointly own all the intellectual property and patents stemming from the joint research. Further details of the deal were not disclosed. The latest agreement also marks Dong-A’s continued efforts to advance in immuno-oncology drug development.
Ligand Pharmaceuticals Inc. unveiled a worldwide OmniAb platform licensing agreement with India's Glenmark Pharmaceuticals Ltd. on Jan. 11, giving the latter access to a suite of platform technologies including OmniChicken, OmniRat, OmniMouse and OmniFlic to discover fully human mono- and multispecific antibodies. San Diego-based Ligand can earn annual platform access payments as well as development and regulatory milestone payments and tiered royalties for each product incorporating an OmniAb antibody. Glenmark will then cover all costs related to the programs. Specific financial terms were not disclosed.

Adimab LLC has agreed to use its proprietary yeast-based discovery and optimization platform to identify fully human antibodies for use against multiple targets chosen by Boehringer Ingelheim GMBH under an agreement announced Jan. 10. Adimab claims the platform launched in 2007 provides unprecedented speed from antigen to purified, full-length human immunoglobulin G antibodies (functional assays within weeks), superior clonal and epitopic diversity, and improved quality and expression. Adimab will grant BI the right to evaluate antibody panels from the collaboration for use in therapeutic products in exchange for an undisclosed upfront payment, research fees and delivery milestones. Further, BI gets an option to exclusively license any antibodies generated from the partnership and will then be responsible for paying Adimab license fees, clinical milestones and sales-based royalties. To date, Adimab has partnered with more than 50 pharma and biotech companies.

SK Biopharmaceuticals Co. Ltd. announced Jan. 8 that it has set up a joint venture with Glycyx PharmaVentures Ltd. to develop the former's constipation candidate relenopride in a rare neurological disease indication. SK Biopharmaceuticals, a wholly-owned novel drug development subsidiary of South Korea's SK Chemicals Co. Ltd., so far has completed a Phase II clinical study of relenopride in constipation and is reviewing plans to progress further development. The joint venture will be 51% owned by Glycyx with the remaining 49% held by SK. It will seek third-party investment and gear up for global clinical trials of relenopride this year. SK Biopharmaceuticals will provide relenopride to the JV, while Glycyx will proceed with the drug development. SK Biopharmaceuticals declined to reveal which rare neurological diseases the two companies will target.

It was a busy week for Harbour BioMed, which announced two licensing deals on Jan. 8 with ImmunoChina Pharmaceuticals and BeiGene (Beijing) Co. Ltd. to provide its patented H2L2 transgenic mouse platform for developing immuno-oncology therapies. Without disclosing financial details, Harbour has granted ImmunoChina and BeiGene rights to use Harbour Mice to develop fully human monoclonal antibodies over a multi-year period.

BeiGene also had a busy Jan. 8 as Mirati Therapeutics Inc. granted the Chinese firm exclusive rights to develop, manufacture and sell the tyrosine kinase inhibitor sitravatinib in Asia (excluding Japan), Australia and New Zealand. BeiGene pays $10m up front and up to $123m in development, regulatory and sales milestones, plus royalties. Sitravatinib inhibits multiple families of tyrosine kinase inhibitors including TAM (TYRO3, Axl, MER),
split (VEGRF2, KIT) and RET. As clinical trials have exhibited positive results studying the therapy as both a single agent for non-small lung cancer and other tumors (Phase I) and in combination with other candidates for NSCLC (Phase II), BeiGene intends to conduct studies of sitravatinib in combination with its PD-1 inhibitor tislelizumab (BGBA317). Tislelizumab is in Phase III for NSCLC and in a number of other trials for additional solid tumors as well as blood cancers.

- Resverlogix Corp. licensed Medison Pharma Ltd. exclusive rights Jan. 8 to market and distribute apabetalone (RVX208) in Israel and the Palestine Authority. Medison will fund all regulatory, sales and marketing activities in the licensed territory. The deal includes ascending double-digit sales royalties, potentially reaching over $100m for Resverlogix.
About the Author

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