ALXN - 1Q21 Earnings Public Q&A

Financial Results

What drove top line strength in the first quarter?

- First quarter revenues (+13% YoY) benefited from continued volume strength across the business; particularly from continued growth in the neurology, PNH, and aHUS businesses, and a strong quarter in the metabolic franchise.
- ANDEXXA sales contributed $29M of revenues in Q1 2021 (~200 bps contribution to YoY growth).

What drove revenue growth in the Asia Pacific (YoY) and Rest of World (QoQ) regions in 1Q?

- APAC growth YoY was primarily driven by increased volume in the Japan neurology business and continued ULTOMIRIS conversion, as well as beneficial order timing in Korea.
- In ROW, QoQ revenue increases were driven by tender and distributor market ordering patterns.

Why were US and Europe revenues down QoQ versus 4Q20?

- The decrease in US revenues QoQ was driven by reduced demand in ANDEXXA and lower sales of SOLIRIS for use in competitor clinical trials.
- European revenues decreased QoQ primarily due to de-stocking in the UK post Brexit inventory build and in Germany post VAT tax increase related inventory build.

1Q Non-GAAP operating margin declined slightly versus prior year, what drove this decline?

- As we have shared in the past, we strive to maintain best-in-class non-GAAP operating margins. First quarter 2021 non-GAAP operating margins remained highly competitive at 59%.[(1)]
- First quarter non-GAAP operating margin decreased year-over-year due to an increase in operating expenses, primarily in R&D to support the growing late-stage development pipeline and those related to the Portola acquisition. [(1)]

What drove the growth seen in Q1 non-GAAP EPS versus prior year?

- 1Q21 non-GAAP EPS growth versus the prior year was driven by top line performance; partially offset by increased operating expenses to support the growing business (primarily in R&D to support the growing late-stage development pipeline and those related to the Portola acquisition). The Q1 non-GAAP effective tax rate and diluted shares outstanding were relatively flat year-over-year. [(1)]

Why is Alexion not providing financial guidance for 2021?

- Given the recently announced agreement to be acquired by AstraZeneca, and with the deal anticipated to close in 3Q 2021, Alexion will not be providing financial guidance for the year.
- We continue to see strong momentum in the business, and we remain on track for our stand-alone long-term ambitions including:
    - $9-10B in global revenues by year-end 2025 (standalone Alexion)
    - 10 launches by 2023
    - Expanding our U.S. Neurology patient volume 4x by year-end 2025 (to ~7,500 total patients)

Why are Caelum Biosciences financials now being consolidated with Alexion financials? Did you acquire Caelum?

- Alexion has not acquired Caelum and still retains the option to do so.
- Under Variable Interest Entity (VIE) accounting standards, it was determined that the changes made to the Caelum contractual arrangement in early March 2021 met the requirement for consolidation. While Alexion continues to own only a minority of Caelum's equity (33% of diluted shares), Alexion is deemed to effectively exercise economic control of Caelum, and therefore we will continue to record 100% of Caelum's operating expenses. Expenses not attributable to Alexion will be presented separately as non-controlling interest.
- The consolidation of CAELUM added operating expenses of ~$3M, diluting Alexion's non-GAAP operating margins by ~20 bps. [(1)]
- In addition, there was a one-time GAAP expense of in-process R&D (IPR&D) for the estimated value of CAEL-101 ($193M).
- Please see our 1Q21 Form 10Q filed today for more details, including in *Note 10 - Caelum Biosciences*.

Commercial Execution

Why were net US neurology patient adds lower than in previous quarters?

- Lower 1Q21 U.S. neurology net patient adds were due primarily to resurgence in COVID-19 cases over the 4Q20 to early 1Q21 and resulting access limitations.
- We have seen signs of demand accelerating beginning in March and continuing into April and expect this trend to continue for the rest of the year as COVID-19 vaccination rates continue to rise and access restrictions ease.
- The neurology franchise is more promotionally sensitive than the PNH or aHUS businesses.
- Recall there is a period of time between patients being identified as candidates for SOLIRIS and beginning treatment.
    - This includes steps such as managing through the coverage / reimbursement landscape, required vaccinations before treatment, and infusion scheduling / logistics. This creates a queue of pending new patients.
    - As COVID began in 2020, this queue was reduced as patients began treatment and new additions to the queue slowed.
- During the quarter, we continued to make progress with the implementation of digital tools and artificial intelligence-guided HCP engagement in the quarter. These practices allow us to reach physicians in a more targeted manner, with a higher probability of success - driving both depth and breadth with neurologists treating gMG and NMOSD patients.
    - We also implemented a new patient support model with the goal of improving the patient experience. This potentially will reduce barriers and the length of time it takes to start therapy.
- The severity of the COVID situation in the US continues to pressure the franchise, but we remain committed to our long-term growth ambition to serve ~7,500 US neuro patients by year-end 2025 and the team's ability to continue navigating COVID-19 related headwinds in 2021.

What impacted ANDEXXA / ONDEXXYA sales performance in 1Q21 as compared to the previous quarter, 4Q20?

- Quarter over quarter, we saw volume decrease, in part due to the COVID-19 pandemic continuing to impact the healthcare system. We continue to roll out our enhanced commercial model and optimize access at our accounts, and we expect to see the benefits of these changes flow through in the future.
- International sales largely did not benefit from an expanded scope of availability in 1Q. as German reimbursement began in February and, within the UK, in England and Wales, reimbursement in gastrointestinal bleeds will begin from May.
- We expect to roll out ONDEXXYA in additional international markets in 2021, including the Japanese launch expected in 4Q21.

ANDEXXA NTAP: What is an NTAP and why is this important for ANDEXXA?

- CMS (The Centers for Medicare & Medicaid Services) has proposed extending the ANDEXXA NTAP for a 4th year covering FY 2022 (10/1/2021 - 9/30/22).
- NTAP stands for New Technology Add-on Payment.
- The NTAP program was created to support timely access to innovative therapies used in the hospital inpatient setting.
- For a new technology to qualify for an NTAP, it must meet three criteria: newness, cost (where the applicable DRG is determined to be inadequate) and demonstrate a substantial clinical improvement.
- The NTAP amount is up to 65% of the cost of the case in excess of the full DRG payment (see below).
- The NTAP is only available for Medicare beneficiaries, but they represent the overwhelming majority of ANDEXXA patients in the US.
- Hospitals may bill for the NTAP once it has been granted by CMS. ANDEXXA's NTAP is currently in place, and this would extend it for a fourth year.
- CMS will finalize the FY 2022 NTAPs in early September 2021.

Background:

- A DRG-code (diagnosis-related group) is a classification system used to calculate pricing for inpatient hospital claims. In general, a DRG payment covers all charges (to Medicare and Medicaid) associated with an inpatient stay from the time of admission to discharge.
- Inpatient use of new treatments like ANDEXXA for Factor Xa inhibitor-related bleeds (or Soliris in NMOSD, our other product with an NTAP) are not covered in DRG-reimbursement to hospitals.
- DRG typically takes three years to catch up with new technologies, leaving the burden of payment on medical institutions.

What proportion of your aHUS treated population has converted from SOLIRIS to ULTOMIRIS?

- ULTOMIRIS for aHUS is launched in our three largest markets - the US, Germany, and Japan.
- Similar to what we achieved with PNH, we have the same best-in-class conversion ambition for our aHUS franchise in these major markets.
- We remain on track to achieve our ambition of >70% conversion within two years of launch in all three of these markets:
    - The US (launched 4Q19) will be the first expected to cross this threshold, as we approach the two-year mark post launch in the fourth quarter of 2021.
    - EU and Japanese approvals came in 2Q20 and 3Q20, respectively, so we expect to reach those benchmarks in 2022.
- We have the same best in class >70% conversion ambition within 2 years of launch in key markets for SOLIRIS indications where we plan also to launch ULTOMIRIS (e.g., gMG and NMOSD).

What is Alexion's sales exposure to government payers in the US?

- Sales to federal and state government programs (Medicare, Medicaid, VA, 340B, PHS, etc.) in the US represent ~60% of 2020 US revenues. The US represented 59% of 1Q21 and full-year 2020 global sales.
    - Medicare, at ~25-30% of US sales, is the largest single component. Alexion Medicare sales are predominantly Part B, as only STRENSIQ is currently available in a self-administered form (Part D).

Has Alexion's growth historically been driven by price increases?

- Alexion's growth in recent years has been volume-driven, without benefit from price increases.
- Our decision to implement a sustainable pricing policy for ULTOMIRIS also means that the ongoing average cost per patient on an annual basis will be lower for ULTOMIRIS than for SOLIRIS in the same indications.

What drove the strong KANUMA growth in 1Q21?

- LAL-D is an ultra-orphan disorder and numbers of new patients added to treatment can be lumpy on a quarterly basis. In 1Q21, we were able to add an unusually large number of patients, but we do not expect this to be the start of a new trend.
- Outside the US, an additional factor to note is that KANUMA ROW sales can be relatively volatile as tender-oriented market order patterns can vary.

R&D Updates

What is the new endpoint for the ALXN1840 Wilson Disease study? Why is there a shift in timeline for top line data (1H21 → 2H21)?

- While clinicaltrials.gov continues to list a primary completion date of February 2021, we currently expect top-line readout in 3Q21.
- At the analyst day in October 2020, we shared our intent to propose changes to the Ph3 trial's endpoints after analyzing new information from the Ph1 / Ph2 trials.
- After consulting with regional regulatory bodies on new primary and secondary endpoints, we have filed amendments to the protocol, and are working on receiving acknowledgement of the changes from IRBs (institutional review boards) at the trial sites. There is no impact to study conduct or integrity as a result of these protocol amendments.
- Once that is secured, we will be able to unblind the data and analyze the study's top-line results.
- Please note that all these prospective changes were made on a blinded basis, in consultation with regulatory authorities, and in light of our analyses of prior trials' data which led to a new understanding of the biology of Wilson Disease.
- Pending positive results, we still expect to file with the FDA later in 2021.
- For context, Wilson Therapeutics originally designed and began the Ph3 trial in 2018 prior to Alexion's April 2018 acquisition of the company.
    - Their original Ph3 design was for 100 treatment-naïve and treatment-experienced patients randomized 2:1 to receive either ALXN1840 (formerly WTX-101) or standard of care (penicillamine, trientine, or zinc) treated for 48 weeks + a long-term extension. The primary endpoint was for non-inferiority versus SoC.
    - After the acquisition, we changed the powering and design to allow for superiority of 1840 over SoC, ultimately enrolling > 200 patients.

- Since doing additional analyses of the Ph1 and Ph2 data, we decided to make the changes to the primary and secondary endpoints to better reflect our evolving understanding of the disease biology and how 1840 acts differently from standard of care.

You've pulled forward the expected top-line readout for ULTOMIRIS in ALS to 1H22 from 2H22. Could you share the reason?

- Despite some initial COVID-related delays in enrolling patients in the trial, there was strong demand from ALS patients and their families, and the trial enrolled more quickly than we had expected.
- This much faster than expected enrollment was the driver of our moving the expected top-line readout date from 2H22 to 1H22.
- Given the high unmet need for patients and caregivers, we wanted to update the community as soon as possible.

What indication(s) do you intend to pursue with ALXN1820?

- We have initiated a Ph1 trial in healthy volunteers early in 1Q21. Once we begin to dose in patients, we will disclose the first indication.
- However, we have talked about multiple potential indications for ALXN1820 across a number of therapeutic areas, including hematology, pulmonology, nephrology and dermatology, where properdin is believed to play an important role.

Why was your Ph3 trial with ULTOMIRIS in COVID-19 patients paused?

- Further enrollment in the global Ph3 study of ULTOMIRIS in adults with severe COVID-19 requiring mechanical ventilation was paused in mid-January, following the recommendation of an independent data monitoring committee and their review of data from a pre-specified interim analysis.
- Available details can be found in the Press Release announcing the study pause.

Why was the ALXN2050 Phase 2 monotherapy study in PNH patients paused?

- In 1Q21, Alexion paused additional enrollment in the Phase 2 study of ALXN2050 monotherapy in PNH patients, pending the receipt of further Phase 1 data, which would allow for further dose escalation in the Phase 2 study.
- We have subsequently received the additional data which allowed us to resume enrolling new patients at higher doses. We expect top line data from this trial in the first half of 2022.

For the ULTOMIRIS SC formulation, you mentioned that you expect to file in the US and EU, but haven't mentioned Japan. Do you intend to file in Japan as well?

- Given different patient preferences (much more preference for self-administered injected drugs in the US and EU vs. Japan) and regulatory requirements, we do not expect to file in Japan at this time.

(1) A reconciliation of GAAP to non-GAAP financial results is provided in the appendix and is available at www.alexion.com.

Forward Looking Statements:

This communication contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. You can generally identify forward-looking statements by the use of forward-looking terminology such as "anticipate," "believe," "continue," "could," "estimate," "expect," "explore," "evaluate," "intend," "may," "might," "plan," "potential," "predict," "project," "seek," "should," or "will," or the negative thereof or other variations thereon or comparable terminology. These forward-looking statements are only predictions and involve known and unknown risks and uncertainties, many of which are beyond Alexion's and AstraZeneca's control. Statements in this communication regarding Alexion, AstraZeneca and the combined company that are forward-looking, including anticipated benefits of the proposed transaction, the impact of the proposed transaction on Alexion's and AstraZeneca's businesses and future financial and operating results, the amount and timing of synergies from the proposed transaction, the terms and scope of the expected financing for the proposed transaction, the aggregate amount of indebtedness of the combined company following the closing of the proposed transaction, are based on management's estimates, assumptions and projections, and are subject to significant uncertainties and other factors, many of which are beyond Alexion's and AstraZeneca's control. In addition, this communication includes forward-looking statements regarding Alexion, including statements regarding: future revenue (including global revenues in 2025 and beyond; expanding patient population (including future US neurology patients increasing by 4x); 10 product launches by 2023; future clinical trial developments (including the timing of commencement and completion of trials); anticipated timing of filing for regulatory approval and receiving regulatory approval and launching products; potential benefits of products and products in development; anticipated benefits of the enhanced commercial model, timing of future product releases; patient conversion ambitions; goals with respect to expanding addressable neurology patient population; the value creation strategy; the building blocks to achieving Alexion's 2025 revenue ambition; new patient support model has potential to reduce barriers and length of time to start therapy; anticipated increased demand for Alexion products for the rest of the year (as COVID-19 vaccination rates rise and access restrictions ease); and potential peak sales for Alexion products. Alexion-related forward-looking statements are also subject to significant uncertainties and other factors, many of which are beyond Alexion's and AstraZeneca's control. These factors include, among other things, market factors, competitive product development and approvals, pricing controls and pressures (including changes in rules and practices of managed care groups and institutional and governmental purchasers), clinical trial results, delays in clinical trials, decisions of government regulators to approve and reimburse for our products; economic conditions such as interest rate and currency exchange rate fluctuations, judicial decisions, claims and concerns that may arise regarding the safety and efficacy of in-line products and product candidates, changes to wholesaler inventory levels, ability to implement commercial and patient models; variability in data provided by third parties, changes in, and interpretation of, governmental regulations and legislation affecting domestic or foreign operations, including tax obligations, changes to business or tax planning strategies, difficulties and delays in product development, manufacturing or sales including any potential future recalls, patent positions and the ultimate outcome of any litigation matter. Additional information concerning these risks, uncertainties and assumptions can be found in Alexion's and AstraZeneca's respective filings with the SEC, including the risk factors discussed in Alexion's most recent Annual Report on Form 10-K, as updated by its Quarterly Reports on Form 10-Q, in AstraZeneca's most recent Annual Report on Form 20-F and in each company's future filings with the SEC. Important risk factors could cause actual future results and other future events to differ materially from those currently estimated by management, including, but not limited to, the risks that: a condition to the closing the proposed acquisition may not be satisfied; a regulatory approval that may be required for the proposed acquisition is delayed, is not obtained or is obtained subject to conditions that are not anticipated; AstraZeneca is unable to achieve the synergies and value creation contemplated by the proposed acquisition; AstraZeneca is unable to promptly and effectively integrate Alexion's businesses; management's time and attention is diverted on transaction related issues; disruption from the transaction makes it more difficult to maintain business, contractual and operational relationships; the credit ratings of the combined company declines following the proposed acquisition; legal proceedings are instituted against Alexion, AstraZeneca or the combined company; Alexion, AstraZeneca or the combined company is unable to retain key personnel; and the announcement or the consummation of the proposed acquisition has a negative effect on the market price of the capital stock of Alexion or AstraZeneca or on Alexion's or AstraZeneca's operating results. 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