4Q & FY 2020 Public Q&A

as of Feb. 3rd, 2021

Financial Results

What drove top line strength in the fourth quarter 2020?

- Fourth quarter revenues benefited from continued strength across the business; particularly from continued growth in the neurology business, strong compliance rates, and ANDEXXA revenues exceeding expectations.
- Fourth quarter revenues increased 15% year-over-year, driven by growth in the neurology business as well as continued strength in the PNH and atypical HUS businesses. ANDEXXA sales contributed an additional $40M of revenues in 4Q 2020.

Full year operating margin exceeded guidance issued with Q3 2020 earnings; what drove operating margin strength in the fourth quarter?

- Fourth quarter 2020 operating margin strength was largely driven by favorable top line performance and continued disciplined operating expense management.

What drove the growth seen in non-GAAP EPS for FY 2020?

- Full year 2020 non-GAAP EPS growth versus the prior year was driven by top line performance. This was partially offset by increased operating expenses to support the growing business (including the margin dilutive effect of the Portola operating expenses) which resulted in a lower operating margin. The FY 2020 tax rate was also higher compared to FY 2019.

Quarter-over-quarter sales in ROW declined ($89M in 4Q vs $148M in 3Q 2020), what drove this?

- As shared during our third quarter 2020 earnings call, third quarter revenues benefited from timing of certain tender and international market revenues. As expected, these revenues did not occur in the fourth quarter.

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 are going into 2021 with strong momentum and we remain on track for our long-term ambitions, including:
    - $9-10B in global revenues by year-end 2025
    - 10 launches by 2023
    - Expanding our U.S. Neurology patient volume 4x by year-end 2025 (to ~7,500 total patients)

Commercial Execution

What drove the stronger 4Q 2020 adds for US Neuro patients vs. 3Q 2020? Should we expect this trend of improvement to continue in 2021?

- We continued to make progress with the implementation of digital tools and artificial intelligence guided HCP engagement in the fourth 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 as well as NMOSD patients.
- The severity of the COVID situation in the US continues to pressure the promotionally sensitive US Neurology business, but we remain committed to our long-term growth ambition to serve ~7,500 patients by year-end 2025 and the team's ability to continue navigating COVID-19 related headwinds in 2021.

What drove the stronger than expected performance by ANDEXXA?

- We were pleased with the results for ANDEXXA, outperforming our 4Q guidance with actual sales of $40M.
- Performance in the quarter was driven by hospital demand. We remain focused on our plans to re-power ANDEXXA's launch by creating access, building advocacy, and generating demand to optimize both new and existing top tier accounts.

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

- ULTOMIRIS for aHUS is launched in our three largest markets - including the US, Germany, and Japan.
- 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 4Q '19) will be the first that we expect 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 2Q '20 and 3Q '20, respectively.
- We have the same 70% conversion ambition within 2 years of launch in key markets for future indications where we plan to launch ULTOMIRIS (gMG and NMOSD).

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

- Sales to federal and state government program payers (Medicare, Medicaid, VA, 340B, PHS, etc.) in the US represent ~60% of US revenues. The US represented 59% of 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. There is some variability as ULTOMIRIS dosing is weight-based, while SOLIRIS' dosing is fixed.

R&D Updates

Can you be more specific on when you expect to see top line data from ALXN1840 beyond 1H 2021?

- While clinicaltrials.gov lists a primary completion date of February 2021, we expect to share top line data in 2Q 2021, allowing time for the database to be locked and data to be cleaned, prior to releasing top line results.

What is driving the delay in top line data from the Phase 1 ALXN1720 program? And why are you adding additional dosing cohorts to the program?

- The healthy volunteer program has been paused for a second time due to COVID-19, given the rising number of cases this past fall/winter. The program is projected to re-initiate in 2Q 2021.
- The data seen so far have suggested that we can get additional inhibition of C5 with higher doses. So we plan to explore an additional dose cohort, including a specific cohort in Japanese patients.
- Given we have agreed with regulators that we can take a direct to Phase 3 approach with 1720 for gMG, and our plans to pursue proof of concept in DM with ULTOMIRIS, we would like to explore the additional dose cohort in the Ph1 study now, versus adding a Ph2 dose exploration study. This timing also allows for further optimization of device development (e.g. auto-injector) before proceeding to pivotal programs. The specific cohort in Japan will also facilitate including Japanese sites in future Ph3 programs.
- We now expect to share top line data from the Phase 1 study in 2H 2021 (vs. 1H 2021 previously).

Why are you initiating a trial with ULTOMIRIS in dermatomyositis (DM), if you intend to also initiate a program with ALXN1720 in DM? Do you intend to commercialize both assets if the programs are successful?

- An adaptive Ph2/3 design for ULTOMIRIS in refractory DM provides us with optionality. While securing faster proof of concept for the role of C5 inhibition in treating DM patients, it also allows us to potentially have a medicine on the market sooner for DM patients given the high unmet need.
    - We expect to initiate the Ph2/3 study with ULTOMIRIS in 2H 2021.
- In addition, based on the Ph2 results of the adaptive Ph2/3 study with ULTOMIRIS, we can decide to pursue a direct to Ph3 study with ALXN1720 in the broader DM population at that time, assuming favorable Ph1 results with ALXN1720. 1720 may provide additional optionality for DM patients and address a broader patient population.

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

- We have initiated a Ph1 trial in healthy volunteers early in the 1Q of 2021. 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 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 is the ALXN2050 Phase 2 monotherapy study in PNH patients paused?

- Alexion has paused additional enrollment in the Phase 2 study of ALXN2050 monotherapy that is underway in PNH patients, pending the receipt of further Phase 1 data (expected in the second quarter of 2021), that will allow for dose escalation in the Phase 2 study.

Is there any update on enrollment of the Ph3 trial for ULTOMIRIS in ALS?

- We now have >75% enrollment in the trial. Patient screening has continued to be extremely strong over the past weeks and we have stopped screening new patients as we expect to be able to fully enroll the trial using the patients that we already have in progress (the study is expected to enroll 354 patients with ALS).

You announced that NIAID would be conducting a trial testing 2040 in COVID patients. Could you please explain why, especially in light of the suspension of the COVID-19 trial for ULTOMIRIS?

- We are pleased that NIAID has decided to start this trial. While we were disappointed by the suspension of the ULTOMIRIS trial in patients with severe COVID-19 requiring mechanical ventilation, we continue to believe that there is a role for complement inhibition in treating COVID-19 patients. The TACTIC-R trial in hospitalized patients with COVID-19 not requiring mechanical ventilation, which includes an ULTOMIRIS arm, continues to enroll.
- 2040, with its inhibition of factor D, provides a different complement mechanism vs. C5 to test in the disease, especially in relation to the activation of micro-angiopathy.
    - Brodsky, et al. in an article in *Blood* (linked here) postulated that SARS-CoV-2 spike proteins bind heparan sulfate and activate the alternative complement pathway (CAP) on cell surfaces. Their model suggested that using an alternative pathway inhibitor (an earlier generation Achillion factor D inhibitor, ACH145951) may prevent both C3c and C5-mediated damage in COVID-19 patients.
- 2040 is administered orally and stored at room temperature.
- There are important differences between the ULTOMIRIS trial and this NIAID study:
    - Patient Severity: The NIAID trial will include a broader patient population than the severe patients enrolled in the ULTOMIRIS trial (NIH Grade 5-7 vs. 7). We believe that the major impact of complement inhibition is going to be shown in earlier stage diseases.
    - Study Design: The NIAID study is designed to identify subtle signals, while the ULTOMIRIS trial had a primary endpoint of mortality. We believe that it is therefore more likely to succeed in providing proof of concept for complement inhibition in this space.
- The NIAID trial to which 2040 will be added as an arm is the ongoing ACTIV-5 / BET trial (wave B study design found here).