CEO on Strategy & Outlook

Open Briefing interview with Interim CEO and Chief Scientific Officer Jonathan Coates

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In this Open Briefing®, Jonathan discusses:

- Rationale for adoption of co-marketing model for ATC
- Importance of ATC approval pathway agreed with FDA and EMA
- Financial position

Record of interview:

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Avexa Limited (ASX: AVX) recently announced its decision to pursue a co-marketing partnership model for the development of its HIV drug apricitabine (ATC). What is the rationale for this decision given the usual path for smaller biotechnology companies is to seek out-licensing or co-development partnerships with larger pharmaceutical companies?

Interim CEO Jonathan Coates
Smaller biotech companies usually seek co-development partners out of necessity. That's because the cost, the risk and the expertise involved in the Phase III trials needed for drug approval are often beyond their reach.

That isn't the case for us. The low cost and risk of the single trial needed to gain regulatory approval for ATC, together with our expertise, mean we can manage the clinical development and approval process in-house. This gives us greater flexibility in looking for partners and means partnering with a company that can market and sell ATC is a viable option. It also gives us the opportunity to achieve a better deal, since co-development deals, where a large pharma assumes a lot of the costs and risks, always result in lower revenues for the small biotech.

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Are there any precedents for a co-marketing arrangement of this kind? What is the profile of your most likely co-marketing partners?

Interim CEO Jonathan Coates
There are several precedents. A recent example is the Swedish company Medivir, which developed an anti-herpes virus product in-house and got approval for it. Medivir now has two co-marketing agreements for the sale of its product in Europe and in North and South America. These sorts of deals are a lot less common because most biotechs don't have the resources or expertise to take a product to approval stage, but it can be done, and done profitably.

We'll be looking for partners with strong sales and marketing experience in niche and specialty products whose entire focus and expertise is in selling and distributing products to pharmacists either regionally or globally. There are many such companies, whose focus is marketing rather than drug development.

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In 2010, Avexa discontinued the ATC programme after unsuccessful licensing negotiations with major pharmaceutical companies. Reasons given for the failure of the talks were the time and capital requirements to get regulatory approval, the difficulty of combining ATC with

other HIV drugs due to the relatively large dose required, and the inability to determine the activity of ATC in combination with other drugs. To what extent might these factors be barriers to gaining a co-marketing agreement?

Interim CEO Jonathan Coates
We believe all these issues have been resolved: our major aim over last two years has been to address these points, whether real or perceived. First, the time and cost to get approval has been significantly reduced following our meetings with the US and European regulatory authorities.

Second, the new trial design does away with the issue of combining ATC with other HIV drugs as we're initially aiming to sell ATC as a standalone product for patients who are resistant to other drugs. This was an issue only in the minds of large pharma, which are focused on selling combination drugs to naive patients, and only want drugs that fit those criteria. In fact, selling speciality products to resistant patients is a market that's wide open to exactly those smaller, specialist companies that would be potential co-marketing partners for us.

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Avexa's ATC patent is due to expire in 2013. Doesn't this severely limit your chances of getting a co-marketing agreement? Couldn't potential marketers simply wait for patent expiry and then take ATC to market themselves?

Interim CEO Jonathan Coates
No. ATC is very well protected. Firstly, we have manufacturing patents that cover ATC out to 2023. That means we hold the knowhow and expertise on manufacturing ATC: it's simply not a molecule that can be made by the current processes manufacturers use, and regulatory authorities are very strict about the way drugs are made.

Secondly, to gain approval a competitor would have to replicate more than 10 years of clinical and pre-clinical research data on ATC, which is just not feasible. Also, once we have approval for ATC, all the data that's part of our regulatory submission will be protected from generic companies for between five and 10 years, depending on the country. A competitor would simply not be allowed to call upon our data in support of a generic version of ATC, even if they're able to make it.

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In the last 12 months Avexa has agreed approval pathways for ATC with both the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA). Under these agreements, Avexa would be able to gain regulatory approval for ATC by successfully completing a 300-patient Phase III trial with a 14-day primary endpoint. Given this is a significantly smaller and shorter trial than usual Phase III trials, what was the basis of your agreements with the FDA and EMA and what conditions are attached?

Interim CEO Jonathan Coates
The basis of all decisions by regulatory authorities such as the FDA and EMA is a scientific analysis of the possible risk to patients compared with the potential benefit. In ATC's case, the authorities have reviewed the data, including the data from the previous Phase IIb/III trial, and concluded that the potential benefit to patients is considerable and that the risk is very low. The regulatory authorities know that new drugs are needed for resistant patients, and the trial design they've approved is specific to ATC. There are no conditions attached to the trial, and our final submission for approval will undergo the usual review processes.

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The previous ATC Phase III trial was terminated early, and there's a perception that it was unsuccessful. How relevant was the data from the previous trial to the regulators' consideration of the new trial?

Interim CEO Jonathan Coates
During our discussions with both the FDA and EMA, the regulators reviewed the data from all our previous clinical work. They clearly see the evidence for ATC, which is why they gave us such a positive way forward.

The previous trial was terminated early because the trial design demanded of us by the authorities at the time turned out not to be adequate. The trial was implemented just as three very highly active anti-retroviral drugs came to market. Those drugs were then included into the therapies of patients on the trial, given they were the best standard of care at the time, but unfortunately under the trial design we had in place, they made it more difficult to see a difference between the group taking ATC and the comparator group.

Because the trial was terminated early, the data couldn't provide statistical significance. But that's not to say that ATC did not work or that the trial was unsuccessful. In fact, both the FDA and EMA have seen all the data out of that trial: they haven't asked us to repeat the trial, they've just asked us to do this other much smaller study with a different design. We take comfort from the fact that the FDA and EMA review hundreds of compounds and hundreds of pages of data every year; they wouldn't have agreed to this one small trial if they had any doubts about the potential benefits of ATC.

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You expect the Phase III trial to run over the 2013 calendar year, with submission of the data to the FDA and EMA toward the end of calendar 2014. What are the risks to this time line and to the successful completion of the trial?

Interim CEO Jonathan Coates
Assuming we can finance the trial, and therefore start on time, the main risks are around slow recruitment or disruptions at our providers, including the clinical research organisations that help us run the trials and the manufacturers to whom we outsource production of ATC. We will of course seek to mitigate those risks as much as possible.

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What is the anticipated cost of the Phase III trial and how will it be funded?

Interim CEO Jonathan Coates
The cost will be in the order of A$30 million, which is around a tenth of the cost of many Phase III trials in this field. Clearly we don't have those funds at the moment, so we're looking at our options.

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You've indicated you expect ATC sales in the range of US$100 million to US$400 million per annum. What assumptions is this estimate based on? How much of this would come through to Avexa under a co-marketing partnership arrangement?

Interim CEO Jonathan Coates
These estimates have been calculated by external analysts assuming that ATC is used for resistant patients and having regard to how many patients might use ATC and to current sales of drugs in a similar space.

Under a co-marketing agreement, we'd expect to see double digit royalties on ATC sales.

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Avexa continues to run an in-house novel HIV integrase inhibitor programme, and has two compounds – a first generation HIV integrase inhibitor and an antibacterial agent – out-licensed to third parties. What progress has been made in these programmes and what steps remain before they can move into the clinic?

Interim CEO Jonathan Coates
The integrase program we're running in-house has progressed well. We have second generation compounds that are active against viruses resistant to current integrase inhibitors, much as ATC is active against viruses resistant to current reverse transcriptase inhibitors. We've improved the compounds' drug-like properties, and the next step will be to start a pre-clinical testing programme to establish the safety of the compounds before we can move closer to the clinic.

The first generation HIV integrase inhibitor is making steady progress in a chemistry sense. However our partner, the Shanghai Institute Organic Chemistry (SIOC) has not yet been able to raise the funding to start clinical development. You have to bear in mind that this is a series of compounds we'd previously dropped as they were not competitive in the US and European markets, being too similar to their competitors. However as the compounds are very easy to make in a chemical sense, SIOC believes that the "me too" market would be competitive in China on a cost-of-goods basis.

Our antibacterial agent AVX13616 is under a confidentiality agreement with Valevia Pharmaceuticals which holds the license for the product. However, I can say that the properties claimed by us have been upheld by Valevia, and progress is being made towards a Phase I trial. Work to broaden the range of therapeutic targets for the compound has also been very successful.

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As at the end of March, Avexa had cash of A$12.9 million, after net cash outflow of A$1.4 million in the March quarter. How indicative is the March quarter cash outflow of the expected levels going forward and do you have adequate cash to continue your research activities and complete the process of securing funding for the Phase III ATC trial?

Interim CEO Jonathan Coates
In addition to the A$12.9 million in cash, we hold just under A$6 million in listed investments, including our strategic shareholding in Allied Healthcare Group (ASX: AHZ).

All our controllable operating expenses have been significantly reduced from the past and our rent contract, which costs A$300,000 per quarter, net of sub-leases, expires in June 2013. Excluding this, our current cash burn is less than A$500,000 per quarter.

Apart from funding the Phase III ATC trial, we have more than adequate resources. Clearly we have to find the funds to conduct the Phase III trial, and we'll be focus on that as soon as we've secured one or more co-marketing partners for ATC.

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Thank you Jonathan.

For more information about Avexa, visit www.avexa.com.au or call Jonathan Coates on (+61 3) 9208 4300.

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