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## Chairman and CEO's Letter

Dear Shareholders,

In the first calendar quarter of 2010, we announced two sets of data around apricitabine (ATC). The results from ATC's Phase III trial will enable resolution around the program's place in the commercial landscape in the near term. Also in this quarter we discontinued our relationship with Tibotec in regard to our HIV integrase program, which is unrelated to ATC. Even though considerable progress has been made to identify lead molecules, the option with Tibotec for the HIV integrase program expired due to potential conflicts with Tibotec's internal programs.

As we discussed at the AGM and in our last newsletter, the sole focus of the management team and Board is to ensure that every avenue is explored to create shareholder value. This can be accomplished in a number of ways. We continue to seek a partner for ATC and these last two data sets are the determining factor for potential partners to make a decision. Other strategic avenues under consideration are M&A transactions, which could potentially achieve a more valuable scenario for shareholders. Essentially, there is absolute commitment to explore all opportunities to serve the interests of Avexa stakeholders.

In February, we reported top line 24 week data on ATC from the Phase III trial as well as 144 week extension data from the ATC Phase IIb study. We are pleased that the compound continues to show durable activity with a strong safety profile for the treatment of patients suffering from HIV.

For our Phase III trial, the top line data showed that more patients reached undetectable viral loads on ATC, although this was not statistically significant because the trial was stopped early and fewer patients were enrolled than originally projected. Avexa expects to present a more detailed analysis of the Phase III results by the end of March. This trial compared ATC to 3TC in drug-resistant HIV patients at 24 weeks and ATC provided a clear clinical benefit to the patients in four key areas:

- The durability of viral load suppression to below detectable levels.
- The ability to improve immunological function by increasing the numbers of CD4+ cells.
- HIV disease progression.
- ATC was extremely safe and well tolerated, with no serious adverse events reported.

The results from the Phase IIb extension study at 144 weeks showed that ATC continues to provide long term benefit to patients. Of the patients who successfully completed the full study, 94 per cent maintained undetectable viral loads up to week 144. Importantly, in these patients, no resistance to ATC was detected and again no ATC-related serious adverse events were observed. Based on the data from both trials, we believe that ATC could be a significant clinical addition to the drugs currently available for the treatment of patients with HIV, and we continue to pursue the best path forward for the compound.

Alongside ATC, the HCV polymerase and antibiotic programs continue to advance and we will continue to explore partnership scenarios for the HIV integrase program.

In moving forward, we are committed to creating shareholder value and are exploring every opportunity to deliver this outcome. On clarification of these opportunities, we will inform the market and will contact you with the details. We thank you for your continued support.

Mr Nathan Drona  
Chairman

Dr Julian Chick  
Chief Executive Officer

# Week 24 Data from Avexa's Phase III Clinical Trial of Apricitabine

Avexa announced the initial results from its Phase III clinical trial of apricitabine (ATC) in February 2010. This was a 48 week double-blinded study in which treatment-experienced HIV-1-infected patients were initially randomised to one of two doses of ATC (800mg or 1200mg, both twice daily) or lamivudine (3TC, 150mg twice daily). All patients also received background antiretroviral therapy that was optimised upon entry into the study. Of special note, as discussed in the report from the SAB meeting later in this newsletter, patients received the highest standard of care for their optimised background therapy, including all the newly available drugs. As reported in June 2009, an independent data and safety monitoring board reviewed the safety and efficacy results when a pre-defined number of patients had reached week 16 of the study and recommended selection of the 800mg ATC dose as the optimum dose. In October 2009, Avexa announced that it would close the study early and analyse the data, after discussions with regulatory authorities and potential partners.

The initial results from the analysis of the week 24 data were released on 4 February 2010 and showed that 53 per cent of

patients in the 800mg ATC arm achieved undetectable levels of HIV-1 RNA (<50 copies/mL). In the 3TC arm, 51 per cent of patients achieved an undetectable viral load at week 24. The number of patients in the ATC arm who lost control of their viral suppression was less than half that seen in the 3TC arm, indicating a more durable response. A decline in CD4+ cells is characteristic of progressive HIV disease – there were increases in CD4+ levels in both arms at week 24, with an average increase of 98 and 73 cells/microlitre in the ATC and 3TC arms respectively.

These beneficial clinical effects of ATC on viral suppression, increased numbers of CD4+ cells and increased durability of the viral suppression resulted in the proportion of patients showing clinical progression of disease being four times less in the ATC arm than in the 3TC arm. While no conclusions as to the statistical significance of these results were made because the trial was stopped early and fewer patients were enrolled than originally projected, these results provide further indications that ATC can improve clinical outcomes for HIV-1-infected patients.

# Week 144 Data from Avexa's Phase IIb Clinical Trial of Apricitabine

Avexa's Phase IIb extension study of ATC (800mg, twice daily) has now concluded and the final (week 144) results of the study are available. Patients in this extension study had already completed the preceding Phase IIb study, where they had received 48 weeks of treatment with ATC or 24 weeks of 3TC followed by 24 weeks of ATC. Patients completing the extension study had therefore received ATC for 120-144 weeks in total.

Thirty-six of the 42 patients enrolled in the extension study completed the study to week 144. Of these 36 patients, 34 patients (94 per cent) had an undetectable viral load, or close to, for the duration of the study to week 144, indicating long-lasting inhibition of viral replication by treatment with ATC in combination with optimised background antiretroviral therapy. In addition, the increases in CD4+ cells observed in the original study were maintained during the extension study. On average, patients had levels of CD4+ cells above 500 cells per microlitre, which is the level where many current guidelines indicate antiretroviral treatment need not be initiated.



ATC is effective in patients with resistance to other commonly used drugs in the treatment of HIV. Importantly, no resistance to ATC itself was detected over the 120-144 weeks of treatment.

Of the patients who had entered the original Phase IIb study with a higher level of drug resistance (more than two thymidine analogue mutations or TAMs), more than 90 per cent achieved undetectable viral loads. This indicates that ATC is effective in patients with resistance to other commonly used drugs in the treatment of HIV. Importantly, no resistance to ATC itself was detected over the 120-144 weeks of treatment.

The excellent safety profile of ATC has now been maintained over three years of treatment. There were no serious adverse events related to ATC and no patient withdrew from the study because of an adverse event related to ATC. ATC was well tolerated over the treatment period, with a high level of compliance throughout the two studies, with more than 95 per cent of patients taking their full dose of ATC consistently over the 144 weeks of treatment.

With the conclusion of the Phase IIb extension study, ATC has been shown to be safe, well tolerated and effective in treatment-experienced HIV-1-infected patients, without causing resistance, over a treatment period of three years.

# Data and Safety Monitoring Board and Scientific Advisory Board Meetings

Avexa held meetings with the Data and Safety Monitoring Board (DSMB) for the ATC Phase III trial and the Scientific Advisory Board (SAB) for ATC during February 2010 in San Francisco, taking advantage of the board members' presence there for the 17th Conference on Retroviruses and Opportunistic Infections (CROI).

An independent DSMB was put in place for the ATC Phase III trial to examine the week 16 data and make a recommendation on the optimum dose of ATC, as well as monitoring the safety data throughout the study. It is made up of individuals with expertise in the treatment and management of patients with HIV-1 infection, statistics and/or ethical aspects of clinical trials. The DSMB supported the decision to close the trial early and enable discussion of the preliminary data with regulatory authorities with a view to establishing an alternative path forward for ATC. As the trial has now been concluded, they were able to share the results of the week 16 dose decision analysis and confirmed that the 1200mg ATC dose was safe and effective but did not provide any additional activity over the 800mg dose. The DSMB were impressed by the safety and tolerability of ATC even up to 1200mg twice daily. The DSMB encouraged Avexa to continue the development of ATC and wished to continue to serve as DSMB members for future studies.

The SAB for ATC is made up of medical investigators in the field of HIV research in Australia, Europe, the United States and South America and provides objective feedback and guidance on the development of ATC. The SAB discussed the difficulty of establishing the activity of new investigational agents within a background of the newly approved drugs such as raltegravir, maraviroc and etravirine. A study presented at the conference on another investigational agent (vicriviroc) showed that they were unable to demonstrate an additional benefit for vicriviroc over and above the background regimen, since the newly approved drugs became available. In this context, the positive trends seen for ATC in the Phase III study (which also included these newly approved drugs in the background regimen) were especially encouraging, considering the much smaller numbers of patients in the Phase III study. The problem of demonstrating the benefit of new agents against the background of new drugs available was widely discussed at the conference, and the SAB discussed alternative designs of clinical trials that would enable the positive attributes of ATC to be clearly shown. Members of the SAB supported Avexa's decision to close the Phase III study early and discuss the results with regulatory authorities such as the FDA. The SAB also reviewed the long term week 144 data for ATC and were impressed by the durability of the response, the lack of resistance even after three years of treatment and the continued excellent safety and tolerability of ATC.

# Avexa's Publications

Publication of scientific work provides independent validation of the value, quality and novelty of the science and its importance from a scientific standing. Avexa endeavours to publish its research in peer-reviewed scientific journals, and the following papers have been published over the last year.

In collaboration with researchers at the School of Chemistry at the University of Wollongong, Avexa has recently published a paper from its antibacterial program in the journal *Angewandte Chemie International Edition* (volume 49, pages 537-540). Titled 'Binaphthyl-based dicationic peptoids with therapeutic potential', the paper describes the design and synthesis of two novel dicationic peptoids that have promising antibacterial activity against a range of microorganisms, including strains resistant to the antibiotics vancomycin, methicillin and linezolid. The journal covers all aspects of chemistry and has a high impact factor, which is a reflection of its importance in the field. It is therefore of note that the paper was accepted for publication in this journal, indicating that the study of these antibacterial compounds is considered of interest to the journal's readers.

The results of a collaboration with Mark Wainberg's laboratory in Montreal, Canada, are described in the paper 'Apricitabine does not select additional drug resistance mutations in tissue culture in human immunodeficiency virus type 1 variants containing K65R, M184V, or M184V plus thymidine analogue mutations' published in the journal *'Antimicrobial Agents and Chemotherapy'* (volume 53, pages 1683-1685). This *in vitro* study showed that HIV-1 already containing certain resistance mutations in the viral reverse transcriptase does not accumulate further mutations in the presence of ATC, which provided further evidence that ATC has little tendency to select for resistance mutations.

Avexa's Dr Susan Cox was invited by the journal *'Expert Opinion on Investigational Drugs'* to write a review on ATC, summarising the pharmacological and clinical data on ATC. *'Expert Opinion on Investigational Drugs'* is a peer-reviewed journal providing a comprehensive guide to the literature published on the most promising and exciting drugs in research and development. Titled 'Apricitabine – a novel nucleoside reverse transcriptase inhibitor for the treatment of HIV infection that is refractory to existing drugs', the review summarised the data available on ATC up to that time, which included the week 48 data from the Phase IIb study of ATC (published in volume 18, pages 199-209).

The results of the Phase I study conducted by Avexa on the effects of administering ATC with ritonavir-boosted tipranavir, another treatment for HIV, were published in the journal *'Clinical Drug Investigation'* (volume 29, pages 721-728) in a paper titled 'Comparison of the pharmacokinetics of apricitabine in the presence and absence of ritonavir-boosted tipranavir: a Phase I, open-label, controlled, single-centre study'. Treatment of HIV requires the use of combinations of drugs to try to suppress replication of the virus as much as possible and prevent the development of drug resistance. There is potential for interactions between the drugs, which may result in altered levels of the drug(s), which, in turn, may lead to decreased effectiveness and/or increased toxicity of the drug(s). This study found that administering ATC with ritonavir-boosted tipranavir led to a small increase in the levels of ATC in the study participants. However, the magnitude of this increase was not considered to be of clinical significance and therefore it is not necessary to adjust the dosing of ATC when it is given with ritonavir-boosted tipranavir.

# Expiry of HIV Integrase Option Period with Tibotec

Avexa has been involved in a worldwide exclusive option agreement with Tibotec Pharmaceuticals for its early-stage HIV integrase program. It was announced at the beginning of March that Tibotec would not exercise its exclusivity option, due to potential future conflicts with its internal programs, and the option was allowed to expire (effective 2 March 2010). During the exclusivity period, Tibotec tested a number of compounds designed and synthesised by Avexa, and showed these to have a high level of potency and activity against HIV strains resistant to another integrase inhibitor, raltegravir, validating Avexa's results. Over this period, considerable progress was made with increasing the selectivity and potency of the program compounds and Avexa now has a number of potent leads with activity against HIV resistant to other integrase inhibitors. Avexa will continue to interact with Tibotec on a non-exclusive basis, but now Avexa will also be able to discuss collaborations and licensing of the program with other parties that have shown interest in the research program.



# Financials

## Interim income statement for the half year ended 31 December 2009

	31 December 2009 \$'000	31 December 2008 \$'000
Finance income	278	1,172
Other revenues from ordinary activities	386	622
<b>Revenue</b>	<b>664</b>	<b>1,794</b>
Contract research and development costs	(4,876)	(16,485)
Raw materials and consumables used	(245)	(237)
Personnel expenses excluding share-based payment expense	(2,006)	(3,600)
Share-based payment expense	(256)	(325)
Occupancy costs	(931)	(628)
Depreciation	(118)	(137)
Asset management expenses	(144)	(106)
Legal and professional services	(255)	(215)
Travel	(184)	(224)
Insurance	(100)	(114)
Intellectual property	(254)	(224)
Merger proposal expenses	-	(172)
Other expenses	(454)	(381)
Loss before income tax expense	(9,159)	(21,054)
Income tax expense	-	-
<b>Loss for the period</b>	<b>(9,159)</b>	<b>(21,054)</b>

## Timetable for the next 12 months

Quarterly Avexa News	June 2010
Annual Report	September 2010

Quarterly Avexa News	December 2010
Quarterly Avexa News	March 2011



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### Editor's Note

We value shareholder feedback.  
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