



ASX Release

Avexa to Present at BIO CEO and Investor Conference Additional Data on ATC's Phase IIb Trial

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Melbourne, Australia - Biotechnology company Avexa Limited (ASX: AVX) announced today that it will present at the 2008 BIO CEO & Investor Conference on Tuesday, February 12, 2008 at 3:30 PM EST at the Waldorf-Astoria hotel in New York. Dr Julian Chick, CEO will provide a general update together with an overview of data from the Phase 2b clinical trial of apricitabine (ATC), the Company's lead anti-HIV drug candidate, recently presented at the Conference on Retroviruses and Opportunistic Infections (CROI 2008), held in Boston on February 4, 2008.

The key points from the scientific presentation are:

- Both the 600mg and 800mg BID doses of ATC, in combination with optimised background antiretroviral therapy (ART), showed superior antiviral activity to 3TC in a population of treatment-experienced HIV-1-infected patients with the M184V mutation which included both first-line failures and patients with multiple prior treatment failures.
- ATC given 600mg or 800mg BID was safe and very well tolerated over the 24-week study period.
- No evidence of development of resistance to ATC was seen.
- Larger, phase 3 trials of ATC in treatment-experienced patients are planned.

The results gathered to date clearly show that ATC:

- Has an excellent safety profile at least equal to 3TC.
- Is superior in antiviral activity to 3TC in failing patients with the M184V mutation.
- Provides clear immunological benefit, increasing CD4 levels to higher levels than 3TC in failing patients with the M184V mutation.
- Has not selected for resistant virus up to week 24.

"These results are extremely encouraging. In conjunction with the ongoing progress being made with the ATC development program, they provide clear indication of ATC's potential " said Dr Julian Chick, CEO .

Avexa anticipates releasing the 48 week data from the ATC Phase 2b trial during the current quarter. Thirty nine of an eligible forty patients remained on ATC therapy post the 48 week trial period.

Technical Data

Background

Apricitabine (ATC) is a novel cytidine analogue nucleoside reverse transcriptase inhibitor (NRTI) which has shown potent reductions in viral load during monotherapy in both treatment-naïve and treatment-experienced patients infected with HIV-1.



ATC has demonstrated activity *in vitro* and in the clinic against viruses containing NRTI resistance mutations, particularly the reverse transcriptase mutations M184V and thymidine-associated mutations (TAMs). AVX-201 is a phase 2b study of ATC compared to lamivudine (3TC) with optimized background (from Day 21) in treatment-experienced patients with HIV-1 containing the M184V mutation.

Primary Objectives

- To evaluate the antiretroviral activity of two doses of ATC versus 3TC in treatment-experienced patients with HIV-1 with the M184V mutation in reverse transcriptase.
- To evaluate the safety of ATC in HIV-1 treatment-experienced patients.

Secondary Objectives

- To evaluate the emergence of mutations in HIV-1 leading to possible phenotypic resistance to ATC.
- To evaluate changes in CD4+ and CD8+ T-cell counts.

Study Design

This Phase 2b trial is a randomised, double-blind, dose-ranging, multi-centre study.

- Patients were randomly assigned to treatment in a 1:1:1 ratio in a blinded fashion to one of three arms:
 - 600mg ATC twice daily (600mg ATC BID arm)
 - 800mg ATC twice daily (800mg ATC BID arm)
 - 150mg 3TC twice daily (150mg 3TC BID arm)
- Enrolment was stratified by the number of TAMs present at screening (<3 TAMs, ≥3 TAMs).

Primary Treatment Period (Day 0 to Day 21)

- On Day 0, patients stopped their existing 3TC or FTC treatment and commenced blinded therapy. No other changes to background ART were permitted during this period.

Continued Treatment Period (Day 21 to Week 24)

- On Day 21, the background ART could be optimised according to the genotype at screening and blinded therapy continued to Week 24. Any approved ART could be used with the exception of 3TC, FTC and zalcitabine.

Open-Label Period (Week 24 to Week 48)

- After Week 24, patients ceased randomized therapy and were offered open-label ATC (800mg BID) to Week 48.



Table 1. Background antiretroviral therapy

Safety population (n=51)	600mg ATC (n=17) N (%)	800mg ATC (n=18) N (%)	150mg 3TC (n=16) N (%)
ART taken during the Primary Treatment Period			
Protease inhibitor	7 (41.2)	8 (44.4)	7 (43.8)
NRTI (excluding 3TC or ATC)	16 (94.1)	18 (100)	16 (100)
NNRTI*	10 (58.8)	10 (55.6)	8 (50.0)
Other antivirals**	1 (5.9)	0	0
ART commenced on Day 21			
Protease inhibitor	15 (88.2)	15 (83.3)	14 (87.5)
NRTI (excluding 3TC or ATC)	15 (88.2)	17 (94.4)	14 (87.5)
NNRTI*	1 (5.9)	3 (13.7)	1 (6.3)
Other antivirals**	1 (5.9)	1 (5.6)	3 (18.8)

*NNRTI = non-nucleoside reverse transcriptase inhibitor

**Enfuvirtide

Viral Load

- With both the 600mg and 800mg doses of ATC, a decrease in viral load was apparent at Day 7, and the viral load continued to decrease with both doses through to Week 24 (Figure 2).
- At Day 21, there were mean decreases in viral load of 0.90 and 0.71 log₁₀ HIV-1 RNA copies/mL in the 600mg ATC and 800mg ATC groups, respectively, which were statistically significant compared to the mean decrease of 0.03 log₁₀ copies/mL in the 3TC group, as previously reported.
- Both ATC arms continued to show a greater reduction in viral load compared to 3TC out to Week 24. The study was not powered to meet this endpoint at Week 24.
- Similar reductions in viral load were shown by the 600mg and 800mg doses of ATC.



Figure 2. Time weighted average log10 change in HIV RNA from Day 0 to Week 24*

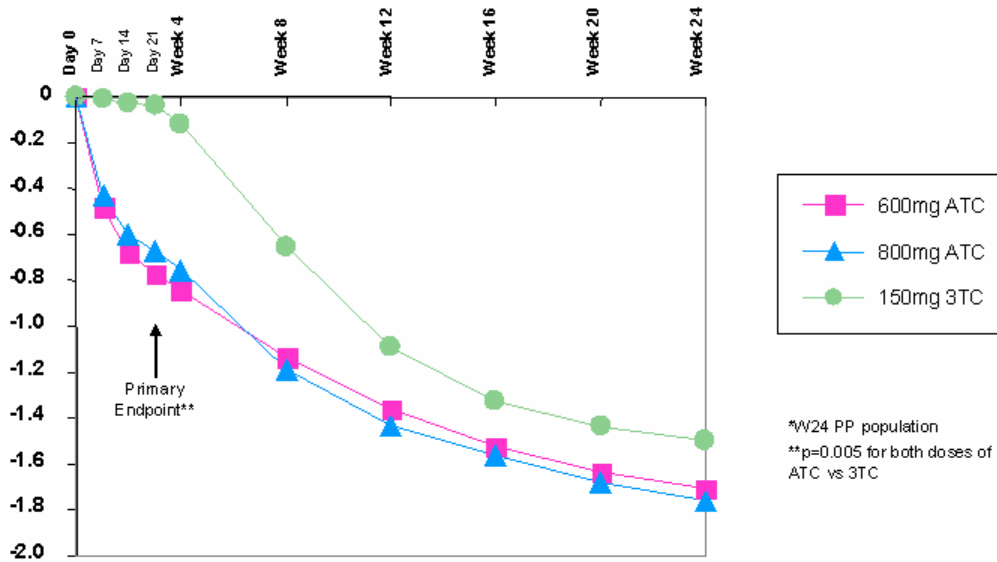


Figure 3. Percentage of patients achieving target viral loads at Week 24

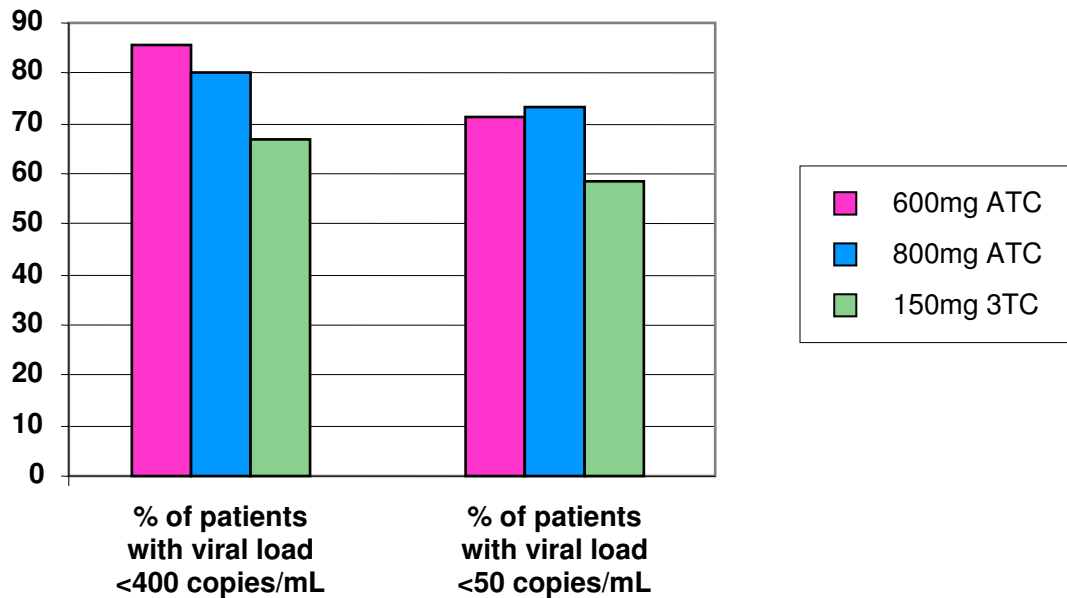




Table 2. Change in CD4+ and CD8+ cell counts at Week 24

W24 PP population (n=41)	600mg ATC (n=14)	800mg ATC (n=15)	150mg 3TC (n=12)
Change in CD4+ cells (cells/ μ L)	145.5	211.5	113.6
Change in CD8+ cells (cells/ μ L)	366.1	375.5	153.9
Change in CD4+/CD8+	0.014	0.084	0.067

Effect of TAMs

Patients with ≥ 3 TAMs at baseline

- The mean reduction in viral load at Week 24 for patients with ≥ 3 TAMs at baseline was -1.71 log₁₀ for the 600mg ATC group compared to -2.16 log₁₀ for the 800mg ATC group.
- The 800mg ATC dose appeared to provide some additional activity compared to the 600mg dose in patients with ≥ 3 TAMs at baseline. The study was not powered to meet this endpoint at Week 24.

Genotype Results

- At Week 24, genotyping was possible for only 8 patients (2 in the 600mg ATC arm, 2 in the 800mg ATC arm and 4 in the 3TC arm) – of these 1 (600mg ATC), 1 (800mg ATC) and 4 (3TC) patients had M184V present.
- No patients were found to have developed the L74V, K65R, Y115F, V75 mutations or additional TAMs during the 24-week period.
- No evidence of resistance to ATC was seen.

Safety

- The most frequently reported adverse events in the study were diarrhea (n=14), nausea (n=9), nasopharyngitis (n=7), hypertriglyceridemia (n=6) and upper respiratory tract infection (n=5), and occurred equally in all three treatment arms.
- 7 patients on ATC reported no adverse events (AEs) at all up to Week 24 compared to none on 3TC.
- 5 serious AEs were reported by 4 patients, all in the 3TC arm.
- 5 patients reported 8 AEs that were possibly related to ATC:
 - diarrhea and dizziness (600mg ATC group)



- mild nausea (600mg ATC group)
- mild pyrosis (800mg ATC group)
- mild anorexia and weight loss (800mg ATC group)
- mild gastric intolerance and moderate diarrhoea (800mg ATC group).
- No patient permanently discontinued ATC treatment owing to a drug-related AE.
- 4 patients had their ATC treatment discontinued temporarily for an AE – only the mild nausea experienced by a patient in the 600mg ATC group was thought to be possibly related to ATC treatment.
- No patients reported grade 3 or 4 laboratory results that were related to ATC treatment.

Discussion

- At Week 24, there was evidence of additional antiviral activity for both doses of ATC compared to 3TC; as expected, since the primary endpoint was at Day 21, this did not reach statistical significance, probably due to the small sample size and the potency of the optimised background ART.
- The potency of the OBR was high, probably reflecting the number of first line failures who moved from an NNRTI-based regimen to a PI-based regimen.
- The reductions in viral load with ATC treatment were accompanied by clinically meaningful increases in the number of CD4+ cells at Week 24.
- Overall, similar activity was seen for the 600mg and 800mg doses, except in patients with ≥ 3 TAMs at screening, where the 800mg dose may have provided some additional activity.
- The adverse event profiles of the 600mg and 800mg ATC BID were similar to each other and to the adverse event profile of 3TC.

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Avexa Limited is a Melbourne-based biotechnology company with a focus on research and development of drugs for the treatment of infectious diseases. Avexa has dedicated resources and funding for key projects including its HIV integrase program and an antibiotic program for antibiotic-resistant bacterial infections. The Company's lead program is apricitabine (ATC), an anti-HIV drug which has successfully completed the 24 week dosing of its Phase IIb trial and continues to progress towards Phase III trials. Avexa has entered into collaboration with TargetDrug in China to identify new CCR5 inhibitors for the treatment of HIV.