AVX754 Overview

Presentation by Dr James Sawyer

Prism Ideas

Clinical Trial Consultants

Avexa

Forward-looking Statements

This presentation includes forward-looking statements that are subject to risks and uncertainties. Such statements involve known and unknown risks and important factors that may cause the actual results, performance or achievements of Avexa to be materially different from the statements in this presentation.

Actual results could differ materially depending on factors such as the availability of resources, the results of pre-clinical proof-of-concept studies, the timing and effects of regulatory actions, the strength of competition and the effectiveness of patent protection.

Additional information regarding risks and uncertainties is set out in the Prospectus dated 15 February 2005 available from Avexa on request.

Dr James Sawyer – Background

- Consultant Pharmaceutical Physician and an expert in the design and implementation of clinical development programs

- Following hospital training positions in General Medicine and Anaesthetics spent 8 years in a variety of international clinical and marketing roles at Sanofi-Winthrop, AstraZeneca and Roche

- Currently Medical Director at Prism Ideas providing drug development and commercialisation consultancy to a variety of large and smaller pharmaceutical companies, specialising in HIV medicine.

- Member of the faculty of pharmaceutical physicians of the Royal College of Physicians and has published across a wide range of therapeutic areas.

- Spend the past 3 years working with Shire Pharmaceuticals on the AVX754 (formerly SPD754) program

Prism Ideas – Overview

- Prism Ideas is a specialist clinical development and medical marketing consultancy

- Founded in 2001 Prism has an international client base including both major Pharmaceutical companies and emerging leaders of the Biotech industry.

- Prism provides strategic input with regards to the design and conduct of development programs. This ensures that the ability of products to meet market needs is appropriately demonstrated.

- Prism manages communication of results arising from these studies to the scientific and clinical community in order to maximise its awareness and understanding.

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Avexa – Product Pipeline

Disease Indication	Research	Lead Compound	Pre-clinical	Phase I	Phase II	Phase III
HIV	AVX754 – NRTI (partner Shire Pharmaceuticals)					
Hepatitis B	Non nucleoside					
HIV	HIV Integrase					
VRI	Antibiotic					

The Clinical Development of HIV

- Phase 1
  - Healthy volunteers
  - Pharmacokinetics (1st safety data in humans)
  - Influence of other drugs
- Phase 2
  - HIV infected patients
  - Treat with new drug alone for a few days (monotherapy)
  - Proof of effectiveness but confirmation required

HIV Clinical Development (cont)

- Phase 3
  - Longer studies (6 months to 1 year)
  - Treatment along with other drugs (clinical requirement)
  - Confirmation of effectiveness and safety in target market
- Phase 4
  - Post launch
  - Product life cycle management
    - Line extensions
    - New indications

Why HIV is a Market Opportunity

- Large number of patients requiring long term treatment
  - Potentially life long for HIV+ children today
- Continuous need for new effective drugs to sustain treatment options
- Little or no expectation of drug acquisition cost containment in developed world
- Low cost of entry into marketplace
  - Highly informed patient and clinician base
  - Rapid uptake of clinically attractive products

HIV Development – Well Defined Needs

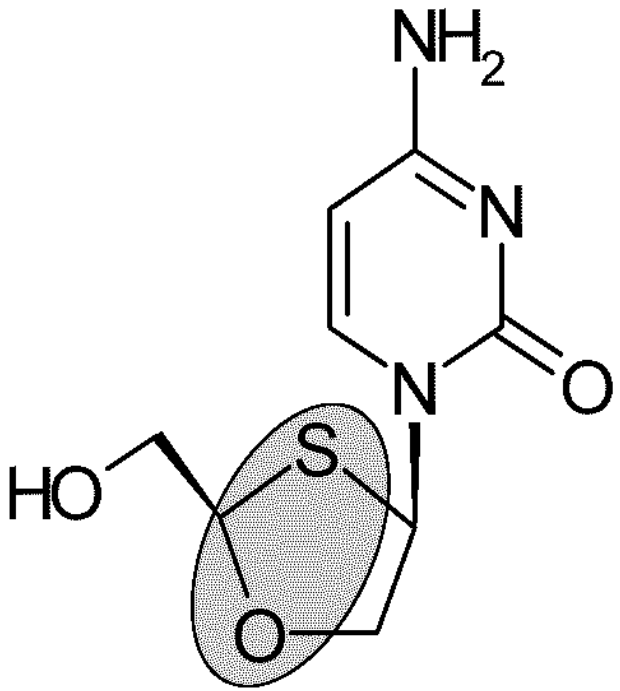
- Short duration clinical studies
  - Reduces development time from industry mean 5.5yrs
- Established outcomes measures to gain approval
- Rapid approval processes in Europe and USA
- No need to provide Health Economics data to support reimbursement

AVX754 Development History

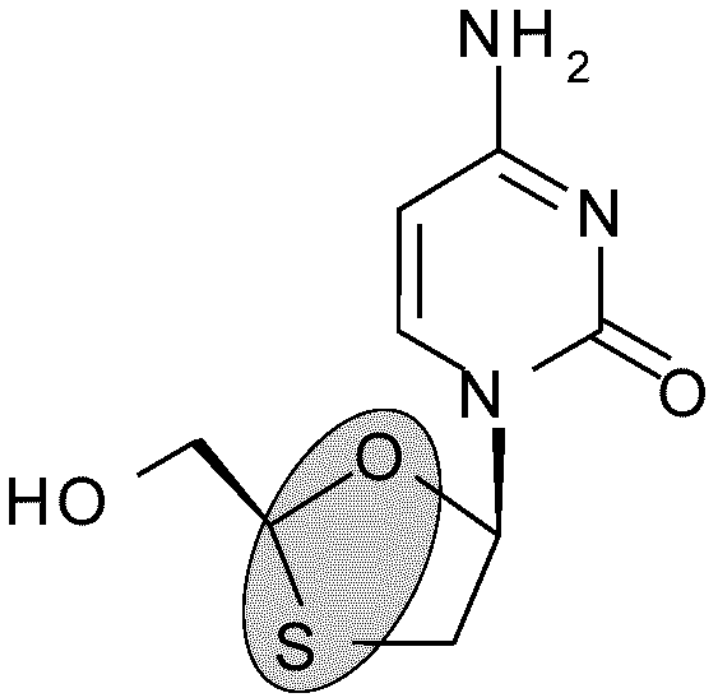
- Development as SPD754
  - Excellent preclinical safety profile
  - Highly promising virology profile
  - 4 PK (Phase I) studies (PK = Pharmacokinetics)
    - Food, Single and Multiple Dose, Drugs used in HIV medicine
  - One study in patients (Phase IIa) completed
  - Investigational New Drug and fast track status granted in USA
- Avexa to complete development (AVX754)

Pharmacology

AVX754



3TC



AVX754 Development History

- Preclinical in vitro studies
  - Highly specific action on HIV
  - Excellent ratio of activity vs. toxicity
    - Comparable/better than 3TC
    - Mitochondrial profile amongst best in class
- Virology data
  - Active against the viruses most commonly resistant to key marketed products
  - Co-dosing with 3TC inadvisable – but clinically unnecessary

Antivirogram Profile of AVX754

Virus Genotype	No. of isolates	Fold difference compared to HIV-1_{IIIB} control						
		AVX754	AZT	3TC	ddI	ddC	d4T	Abacavir
WT	5	1.3±0.8	1.8±0.7	1.0±0.5	1.3±0.5	1.6±0.7	1.6±1.8	1.4±1.0
AZT^{R*}	5	1.7±1.2	>58±49	4.1±1.7	2.5±2.4	0.96±0.6	<1.6±1.2	<3.2±2.0
$3TC^{R}$	5	1.2±0.6	1.1±0.6	>39	1.4±0.4	2.6±1.0	0.58±0.11	1.9±0.6
AZT^{R} / $3TC^{R}$	8	3.3±2.5	25±26	>39	2.0±1.6	3.2±1.5	1.6±0.5	6.3±5.2
Q151M+M184V	5	24±2	>71±36	>39	27±18	11±5	8.3±3.0	17±14
Q151M	5	21±2	>66±36	14±14	23±9	14±7	17±6	20±13
69 insertions	7	8.0±5.8	>72±45	>34±22	10±10	5.8±3.4	8.6±6.9	19±11
$Abacavir^{R}$	5	1.9±0.7	1.8±0.7	>39	4.5±2.1	2.9±0.9	1.1±0.4	14±6
$d4T^{R}$	5	4.2±2.6	>38±45	>27±20	3.9±2.2	2.8±2.1	4.1±1.2	11±7

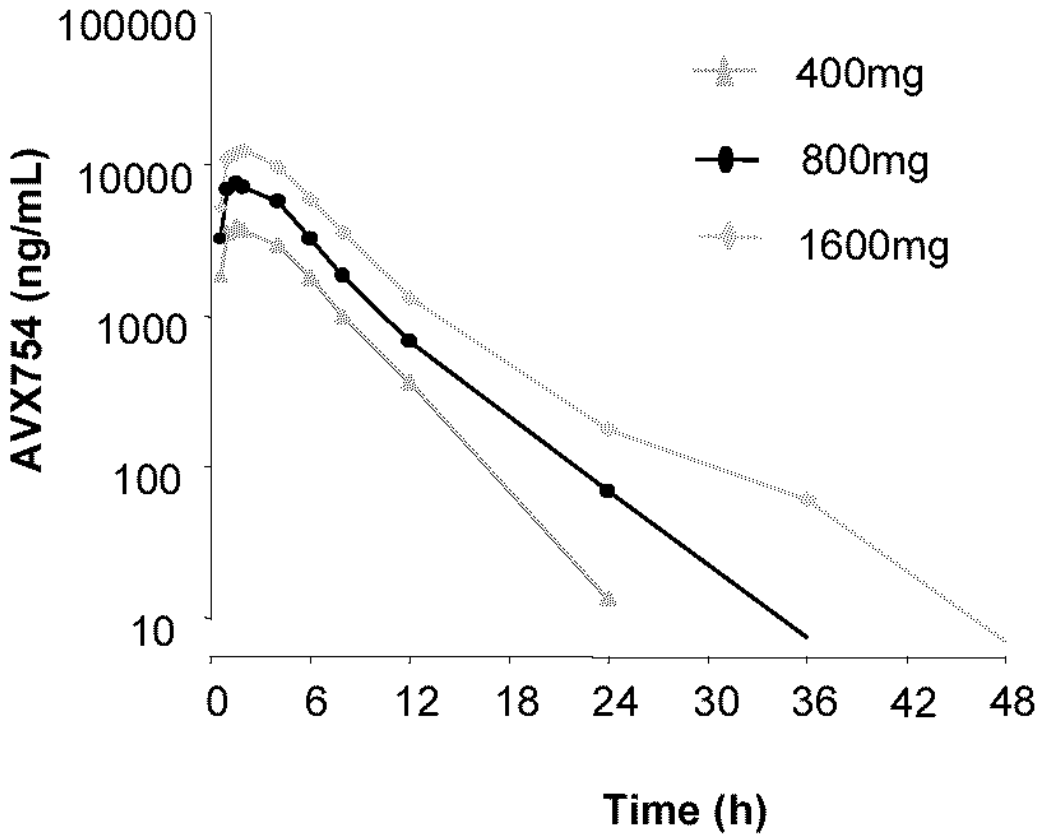
* R: resistant

Taylor DL, Ahmed PS, Tyms AS, et al. Drug resistance and drug combination features of the human immunodeficiency virus inhibitor, BCH-10652 [(+/-)-2'-deoxy-3'-oxa-4'-thiocytidine, dOTC]. Antivir Chem Chemother 2000;11:291–301

AVX754: Summary of In Vitro Virology

- Good in vitro activity against
  - Wild-type HIV-1 strains
  - Viruses resistant to other treatments
    - AZT, 3TC
- Antagonism between AVX754 and 3TC is clinically immaterial
- Reduced activity vs. other resistant virus types does not impact market opportunity

Single Dose Pharmacokinetics



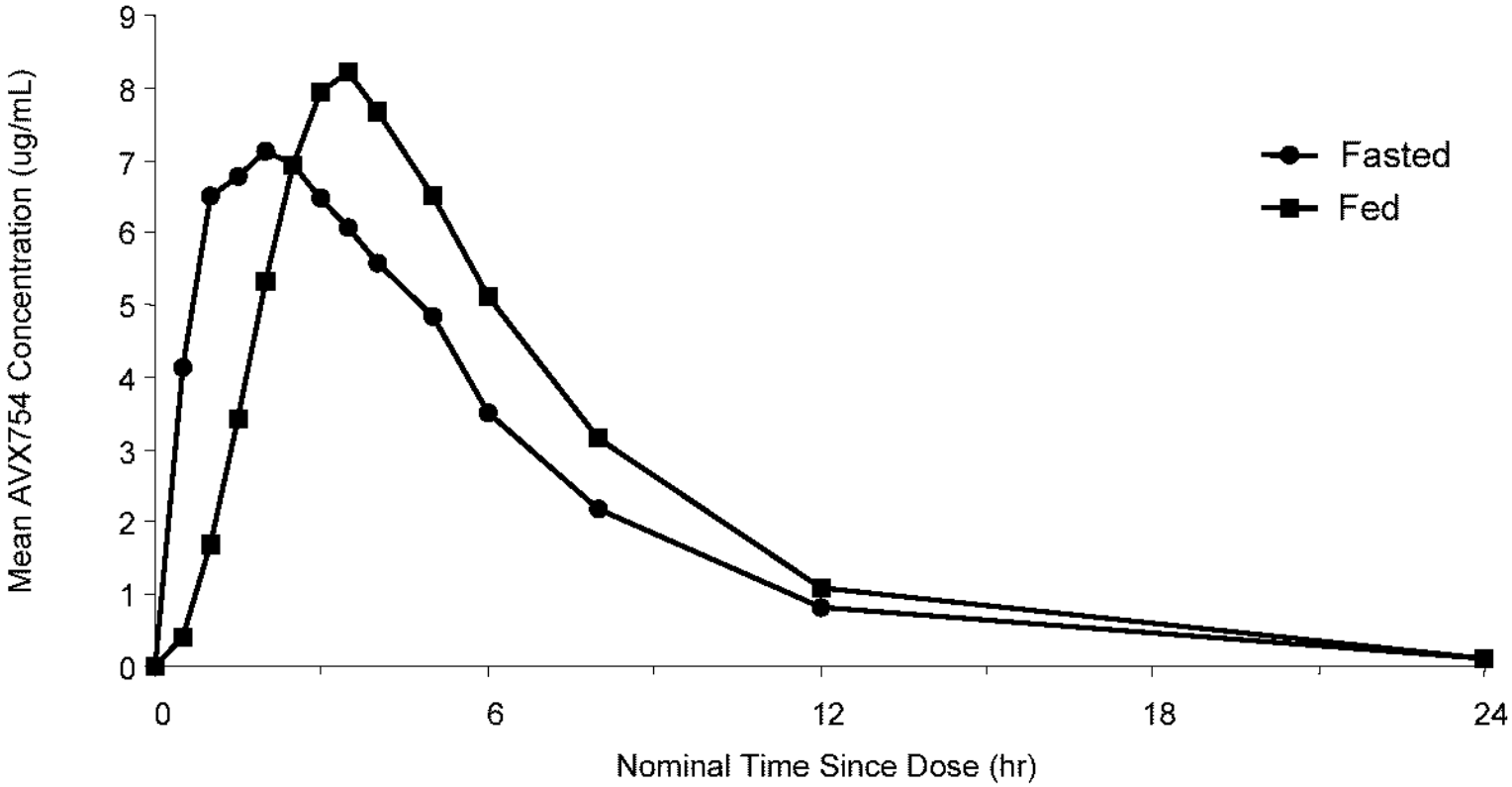
- Linear
- M=F
- Bioavailability 65-80%
- $T_{1/2}$ approx 6 hours
- Primary route of excretion
  - Renal
  - Some active transport
- No enantiomeric conversion

Francis RJ et al Pharmacokinetics (PK) of SPD754, a new cytidine analogue, in healthy volunteers [abstract 528]. Antiviral Ther 2003; 8 (Suppl 1):S325

Interactions

- Food
  - No effect
- 3TC/FTC
  - No co-dosing but no clinical rationale for this either
- Other commonly co-prescribed drugs
  - No expectations of any need to alter AVX754 dose when co-dosed with other anti HIV medications

No Effect of Food on AVX754 PK



AUC ↑ 13% (95% CI 5 to 23%) Cmax ↑8 % (95% CI -2 to 19%)

* Holdich T, Dennis K. Investigation of the influence of food upon the pharmacokinetics of SPD754 [abstract 4.1.6]. Abstracts of the 9th European Aids Conference, Warsaw (25–29 October 2003)

Summary of Clinical Pharmacology

- Highly predictable PK
  - Absolute oral bioavailability of 62-85%
  - Plasma half life ~ 3 hours
  - Low intersubject variability
  - No influence of gender
- No demonstrable hepatic metabolism
- Cannot be co-administered with 3TC/FTC
- Triphosphate intracellular half life ~ 6.5 hours

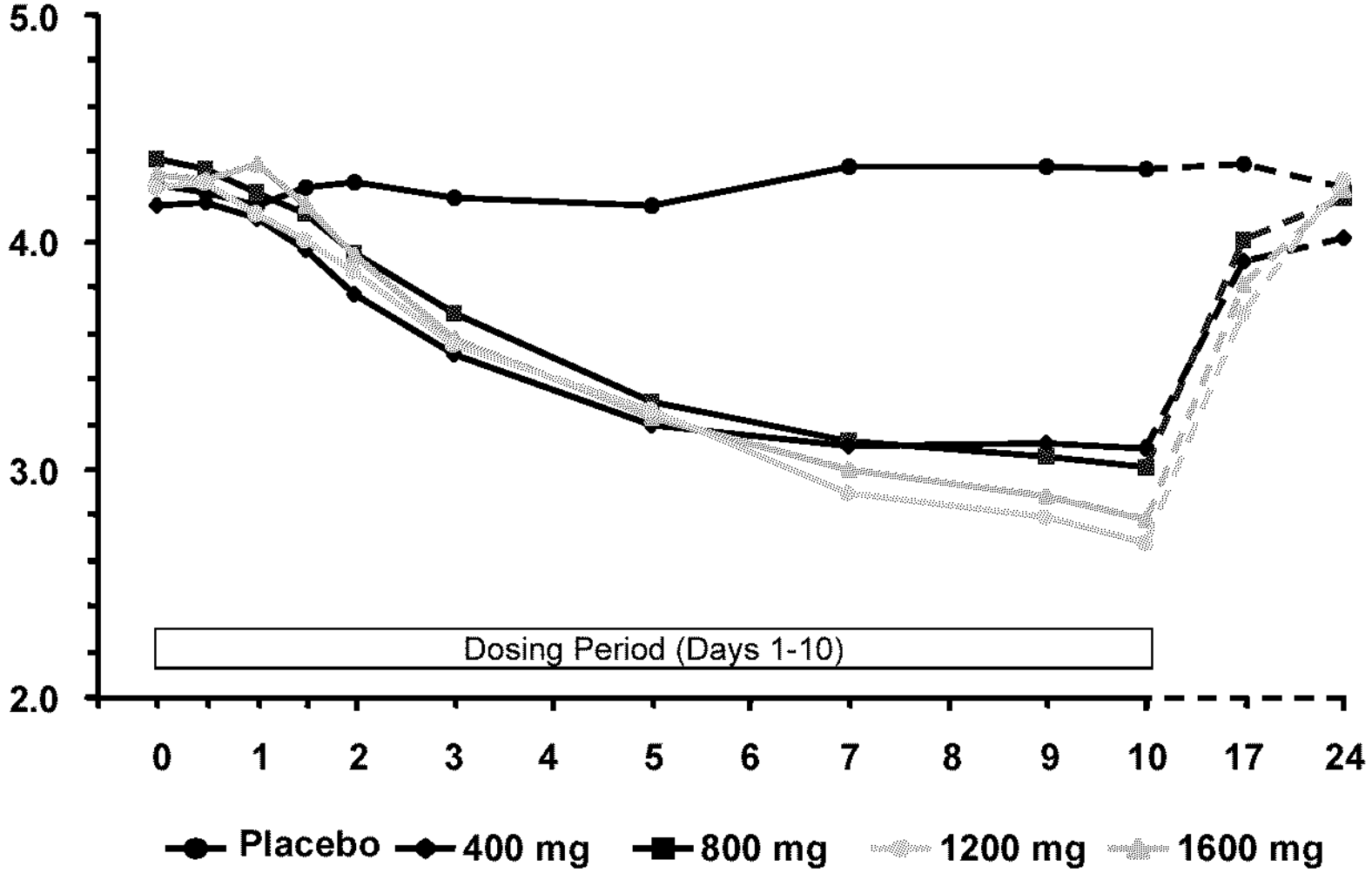
Clinical Evaluations

- Safety and tolerability
- Efficacy
  - against wild type
  - against viruses harbouring mutations
- Clinical virology

Summary of Adverse Events

- Generally well tolerated
  - No SAE
- Most common AE similar frequency to controls
  - Headache
  - Nasal congestion
  - Occasional rash
- Laboratory data unremarkable

Monotherapy in Treatment Naïve Patients



Cahn P, et al. Antiviral HIV-1 activity of SPD754, a new NRTI: Results of a 10 day monotherapy study in treatment naïve HIV patients [LB15]. 2nd International AIDS Society Conference on HIV Pathogenesis and Treatment, Paris (13–16 July 2003a

Review of Monotherapy Study Data

	AVX754	TDF	ABC	3TC	AZT	FTC†
7 days	1.1–1.4	0.85	1.0			
10 days	1.18–1.65	1.05				
12 days				1.45		1.7
14 days				1.4*	0.6	
28 days		1.57	1.55			

* 600mg qd

Log reduction in VL observed in ART-naïve patients at subsequent market dose

AVX754 - Conclusions

- Excellent preclinical tolerability profile
- Activity against NRTI-resistant viruses
  - with up to 5 TAMs
  - with and without M184V
- Comparable with best in class in monotherapy
- Likely to address unmet need in ART-experienced patients
- Potential role in ART-naïve patients
- High probability of AVX754 reaching the market
  - Existing data reported consistent with ≥ 80% chance of AVX754 being successful in Phase IIb study
  - All HIV drugs that have successfully completed phase IIb to date have subsequently reached the market
    - there is no reason to suspect this will be different for AVX754
- Estimated to be on market by 2009

AVEXA

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