

Alchemia Limited

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ASX:ACL

Annual General Meeting  
21<sup>st</sup> November 2008

Alchemia

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# Overview

- Founded 1995, listed on ASX (ASX:ACL) Dec 2003
- Small molecule biopharmaceutical company n = 20
  - Generic fondaparinux – expected launch 2009
    - Manufacture and marketing agreement with Dr Reddy's
  - HyACT™ - tumor-targeting technology
    - Successful phase II trial of HA-irinotecan in colorectal cancer
    - IND open for Phase III
    - Multiple oncology applications e.g. mAbs

# Pipeline

Therapeutic area	Drug	Action	Disease/ condition	Stage	Estimated date	Partner
Cardiovascular	Generic fondaparinux	Indirect factor Xa inhibitor	VTE	Preparing to file	FY 2009- ANDA CY 2009- Market launch	Dr Reddy's
Oncology	<i>HA-Irinotecan</i>	Topoisomerase I inhibitor	Colorectal cancer	Clinical - Ph II complete	CY 2008 - IND CY 2009- Phase III	
Oncology	HyACT® antibodies	Various	Cancer	Preclinical	–	

# Events during past year



## Generic Fondaparinux

- Completion of technology transfer to Dr Reddy's
- All technical issues in commercial scale-up now resolved
- Preparation for filing of DMF and ANDA well advanced
- Granting of key US patent for synthetic process

## HyACT/Oncology

- Successful meetings with US and EU regulators
- FDA approval of IND for Phase III registration trial
- New clinical strategy after new data presented at ASCO
- Granting of key HyACT patent in EU
- Formation of Clinical Advisory Board

# Events during past year



## Company restructuring

- 60% reduction in headcount
- 50% reduction in cash burn to \$0.5m per month
- Sufficient cash for 2 years of operations
- Exploring opportunities to extract value from VAST drug discovery platform
  - Main VAST screening library will be completed shortly
  - UQ collaboration has yielded analgesic molecules with novel profiles

Generic fondaparinux

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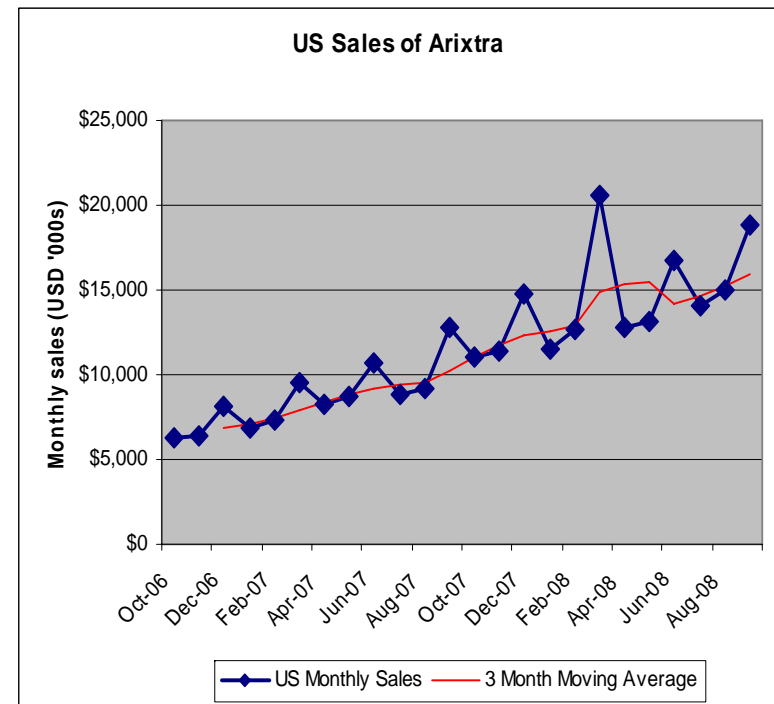
A unique generic opportunity

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# fondaparinux sodium - background

- Marketed by GSK as Arixtra™
  - US MAT to September \$172m (+70%)\*
  - Launched in US in 2003
  - US patents expired 2002
- Factor Xa inhibitor
  - Once-daily injectable anticoagulant
  - Approved for all major indications, 'approvable' for ACS Feb 2007
- US data exclusivity expired
  - EU exclusivity expires 2012



\*Source: IMS Data



# Fondaparinux – unique opportunity

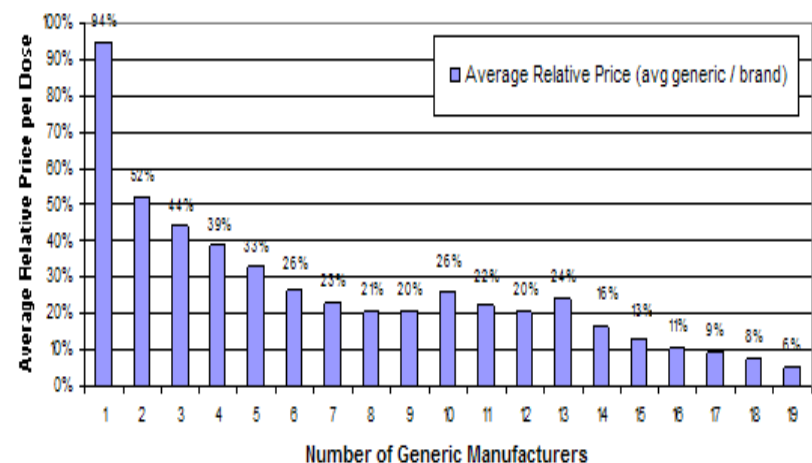


- API very difficult to manufacture at scale
  - Originator (Sanofi) took >10yrs to scale-up synthesis
- Alchemia has developed a novel fondaparinux synthesis
  - Patent protected (granted in US)
  - Successful manufacture at commercial scale
- Approval via ANDA route, paragraph II
  - Fully synthetic molecule
  - Will not face same regulatory issues as generic LMWHs
- Likely to be first, and potentially only, generic
  - No other sources of API identified

# Fondaparinux – market dynamics

- Similar dynamics to Paragraph IV generic filings
  - First generics typically gain 40%+ Rx share
  - Prices remain high
  - Low SG&A costs
- But exclusivity >> 180 days
  - Long lead-time for other generics
  - High cost of entry

Generic Competition and Drug Prices



Source: FDA analysis of retail sales data from IMS Health, IMS National Sales Perspective (TM), 1999-2004, extracted February 2005

# Current status



- API manufactured under exclusive agreement with Dr Reddy's Laboratories, Hyderabad
  - Dr Reddy's is #3 in US for number of approved DMFs
- Partnered with Dr Reddy's Inc. for US market
  - 60% share of profit to Alchemia under certain conditions
  - Minimum 50% share of profit
  - Reddy's has first rights for EU market
- DMF and ANDA in preparation for filing
  - Launch anticipated H2 2009

# Economics of generic fondaparinux

Sales of brand\*\*



Act. 2007 US\$119m

Est. 2008 US\$200m (+67%)

Fcst. 2009 US\$250-300m\*

Sales of generic



Est. 40-50% Rx share

~20% discount to brand

Profit to Alchemia



50%-60% share of profit

= approx 30-35% of generic sales

\*excluding any impact on sales of launch of ACL generic

\*\* based on IMS data

November 08

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# Alchemia

## Alchemia Oncology

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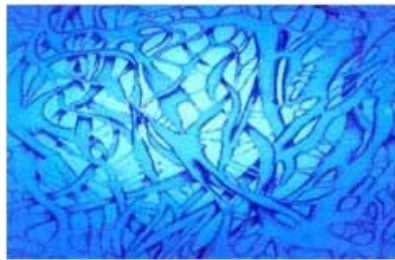
HyACT and HA-irinotecan

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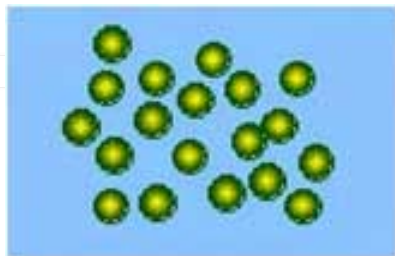


# HyACT<sup>®</sup> Technology Platform

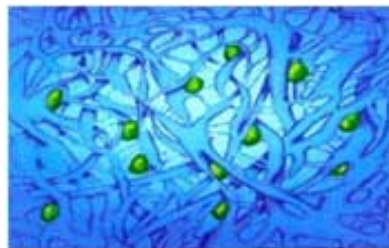
Hyaluronic acid (HA) used to target chemotherapy agents to tumors



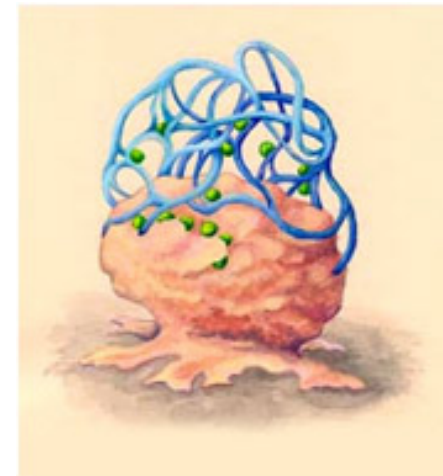
Hyaluronate (HA)



Anti-cancer drug



The drug is formulated within HA matrix.

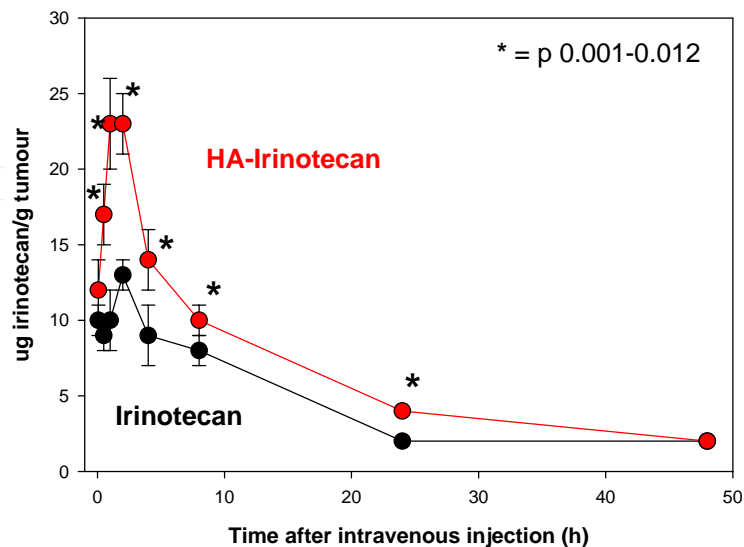


HA selectively binds to cancer cells via HA receptors (CD44) delivering more drug to tumor.

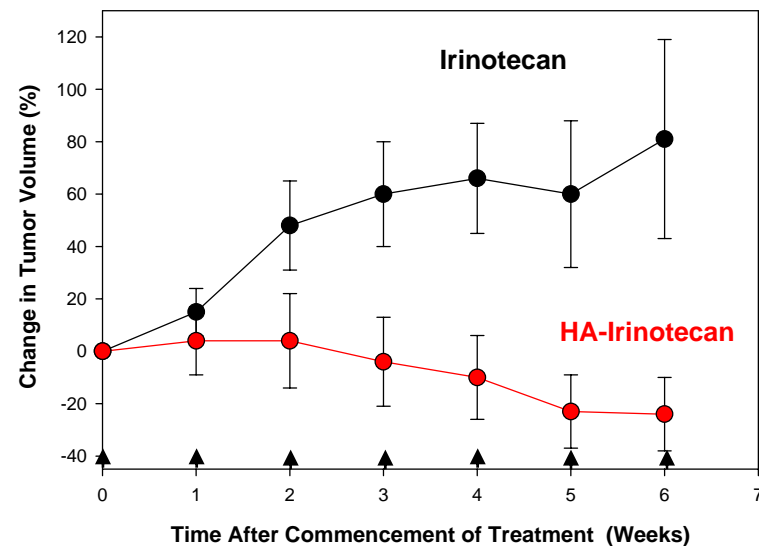
# Preclinical Efficacy of HA-irinotecan

- HA-irinotecan delivers 2-4-fold more drug to the tumor
- HA-irinotecan increases survival in models of human colon cancer

Intratumoral concentration of irinotecan in mice treated with irinotecan or HA-irinotecan



GEO Colon Tumours treated with Irinotecan or HA-Irinotecan



# HyACT Platform



- Tumor targeting through Hyaluronic Acid (HA) receptors
  - Activated CD44 over-expressed in majority of tumor types
  - CD44<sup>+</sup> is an established marker for cancer stem-cells
  - Enhancement of activity dependant on CD44 expression
- Hyaluronic acid is approved for human use
  - Used in eye and knee surgery and as dermal filler
  - Naturally occurring polysaccharide
  - GMP material available at scale from bacterial fermentation
- Enhanced anti-tumor effects seen with multiple agents
  - Water-soluble small-molecule drugs and biologicals



# HyACT – human experience



Test Compound	Patient Population	Number of patients	Safety
<b>Phase I studies</b>			
Hyaluronic acid (HA)	Healthy volunteers	8	√
Hyaluronic acid (HA)	Healthy volunteers	24	√
HA-fluorouracil	Metastatic Colorectal	14	√
HA-doxorubicin	Metastatic Cancers	16	√
HA-irinotecan	Metastatic Colorectal	13	Reduced diarrhea and neutropenia
<b>Phase II study</b>			
HA-irinotecan	Metastatic Colorectal	80	Equivalent to irinotecan

# HA-irinotecan - Phase II trial summary

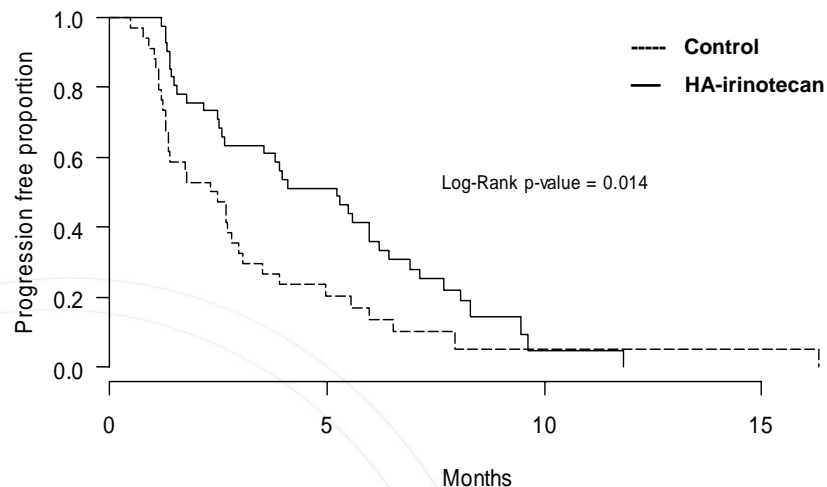
- 2<sup>nd</sup> line mCRC, 5-FU failures (85% FOLFOX), ECOG 0-1
  - 80 patients, 1:1 randomization
    - irinotecan 350mg/m<sup>2</sup> vs HA-irinotecan (350mg/m<sup>2</sup> irinotecan, 1000mg/m<sup>2</sup> HA) every 3 weeks
    - Well matched demographics and prior treatment
  - Significant increase in PFS (+116%, p=0.017)
  - Significant increase in TTF (+123%, p=0.007)
  - Significant increase in disease control by RECIST (76% vs 46%, p=0.053)
  - Trend towards increase in OS (10.0m vs 8.0m, p=0.2)
- No difference in toxicity
- No difference in plasma PK of irinotecan or SN-38
- No difference in dose intensity per patient per cycle

# HA-irinotecan Phase II - Efficacy



- Significant increase in progression-free survival (5.2 vs 2.4 months)
- Significant increase in time to treatment failure (4.0 vs 1.8 mths)

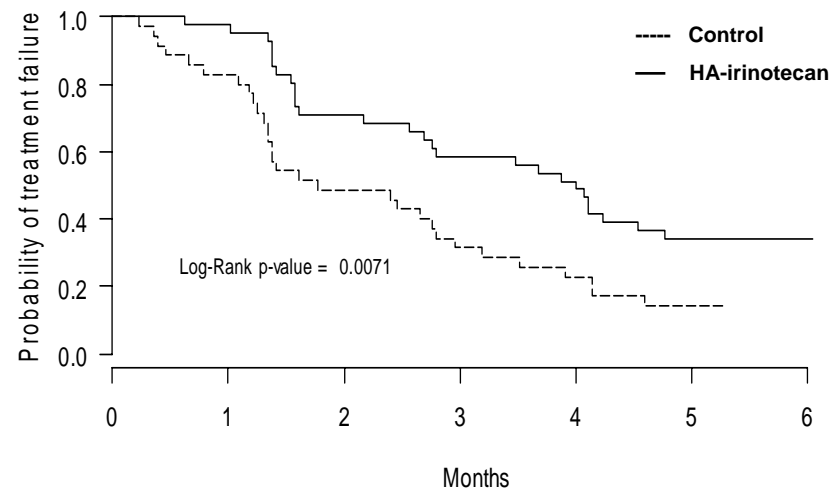
Progression-free survival (PFS)



Hazard ratio 0.46 p= 0.0107

After adjustment for prognostic factors

Time to treatment Failure (TTF)



Hazard ratio 0.49 p= 0.024

After adjustment for prognostic factors

# Major treatments for mCRC

## 1<sup>st</sup> Line mCRC

**FOLFOX/CAPOX  
+/- Avastin<sup>®</sup>**

## 2<sup>nd</sup> Line mCRC

**FOLFIRI**

**PFS ~2.5m**

**Irinotecan +  
Erbitux<sup>®</sup>**

**PFS ~4.0m**

## 2<sup>nd</sup> Line after CRYSTAL

**Kras mutants**

**FOLFIRI**

**PFS ~2.5m**

**Kras wild-type**

**Irinotecan +  
Erbitux<sup>®</sup>**

**PFS ~6.0m**

# HA-irinotecan - Phase III plans



- 505(b)(2) route, single pivotal trial required
- IND open for HA-irinotecan + Erbitux vs irinotecan + Erbitux
  - 740 patients, 1:1 randomization, blinded
  - 2<sup>nd</sup> line mCRC, K<sup>ras</sup> wild-type, EGFR<sup>+</sup>
- Opportunity after ASCO for FOLFIRI vs FOLF(HA)-iri\*
  - Approx. 40-50% patients ineligible for Erbitux 2<sup>nd</sup> line
  - 350 patients, 1:1, blinded, 2<sup>nd</sup> line mCRC
  - Smaller, shorter, lower cost study

# Alchemia - Financial Summary



- Cash on hand Sep 2008      A\$ 12.3 million
- Cash burn after restructure      A\$ 6.0 million pa
  
- Capital structure
  - Ordinary shares (06/08)      160 million
  - Unlisted options      7.5 million
  - Top 20 holders own      >65 %
  
- Current price      A\$ 0.13
- Market Cap      A\$ 22m

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# Summary

- Preparing DMF and ANDA filing for fondaparinux
  - Launch anticipated in H2 2009
  - Significant revenue opportunity
- Preparing for pivotal Phase III trial of HA-irinotecan
  - Opportunity to commence trial in H1 2009
- Multiple opportunities for HyACT technology
  - Supergenerics
  - Lifecycle management
  - Antibodies
- 2 years cash, sufficient to reach fondaparinux revenues