

# Alchemia



Alchemia Limited  
(ASX:ACL)

*January 2014*

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- Publicly-listed, (ASX: ACL) commercial and late-stage biopharmaceutical drug development company
- Lead oncology asset, HA-Irinotecan, in ongoing pivotal Phase III trial for mCRC with results expected by 2Q CY2014
- Robust pipeline leveraging HyACT and VAST platforms
  - HyACT generating strong oncology programs:
    - Pivotal phase III mCRC drug trial nearing completion
    - Phase II oncology trials ongoing (SCLC & mCRC)
  - VAST small molecule drug discovery platform
- Fondaparinux, FDA approved difficult-to-manufacture sterile injectible product on market, generating free cash flow
- Multiple industry partners
  - Dr Reddy's Laboratories
  - Merck Serono
  - AstraZeneca
- Strong financial position – funded through PIII

# Pipeline



DVT is deep vein thrombosis  
PE is pulmonary embolism

mCRC is metastatic colorectal cancer  
SCLC is small cell lung cancer



**Cardiovascular**



**Oncology**



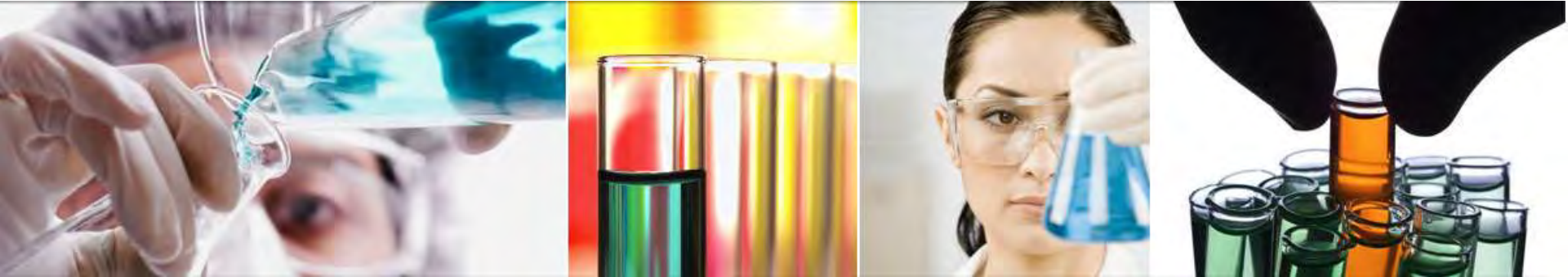
**Various Therapies**

- **Oncology (HyACT assets)**
  - Results of pivotal HA-Irinotecan Phase III trial 1H CY2014
  - Subsequent filing of NDA for HA-Irinotecan for mCRC
  - Potential partnership for HA-Irinotecan
  - Potential launch of new HyACT-enhanced chemotherapy clinical trials
  
- **Fondaparinux**
  - Stabilization and potential growth in fondaparinux profit share
  - Potential manufacturing cost improvements for fondaparinux
  - New regulatory approval and launches in new markets for fondaparinux
  
- **VAST**
  - Potential for additional VAST collaborations with pharmaceutical companies

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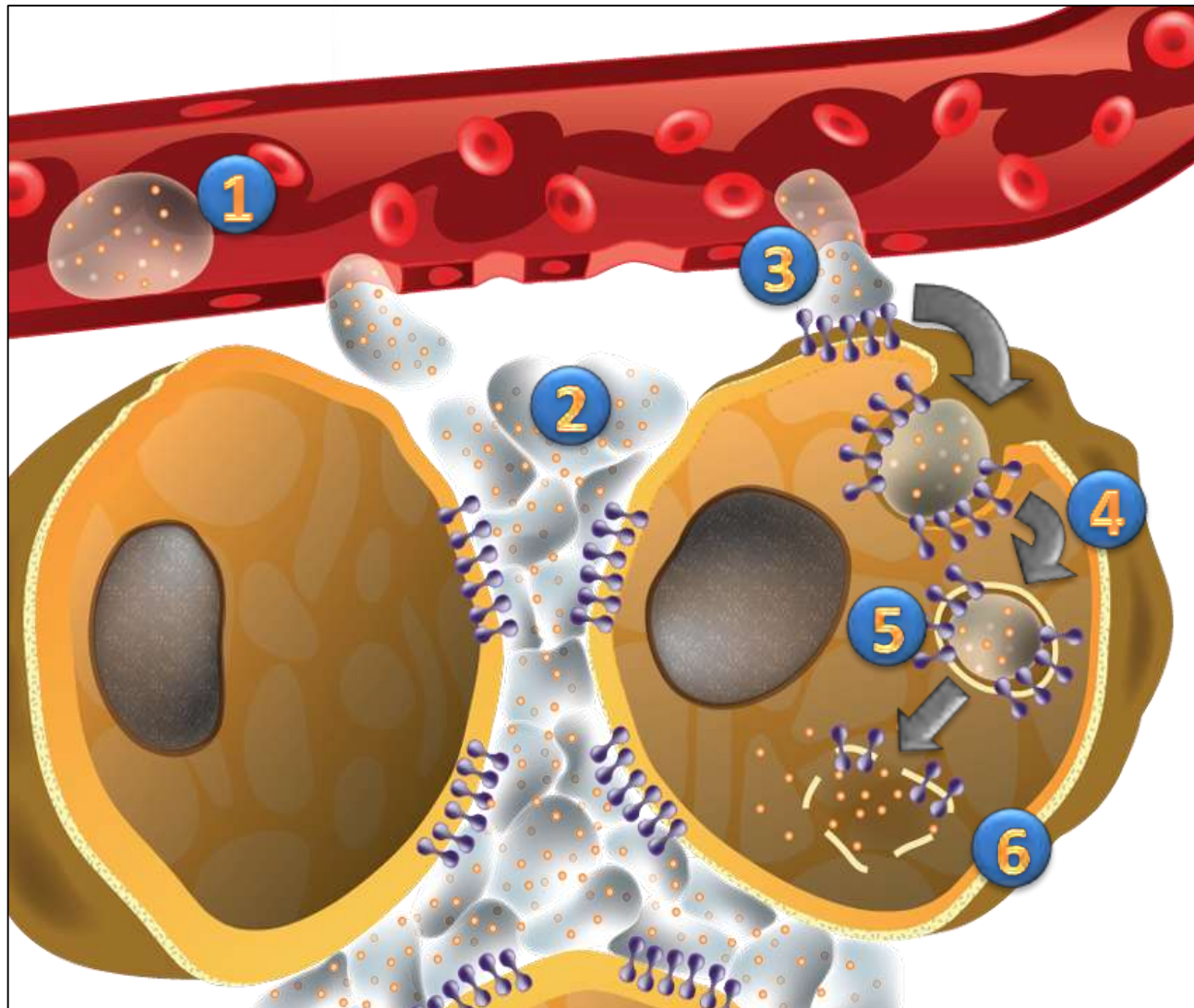
# Drug Development and Discovery Platforms - HyACT, VAST

# Alchemia



- Platform formulation technology with potential to generate additional assets across broad range of oncology targets, including chemotherapies and targeted biologics
- HyACT targets tumor cells through unique dual mechanism of action
  - Drug depot formation around cancer cells increasing the concentration and exposure to drug
  - Hyaluronic acid directly binds to cancer target CD44, triggering internalization of HyACT drug resulting in up to 1000x more anti-cancer drug in tumor cells
- Additive to existing chemotherapeutics without altering their administration or safety
- Could be used for many different chemotherapies and targeted therapies
- HyACT drugs pose lower risk of development compared with a “new chemical entity,” while still targeting similar pricing
- Lead HyACT product candidate, HA-Irinotecan, is in a pivotal Phase III clinical trial

# HyACT Dual Mechanism of Action

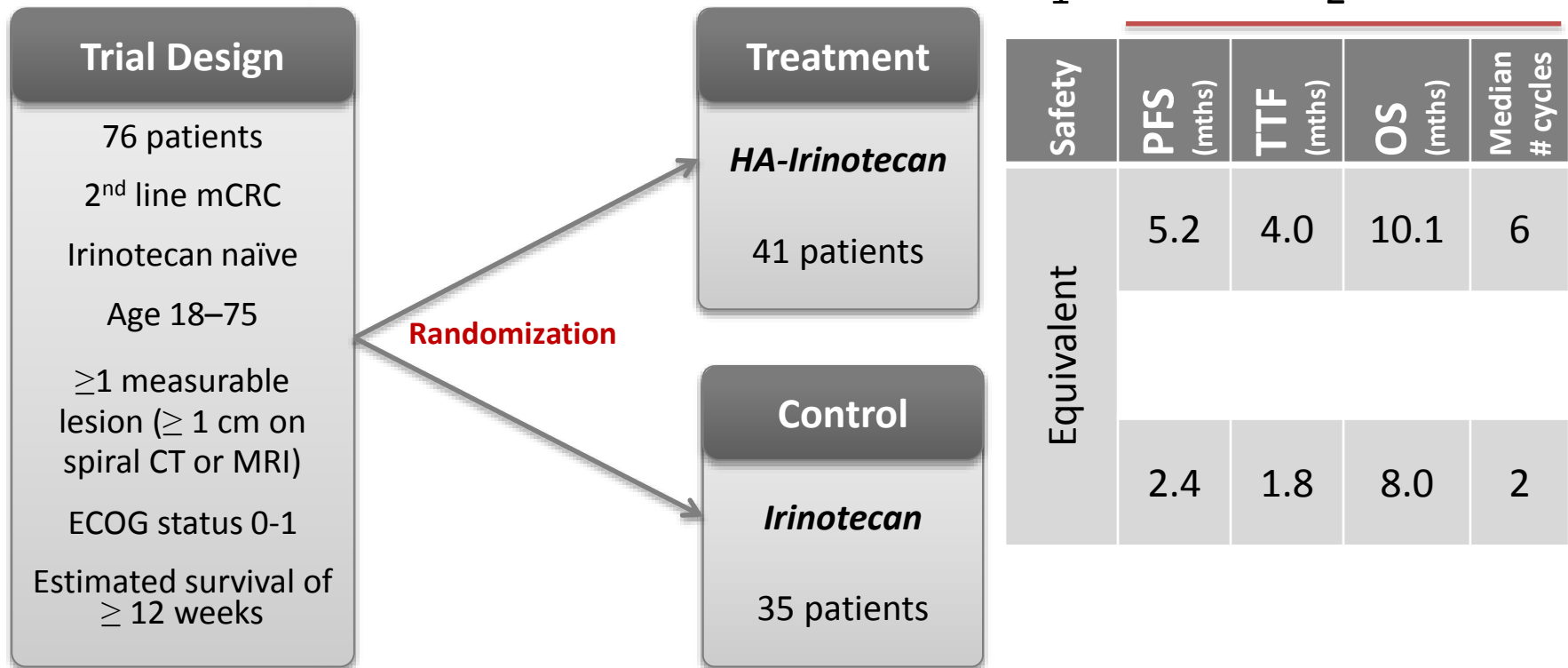


- 1 Entry to tumor environment through leaky vasculature
- 2 HyACT-targeted drug forms 'depot' in tumor microenvironment
- 3 Binds with high avidity to activated CD44
- 4 Binding induced endocytosis
- 5 HyACT-targeted drug held within lysosome
- 6 Breakdown of HyACT and vesicle to release drug internally



- First drug candidate to be developed using HyACT development platform, currently nearing completion of pivotal Phase III clinical trial (end of 1H CY2014)
- Phase III Alchemia-sponsored trial: patients with 2nd/3rd line metastatic colorectal cancer (mCRC)
  - Pivotal Phase III trial completion estimated by mid-2014
  - FDA submission expected 2H CY2014 utilizing 505(b)(2) pathway
  - Approval expected 2015 (US), 2016 (EU)
- Tumor-targeted version of existing chemotherapy, irinotecan
- Irinotecan marketed by Pfizer as Camptosar®; peak sales US\$970M prior to patent expiry (US) in 2008
- Investigator-sponsored phase II trials: Small Cell Lung Cancer (SCLC) & mCRC in combination with Erbitux®
  - Show effect of HA-Irinotecan on cancer stem cells
  - Show safety of HA-Irinotecan with Erbitux
- Proof of concept for HyACT platform tumor-targeting technology

*HA-Irinotecan provided 12 week extension in PFS with no change in safety, dosing schedule or PK compared with irinotecan alone*

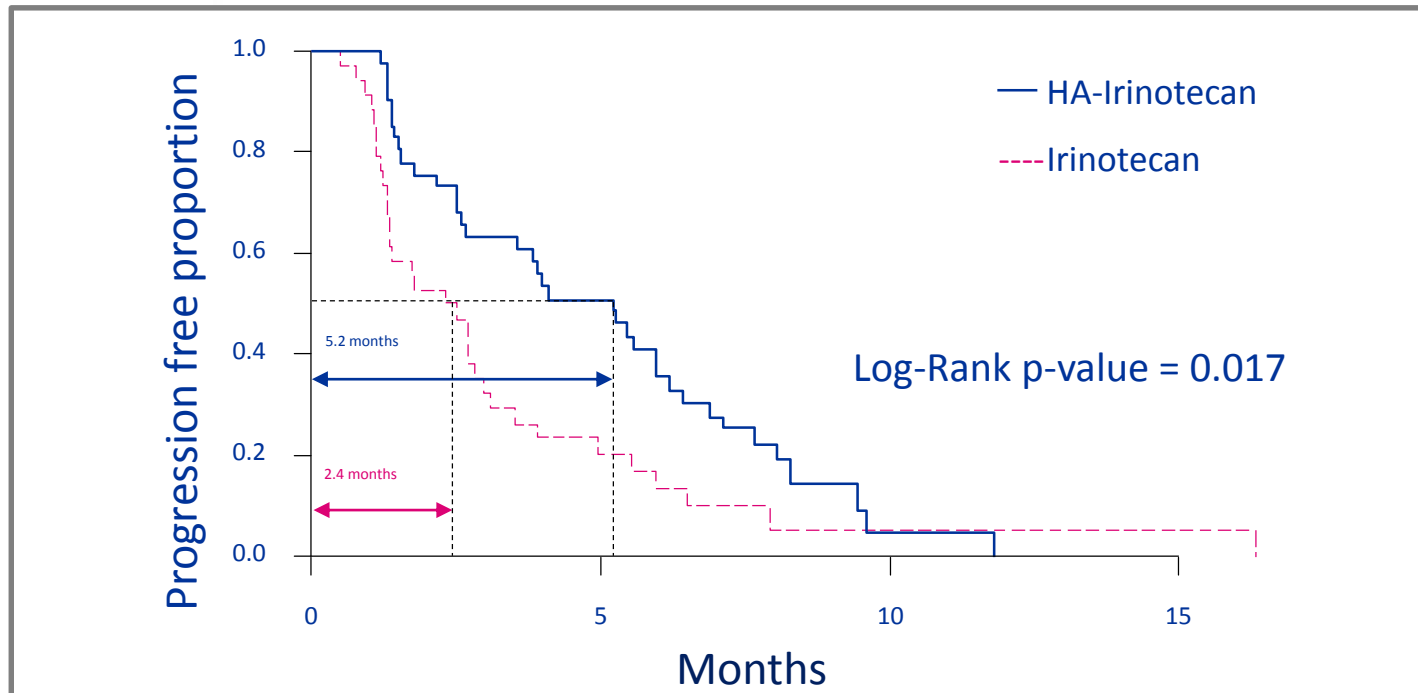


*Cancer Chemotherapy Pharmacology. 67:153-63*

# Phase II Head-to-Head Results Encouraging

(Trial Completed)

Statistically significant increase in Progression Free Survival (PFS) of 5.2 vs. 2.4 months ( $p=0.017$ )

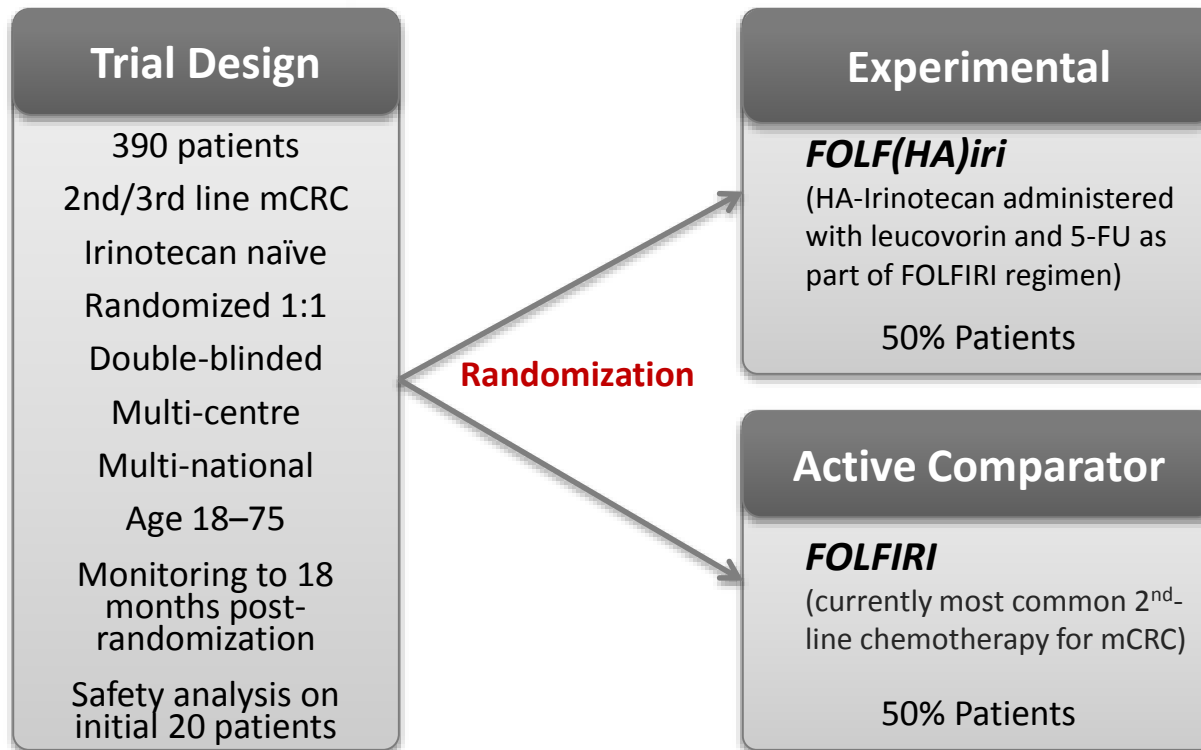


## ➤ Other Key Results

- Hazard ratio for PFS of 0.56 ( $p=0.019$ )
- Increase in DCR (76% vs. 46%,  $p=0.053$ )
- Trend towards increased overall survival (10.1 vs. 8 months) ( $p=0.196$ )
- Longer Time to Treatment Failure (4.0 months vs. 1.8 months) ( $p=0.007$ )
- HA-Irinotecan patients treated for significantly more cycles (six vs. two) ( $p=0.005$ )
- No significant increase in toxicity was observed

- HA-Irinotecan effective and safe in 2nd line patients
- No difference in toxicity profile versus irinotecan
- Observations for HA-Irinotecan patients when compared with irinotecan:
  - Significant increase in time to disease progression
  - Had significant increase in time to treatment failure
  - Had demonstrably improved tumor-control data (RECIST, Choi)
  - Were able to receive more drug via increased cycles of therapy
  - Had trend toward better overall survival

*Trial powered to detect  $\geq 6$  week extension in PFS.  
415 patients fully enrolled, expected completion 2Q CY2014*

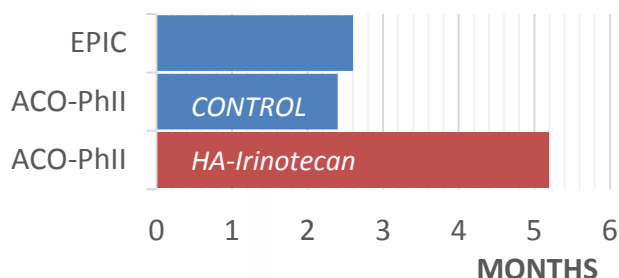


**ClinicalTrials.gov Identifier:  
NCT01290783**

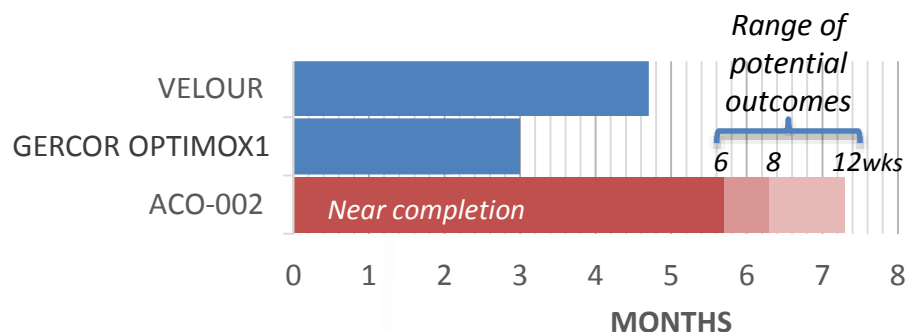


## HA-Irinotecan performance in clinical trials compared with standard chemotherapy

2<sup>nd</sup>/3<sup>rd</sup> Line mCRC Irinotecan Single Agent PFS



2<sup>nd</sup> Line mCRC FOLFIRI Regimen PFS



- 12 wk (116%) improvement in PFS observed in Phase II study (single agent HA-Irinotecan)
- Phase III target improvement of 8-12 wks would be a significant (46-70%) improvement in efficacy
- HA-Irinotecan could be used as a 'drop in' replacement for irinotecan as part of FOLFIRI
- Compelling choice for clinicians when considering which chemotherapy regimen to use

# HA-Irinotecan – Targeting Major Market

- Target endpoint is 8 - 12 week improvement in PFS
- PFS improvements from other commercial pharmaceuticals:
  - Avastin – (2nd line mCRC) PFS improvement of 10.5 weeks
  - Erbitux – (1st line mCRC) PFS improvement of 6.5 weeks
- Peak sales estimates for HA-Irinotecan:
  - 8 week PFS generates peak sales estimate of \$465M
  - Further, expanded use (1st line mCRC) of HA-Irinotecan generates estimated peak sales over \$1.5B (would include additional trial(s))
- Expect up to 90% gross margin for US market (price depending)



2012 total sales of over \$6B (includes other cancers)\*



2012 total sales of \$1.85B (includes other cancers)\*

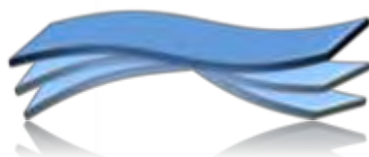
\*Source: Bloomberg

- Small Cell Lung Cancer (SCLC)
  - 26 patients out of targeted 40 patients recruited to investigator-sponsored Phase II trial
    - 2 trial sites in Australia
  - Primary endpoints are safety and clinical activity
    - Safety measured by the incidence of grade 3 or 4 toxicity
    - Clinical activity of HA-Irinotecan combined with carboplatin
  - Early encouraging signs of clinical activity of HA-Irinotecan combined with carboplatin
  
- ‘CHIME’ Trial: Cetuximab Hyaluronic Acid Irinotecan In Metastatic Colorectal Cancer
  - Joint funded, investigator sponsored Phase II trial using HA-Irinotecan in FOLFIRI regimen administered with Merck Serono’s Erbitux
  - Primary endpoint is safety, with several efficacy secondary endpoints

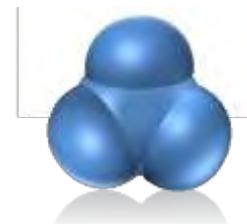


- Licensing activities underway
  - Potential partnership deal for HA-Irinotecan
  - There are very few late stage oncology clinical assets available for licensing
  - Licensing would enable further de-risking
  
- HA-Irinotecan Phase III trial important milestones
  - Top line data projected 2Q CY2014
  - Submit New Drug application to both USA and Europe regulatory agencies 2H CY2014
  - US: Potential approval 2H CY2015
  - Europe: Potential approval 1H CY2016

**Classical pharma small molecule shapes**



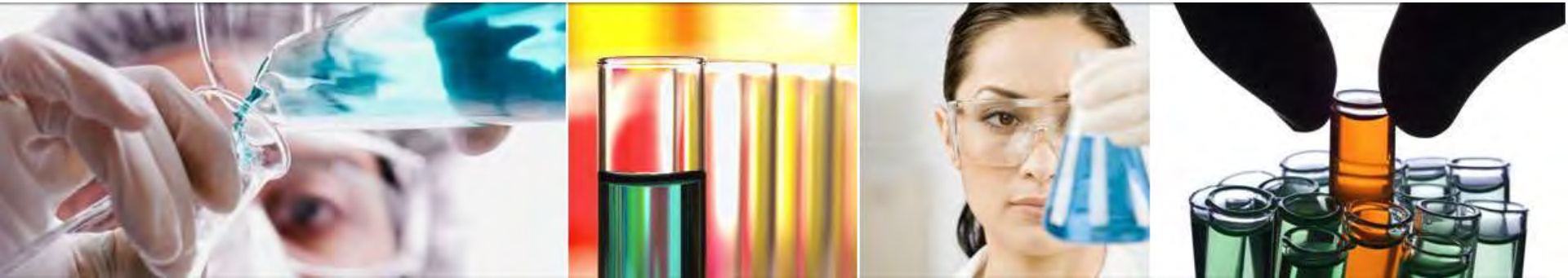
**VAST shapes**

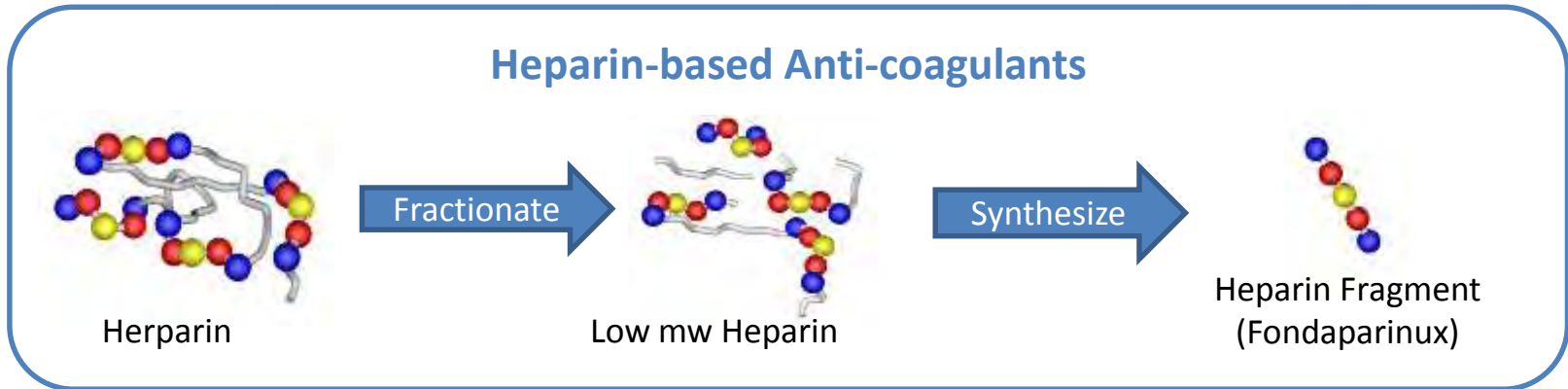


- Drug discovery technology with an array of diverse compound shapes
- Proven platform, enabling the development of a commercial manufacturing process for fondaparinux
- Financially efficient with a focus on productivity through partnerships and grants
- \$240M strategic collaboration with AstraZeneca (April, 2013)
- Grant funding to support internal collaborative drug discovery programs
- Collaborations with WEHI (oncology), UQ (pain) and MIPS (allosteric modulation)

# Generic Fondaparinux

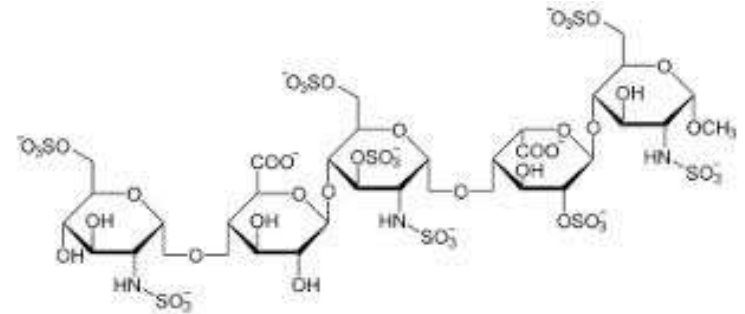
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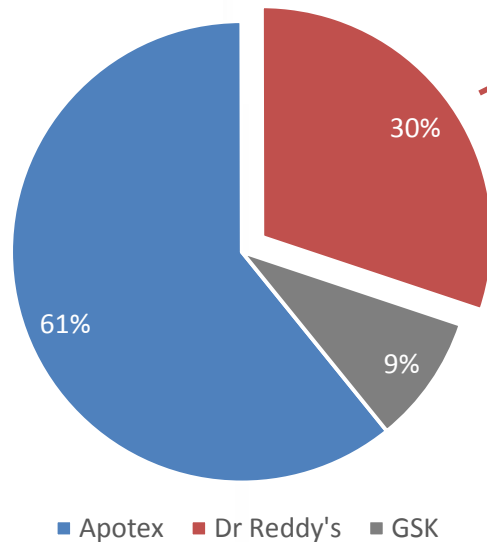


## **Fondaparinux: Not a typical generic**

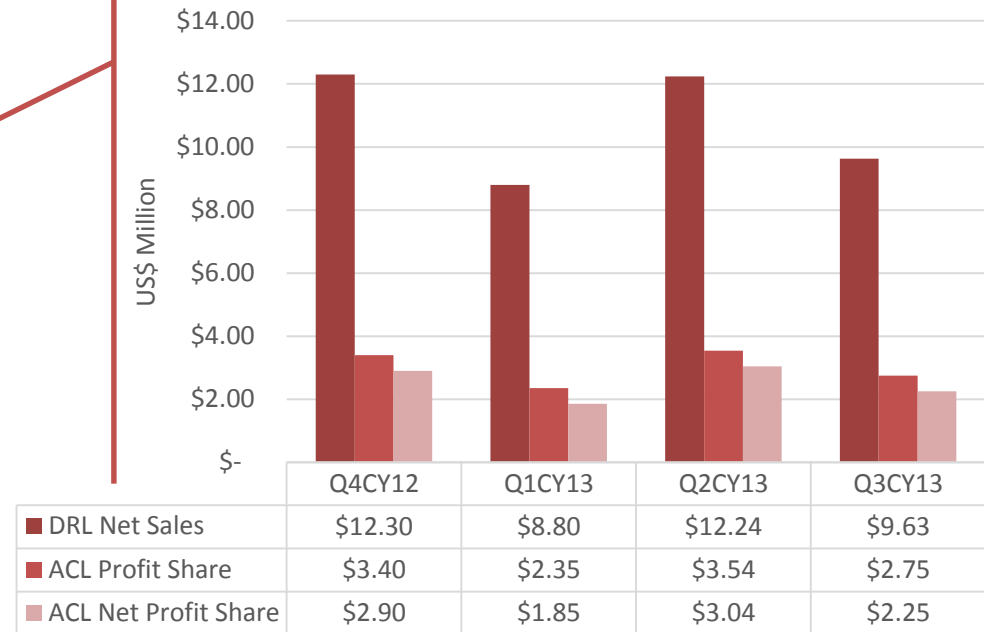
- Very difficult to synthesize: 60+ steps
- Even more difficult to scale up to production level
- Patent protection for synthetic route – expiry 2023
- Know how protection on scale up manufacturing – no expiry
- Sole independent generic on the market alongside Arixtra<sup>®</sup> (GSK, now Aspen) & Apotex Authorised Generic



Market Share by Volume  
(Quarter ending September 30, 2013)



Profit Share to Alchemia



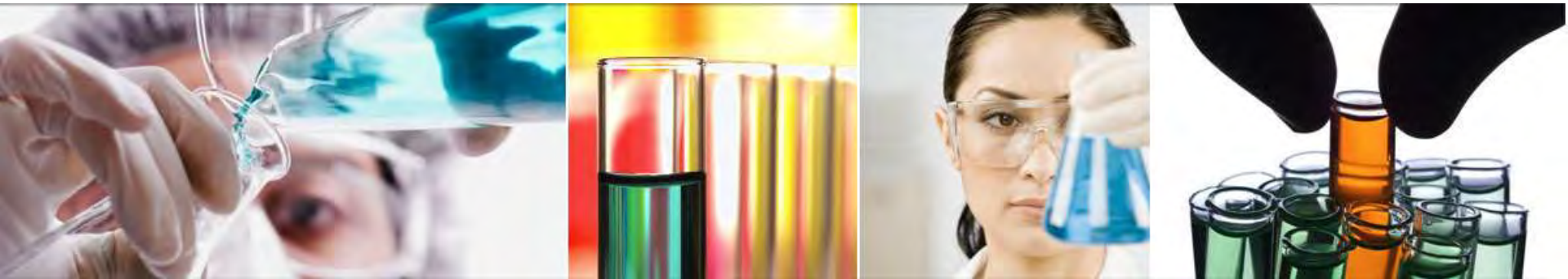
- ~30% market share (total retail + institutional)
- ~50% market share (retail)
- Profit share of between \$2.35M and \$3.40M to Alchemia per quarter
- September 30, 2013: Aspen acquired rights to GSK's injectable thrombosis brands, including Arixtra, and its manufacturing facility for \$970M

\* Source: IMS

- Potential growth/stabilization of profit share
  - Continued competitiveness by Dr Reddy's U.S. sales force
  - Improvement in manufacturing costs
    - Economies of scale and process improvements
    - Expiry in December 2014 of Alchemia's agreement with Dr Reddy's to contribute \$0.5M per quarter for process and production improvements (as announced September 2012)
  - Profit share arising from ROW sales
  - Potential changes in market dynamics
  
- Pursuing options to best create shareholder value, including assessing the potential monetization of fondaparinux
  - De-risks assets and provides potential upside for shareholders

# Corporate Summary

# Alchemia



➤ **Charles Walker – Chief Executive Officer**

- Appointed CEO February, 2013, following two years serving as Alchemia’s Chief Financial Officer
- 20 years of life sciences expertise, beginning career in pharmacology in the UK
- 10+ years experience in corporate finance, executive over 40 successful corporate transactions
- Co-founded life science investment banking firm in UK sold to Nomura International plc in 2005

➤ **Thomas Liquard – Chief Operating Officer**

- Joined Alchemia in 2013; Responsible for commercial and corporate development
- 10+ years of life sciences commercial experience, including 7 years at Pfizer, Inc. in New York
- Deep experience across the pharma industry value chain, from clinical development to late stage commercialization, and across multiple therapeutic areas including oncology
- Experienced in business development transactions (licensing, M&A), new product planning, portfolio development and commercialization for both 505(b)(2) and NCE assets

➤ **Tracey Brown, PhD – Chief Scientific Officer, Vice President of Oncology**

- Joined Alchemia in 2006 as a result of Company’s acquisition of Meditech Research Limited
- 30 years international experience in both translational research and drug development where she has taken drugs from conception through to marketing approval
- Inventor of HyACT platform and has been responsible for all pre-clinical, clinical and regulatory activities.

➤ **Wim Meutermans, PhD - Head of Discovery**

- Joined Alchemia in 2000 and directly responsible for all small molecule drug discovery projects
- 20 years of experience in all non-clinical aspects of drug discovery and one of key inventors of VAST discovery platform
- Obtained PhD from Katholieke Universiteit Leuven in Belgium

➤ **Imran Ahamed, CPA – Group Financial Controller**

- Appointed Group Financial Controller in February 2013, following one year as Alchemia Oncology’s Financial Controller
- Brings 20+ years of accounting and finance experience to Alchemia, having held senior finance positions in investment banking, manufacturing, retail and wholesale sectors in Asia, Southern Africa, the Middle East and Australia



## ➤ **Nathan Drona – Chairman**

- Brings 15 years of experience across investment banking, most recently as Managing Director of Challiss in New York and Sydney.
- Has executed 25 global banking and M&A engagements in biotech related fields, leading to the award of the “Pharmaceutical Buy-Side M&A Advisor of the Year” by Frost & Sullivan in 2005.
- Previously spent two years as Chairman of the Board of Directors of ASX-listed Avexa, where he oversaw the Phase III clinical trial of a nucleoside analogue with over 300 patients in 130 specialist HIV centers in 15 countries.

## ➤ **Tracie Ramsdale, PhD**

- One of original founders of Alchemia and has led development as General Manager and CEO from 1998-2007; board member since 2003
- Holds Master of Pharmacy from Victorian College of Pharmacy and a PhD in Biochemistry from the University of Queensland.
- Previously served as Principle Investigator and Commercial Manager of the Centre for Drug Design and Development at University of Queensland, prior to which she held research appointments at Victorian College of Pharmacy and Bond University.
- Currently an adjunct Professor at the School of Chemical and Molecular Biosciences, University of Queensland, a member of the Australian Federal Government's Advisory Council on Intellectual Property and a Fellow of the Australian Academy of Technological Sciences and Engineering.

## ➤ **Susan Kelley, MD**

- Served on the Board of Directors of ArQule, Inc. since April 2011.
- Previously experience at Bayer Healthcare Pharmaceuticals and Bayer-Schering Pharma in Germany and the United States, serving as Vice President, Global Strategic Drug Development, Cancer; and Vice President, Global Clinical Development and Therapeutic Area Head-Oncology.
- Prior to that, served as Chief Medical Officer of the Multiple Myeloma Research Foundation/Consortium.
- Most recently served as an independent consultant to the pharmaceutical and biotechnology industries in the field of oncology drug development and strategy.

## ➤ **Tim Hughes**

- Brings 30+ years of experience in investment banking and fund management.
- Most recently served as Investment Counsel at NGS Super and as a commentator on economics and finance for a News Corporation paper.
- Previously spent 13 years as a senior executive at Rothschilds as a board director and executive committee member.

○ Market capitalization	A\$178M
○ Current Share price (as of Jan 10th)	A\$0.55
○ Cash on hand at Sept 30 <sup>th</sup>	A\$10.0M*
○ No debt	
○ Capital structure	
- Ordinary shares outstanding	324,338,515
- Options outstanding	7,177,500
- Fully diluted	331,516,015
Substantial shareholder (Orbis/Allan Gray)	18.2%
Management and directors (excluding options)	1.1%

*\* Note that this sum excludes A\$8.8M received as part of the R&D Tax incentive program in October 2013*

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  - Results of pivotal HA-Irinotecan Phase III trial 1H CY2014
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  - Potential partnership for HA-Irinotecan
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- Fondaparinux
  - Stabilization and potential growth in fondaparinux profit share
  - Potential manufacturing cost improvements for fondaparinux
  - New regulatory approval and launches in new markets for fondaparinux
  
- VAST
  - Potential for additional VAST collaborations with pharmaceutical companies

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- Drug development company entering transformative 2014
  - Strong financial position
  - First product already developed, launched and generating free cash flow, currently funding internal R&D
  - HA-Irinotecan approaching pivotal trial read out and potential filing in the US
  - Platform technologies proven to deliver new products
  - Established global pharma partners
- Significant near-term milestones, including Phase III data read-out for HA-Irinotecan in mCRC and potential for third major partnership deal (HA-Irinotecan)

# Alchemia



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