
Cellomatics
BioSciences
Our expertise, your discovery


KRISANI Bio
Beyond Innovation

Highlights

- Procysbi (Cysteamine delayed release formulation) of Raptor Pharma is an approved drug by the US FDA. Horizon Pharma had acquired Raptor Pharma for USD 800 million; September 2016.
- Cysteamine (Raptor Pharma) Cost of Therapy: $2,091.60/day, $62,748/30 days, $752,976 - year
- CB-ND-002: US Patent granted, Strong Patent Protection: 2032
- With significant data already available for the components of CB-ND-002, we believe this New Molecular Entity (NME) could qualify for the 505(b)(2) approval process which would result in a shorter time to market, less development cost, and a lower risk of failure than the standard approval process.
- CB-ND-002 is projected to have the better efficacy, bio-availability and safety profile compared to the marketed products and recently approved by the US-FDA. Utilizing the pharmacologically active endogenous molecule will enable the approved therapeutic to enhance the therapeutic pharmacokinetic profile, obtaining the similar therapeutic effect with the lower dosage and thereby alleviating the side effect profile
- Significant value inflection and out-licencing opportunity already being explored after completing a dosage ranging pharmacokinetic study and proof-of-concept trial
- Strong IP: composition-of-matter and use patents obtained; multiple layers of IP (composition of matter, method of use, formulation, process patents)

Strengths of Cellomatics BioSciences – Krisani Biosciences Collaboration -

- Highly De-Risked Business Model
  - Rx business focused on large unmet medical and market needs with reduced risk and high reward I.P backed product design and development
  - The product developed has the ability to qualify for 505(b)2 approval process and therefore requires low investment, less time frame for development, low risk of failure, less development cost and high reward
- Highly experienced team comprising entrepreneurs and leading industry experts including inventors – right blend of experience and energy

Opportunity

- **Unique Value Proposition**
- **Overview of KrisaniBio**
- **New Drug Discovery**

Our Unique Proposition -

- Cellomatics BioSciences and KrisaniBio collaboration seek to significantly enhance the value proposition of new drug discovery in different unmet need therapeutic areas:

  - Proprietary and Innovative Platform based drug discovery and development
  - Designed & Developed I.P. backed Portfolio of novel potential therapeutic molecules
  - Drug candidates resulting have lower regulatory hurdles and mitigate the risk of product registration and launch
  - Cost and time to develop products is significantly reduced due to the use of existing and established molecules in some of our portfolios

Opportunity

- Unique Value Proposition
- **Overview of Cellomatics BioSciences and Krisani Biosciences**
- New Drug Discovery

Cellomatics BioSciences – An Overview

- Cellomatics Biosciences Ltd. is a laboratory-based Contract Research Organisation (CRO) specialised in Oncology, Immunology/Inflammation, and Respiratory.
- We provide bespoke pre-clinical/early discovery phase laboratory services to support academic groups, pharmaceutical and biotechnology companies in their R&D studies and biomarker research.
- The Company
  - Founded in 2015 and Privately owned
  - Operating out of Biocity, Nottingham
  - Experienced Management team with track record of delivering complex scientific projects and peer reviewed international publications
  - Completed over 50 successful scientific projects in collaboration with over 20 sponsors
  - Links with leading UK Universities
  - Fully serviced laboratory with Specialised personnel
  - National and International partners

About Us

Vision

Integrated *in vitro* testing; from experimental conception to project delivery

Mission

- To revolutionise drug discovery research by providing integrated, cost-effective laboratory services including assay design consultancy, logistics support, bespoke high quality assay development/validation and data analysis.
- To be a responsible and trusted laboratory-based CRO partner with Quality, Flexibility, Reliability and Customer support as our indispensable asset.

Our Senior Scientific team

Dr Shailendra Singh PhD, MBBS, MRes
Founder and Chief Executive Officer

- Over 15 years of experience in research and development
- Experience in the management of Technical team and directing the laboratory operations at the strategic and commercial level.
- Strong track record in conceptualising, designing, implementing and setting up R & D Facilities
- Experience in fund-raising and collaborative ventures with industry and Biotech.

Prof David Lambert PhD, BSc
Non-Executive Director

- Over 30 years of experience in research and development
- Professor of Anaesthetic Pharmacology – University of Leicester
- He has ~250 publications (excluding abstracts) with h-index 35. Publications include book in 3rd edition and one patent.
- Awarded Humphry Davy medal, an eponymous chair and Fellowship by election by Royal College of Anaesthetists.

Opportunity

- Unique Value Proposition
- Overview of Cellomatics BioSciences and Krisani Biosciences
- New Drug Discovery

New Drug Discovery Pipeline

- **Nephropathic Cystinosis** -
  - Prodrug - Cysteamine of EPA
    - CB-ND-002 (4 potential indications – Nephropathic cystinosis, Huntington's Disease, NASH, Radiation Sickness)

CB-ND-002

Nephropathic Cystinosis

Orphan Category: Nephropathic Cystinosis

Description

- Nephropathic cystinosis (NC) is a genetic error of metabolism disabling the mechanism for clearing the amino acid cystine, a breakdown product of cellular proteins. This results in an accumulation of cystine crystals in all organs and tissues.
- Condition is usually diagnosed in early childhood when patients exhibit poor growth, vision problems (photophobia) and specific kidney problems (called Fanconi syndrome) that result in increased urination, thirst and dehydration. If untreated, NC destroys major organ systems including the kidneys, eyes, liver, muscles, pancreas and the brain. Additional complications include muscle wasting, poor growth, difficulty swallowing, diabetes and hypothyroidism.

Incidence

- NC is a rare disease with an incidence estimated to be 1 case / 100,000-200,000 living births. It is estimated to have around 500 patients in US and 2,000 worldwide with therapy cost of ~$750,000 per annum

Therapy & Reactions

- Cysteamine therapy may delay and/or prevent kidney transplant and other clinical manifestations of disease. Goal of cysteamine treatment of NC is to reduce cystine levels in cells. However, patient compliance is challenging due to frequent dosing and gastrointestinal side effects.

CB-ND-02: Design Concept

PRODRUG OF CYSTEAMINE AND EPA

- **CYSTEAMINE:**
  - Approved Molecule by the US-FDA and EMA for the treatment of Nephropathic Cystinosis
  - Extensive research has been conducted at Harvard Medical College and MIT research labs to investigate the Cysteamine potential in NASH and Huntington's Disease
  - Has the potential for the therapeutic treatment of NASH

- **EPA (Component of Omega 3)**
  - GRAS listed
  - Protective effects on the neurons
  - Prevents Inflammation and ROS generation

CB-ND-02: Studies Conducted

- Chemical Synthesis Process and Other Analytical Parameters standardization efforts for Optimization were ongoing for DMF & CMC filings
  - Obtained 99.98% pure compound with Robust Stability (In-house and GVK BIO)

- Selective Evaluation of the compounds in animal model to Investigate the Prodrug behavior and PK

- Preliminary safety analysis was also conducted
  - All the animal studies were conducted at Charles River Labs, UK and Finland

CB-ND-02: PK STUDY

Summary of Study

- The aim of the study was to evaluate pharmacokinetic profile of plasma and brain concentration of KB-ND-002, Cysteamine and Eicosapentaenoic acid in CD-1 male mice
- Reference compounds are administered by oral gavage (10ml / kg) per oral.
- Mice in each experimental group are treated for PK analysis for the following 10 time points:
  - 0, 15, 30, 60 min, 1.5, 2, 3, 4 and 5 hrs

Test System

Species / Strain	CD-1 Male Rats
Source	Charles River Labs, USA
No. of animals	160
Weight	20 – 30g

- Parameter estimation was performed on mean plasma and brain Eicosapentanoiec acid, KB-ND-002 and Cysteamine concentration vs nominal sampling time values from 3 animals per timepoint. Parameter estimates were derived for each analyte, and matrix using a non-compartmental approach in WinNonlin Enterprise version 5.2.1 (Pharsight Corp., Mountain View, California, USA).
- A WinNonlin regression analysis was performed with each concentration vs time profile reviewed by means of visual inspection to appropriately characterize the apparent terminal elimination phase and optimize the reliability of the lambda-z estimation.

CB-ND-02: PK STUDY RESULTS

- The Cmax study results indicated that higher level for CB-ND-002 at 112 mg/kg dose as against Cysteamine, the current standard of care
- Even the Terminal Elimination Half Life (T1/2) for CB-ND-002 was higher at 16.17 hrs compared to Cysteamine's 6.53 hrs

Matrix	Treatment (Group)	Dose (mg/kg)	Cmax (ng/mL)	Cmax/D (ng/mL)/ (mg/kg)	Tmax (h)	AUC(0-t) (ng.h/mL)	AUC(0-t)/D (ng.h/mL)/ (mg/kg)	AUC(0-inf) (ng.h/mL)	AUC(0-inf)/D (ng.h/mL)/ (mg/kg)	T1/2 (h)	Rsq
Plasma	CB-ND-002 (Group 1)	60	318	NC	5.00	806.6	NC	NC	NC	NC	NC
	CB-ND-002 (Group 2)	112	244	NC	0.25	724.6	NC	4403 #^o~+	NC	16.17 #^o~+	0.11
	CB-ND-002 (Group 3)	225	150	NC	0.25	653.1	NC	2319 *#o	NC	9.25 *#o	1.00
	Cysteamine (Group 4)	112	173	NC	0.50	628.1	NC	1577 #o~+	NC	6.52 #o~+	0.26
	Eicosapentanoiec Acid (Group 5)	112	2440	21.8	1.00	3276	29.25	4715 #o~+	42.10 #o~+	3.27 #o~+	0.73
Brain	CB-ND-002 (Group 1)	60	810	NC	0.50	3773	NC	36940 #o	NC	32.09 #o	0.85
	CB-ND-002 (Group 2)	112	808	NC	4.00	3819	NC	NC	NC	NC	NC
	CB-ND-002 (Group 3)	225	781	NC	3.00	3683	NC	30630 *#^o~+	NC	25.27 *#^o~+	0.67
	Cysteamine (Group 4)	112	833	NC	5.00	3942	NC	NC	NC	NC	NC
	Eicosapentanoiec Acid (Group 5)	112	1110	9.93	1.00	4672	41.71	NC	NC	NC	NC

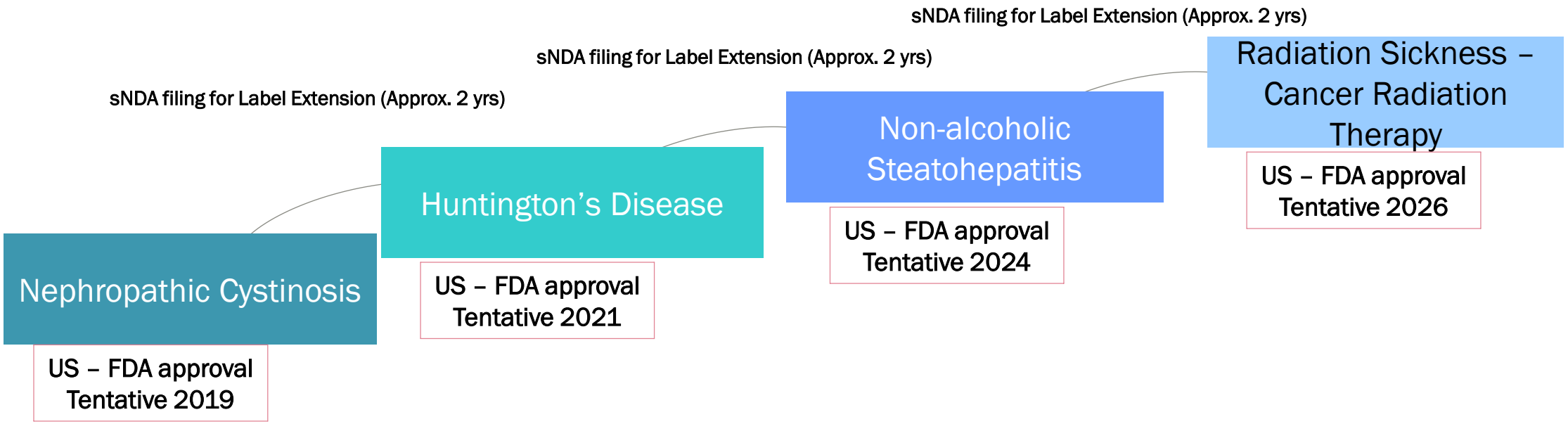
*** < 4 data points used to determine terminal elimination slope; #the terminal elimination slope covered < 2 half-lives (T1/2 as determined by the regression), ^Cmax included as the first point of the terminal elimination slope; ° the AUC extrapolated > 20%; ~ the regression line fitted to the terminal elimination phase data is of poor fit (Rsq <0.80), + estimation of terminal elimination phase slope by WinNonlin considered by pharmacokineticist to be unreliable; AUC(0-inf), AUC(0-inf)/D and T1/2. NC = not calculable**

CB-ND-02: Intellectual Property

- Filed a Worldwide Patent Application – PCT covers 108 countries
- Filed a National Patent Application with the USPTO and Indian Patent Office
- US Patent no. US8871805B2, US844570713B1

Disease Category	Date of Filing	Patent Region	Patent Number
Nephropathic Cystinosis	July 8, 2010	US	US8871805B2, US844570713B1

CB-ND-02: Indications Potential



Precedent - Horizon Pharma plc Completes Acquisition of Raptor Pharmaceutical Corp.

DUBLIN, Ireland, Oct. 25, 2016 (GLOBE NEWSWIRE) -- Horizon Pharma plc (NASDAQ:HZNP) a biopharmaceutical company focused on improving patients' lives by identifying, developing, acquiring and commercializing differentiated and accessible medicines that address unmet medical needs, today announced that it has completed the acquisition of Raptor Pharmaceutical Corp. (NASDAQ:RPTP).

Strategic rationale:

- Strengthens Horizon Pharma's focus on rare diseases and provides expansion into Europe and other international markets.
- Adds PROCYSBI® (cysteamine bitartrate) delayed-release capsules and QUINSAIR™ (aerosolized form of levofloxacin) global rights, with PROCYSBI having strong patent protection through 2034.
- Diversifies revenue with 11 medicines across three business units: orphan, rheumatology and primary care.

Horizon Pharma plc Completes Acquisition of Raptor Pharmaceutical Corp.

Financial impact

- Including the expected impact of the Raptor acquisition for the remainder of 2016, Horizon Pharma is raising its full-year 2016 net sales guidance on a GAAP basis, including the previously announced $65 million settlement with Express Scripts as a one-time reduction, to approximately $980 to $985 million.
- Horizon Pharma is raising its net sales guidance on a non-GAAP adjusted basis to approximately $1.045 to $1.050 billion excluding the $65 million settlement. The exclusion of the $65 million settlement from GAAP net sales guidance is the only adjustment reflected in Horizon Pharma's full-year 2016 non-GAAP adjusted net sales guidance.
- Net sales from Raptor medicines for the last two months of 2016 are expected to add between $20 and $25 million to Horizon Pharma total net sales.
- Including the expected impact of the Raptor acquisition for the remainder of 2016, Horizon Pharma is confirming its full-year 2016 adjusted EBITDA guidance of approximately $450 to $460 million.

Vision for CB-ND-002

- To develop once-a-day formulation with sustained response and efficacy
- To further improve the acute (tolerability – nausea, vomiting, diarrhoea) and chronic (gastric and intestinal ulceration, bleeding) Adverse Effect profile of currently available PROCYSBI®
- Improve the compliance in paediatric population and reduce the healthcare burden

info@cellomaticsbio.com
+44 (0) 115 7870081
www.cellomaticsbio.com
634 Innovation Centre
Biocity Nottingham NG1 1GF
UK