# Shire acquisition of ViroPharma

- Strategic move to strengthen Shire's Rare Disease business
- Augments already strong growth prospects

**Flemming Ornskov, MD**
Chief Executive Officer

**Graham Hetherington**
Chief Financial Officer

Shire

**Our purpose**
We enable people with life-altering conditions to lead better lives.

## CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS

**Statements included in this communication that are not historical facts are forward-looking statements. Forward-looking statements involve a number of risks and uncertainties and are subject to change at any time. In the event such risks or uncertainties materialize, results could be materially adversely affected. The risks and uncertainties include, but are not limited to, that:**

- **Shire's proposed acquisition of ViroPharma may not be consummated due to the occurrence of an event, change or other circumstances that gives rise to the termination of the merger agreement;**

- **a governmental or regulatory approval required for the proposed acquisition of ViroPharma may not be obtained, or may be obtained subject to conditions that are not anticipated, or another condition to the closing of the proposed acquisition may not be satisfied;**

- **ViroPharma may be unable to retain and hire key personnel and/or maintain its relationships with customers, suppliers and other business partners pending the consummation of the proposed acquisition by Shire, or ViroPharma's business may be disrupted by the proposed acquisition, including increased costs and diversion of management time and resources;**

- **difficulties in integrating ViroPharma into Shire may lead to the combined company not being able to realize the expected operating efficiencies, cost savings, revenue enhancements, synergies or other benefits at the time anticipated or at all;**

**and risks and uncertainties detailed from time to time in Shire's or ViroPharma's filings with the U.S. Securities and Exchange Commission, including their respective most recent Annual Reports on Form 10-K.**

## ADDITIONAL INFORMATION AND WHERE TO FIND IT

**This communication is for informational purposes only and does not constitute an offer to purchase or a solicitation of an offer to sell ViroPharma common stock. The offer to buy ViroPharma common stock will only be made pursuant to a tender offer statement (including the offer to purchase, letter of transmittal and other related tender offer materials). Investors and security holders are urged to read both the tender offer statement (which will be filed by Shire subsidiaries with the Securities and Exchange Commission (SEC) and the solicitation/recommendation statement on Schedule 14d-9 with respect to the tender offer (which will be filed by ViroPharma with the SEC) when they become available because they will contain important information, including the terms and conditions of the offer. Investors and security holders may obtain a free copy of these materials (when available) and other documents filed by Shire and ViroPharma with the SEC at the website maintained by the SEC at www.sec.gov. The tender offer statement and related materials, and the solicitation/recommendation statement, may also be obtained (when available) for free by contacting Shire Investor Relations, at [+1 781 482 0999 or +44 1256 894157].**

**Copies of these materials and any documentation relating to the tender offer are not being, and must not be, directly or indirectly, mailed or otherwise forwarded, distributed or sent in, into or from any jurisdiction where to do so would be unlawful.**

# Compelling strategic rationale

**Flemming Ornskov, MD**
**Chief Executive Officer**

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# Compelling acquisition rationale

- **Excellent strategic fit with Shire's rare disease expertise**
- **Augments Shire's already strong growth profile**
- **Adds CINRYZE® (C1 esterase inhibitor [human]) – a growing product which is complementary to FIRAZYR® (icatibant injection)**
- **Shire expects annual cost synergies of approximately $150 million by 2015**
- **Immediately accretive to Non-GAAP EPS and enhances earnings growth profile**
- **Shire expects transaction to deliver ROIC in excess of weighted average cost of capital**

# ViroPharma Incorporated background

**History**

- Founded in 1994, with a commitment to the development and commercialization of innovative products that address unmet needs
- The company has grown through a focus on Business Development, most recently acquiring Lev Pharmaceuticals Inc. in 2008 and DuoCort Pharma AB in 2011

**Products**

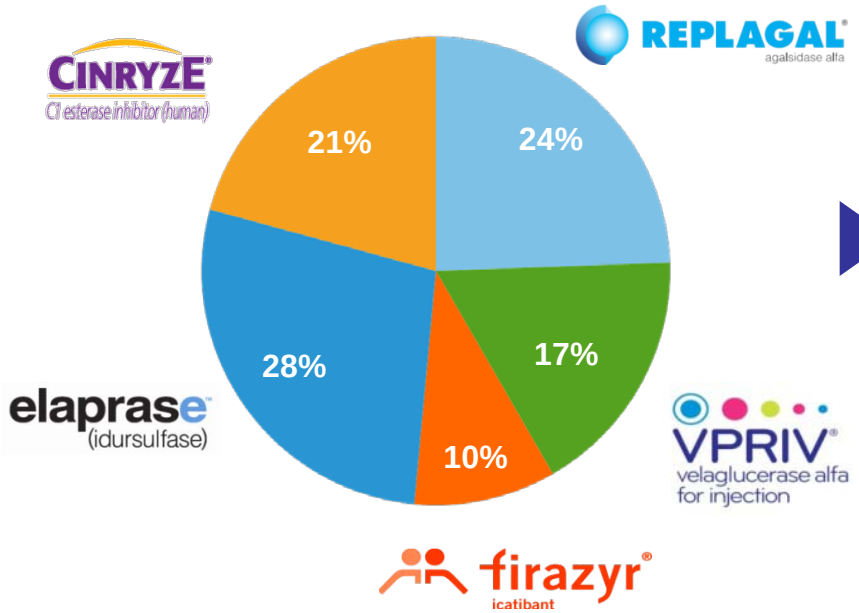
- Key product is CINRYZE indicated for routine prophylaxis against angioedema attacks in adolescent and adult patients with Hereditary Angioedema (HAE)
- Other marketed products include BUCCOLAM® (midazolam oromucosal solution) and PLENADREN® (Hydrocortisone, Modified Release Tablet)
- Additional pipeline assets

**Facts**

- NASDAQ listing
- 410 employees as at 31 December 2012
- Head office in Exton, PA with other locations in countries throughout the EU
- Manufacturing rights to CINRYZE held by Sanquin, based in the Netherlands

# Expected to create a growing ~$2 billion Rare Disease business

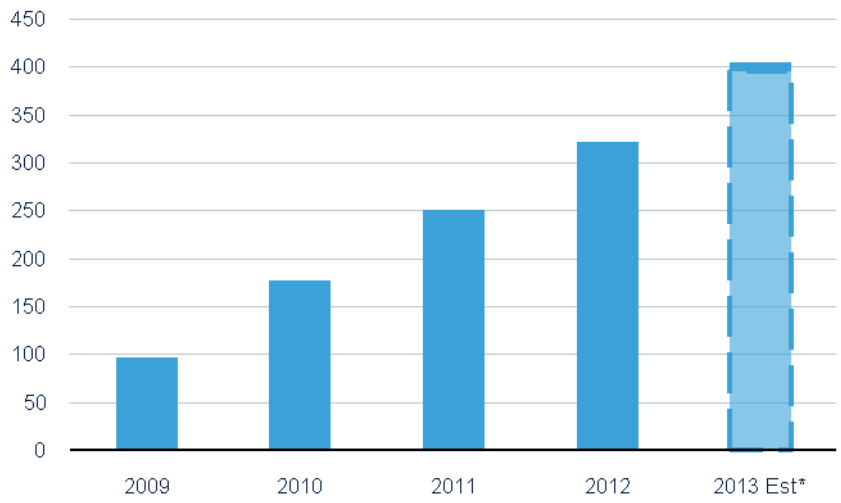
**On closing, CINRYZE will make an immediate and significant contribution to the Rare Disease business…**




Sales estimates based on 2013 consensus sales forecasts[1]

**… supported by a track record of significant growth**

**Cinryze US sales since launch ($m)**

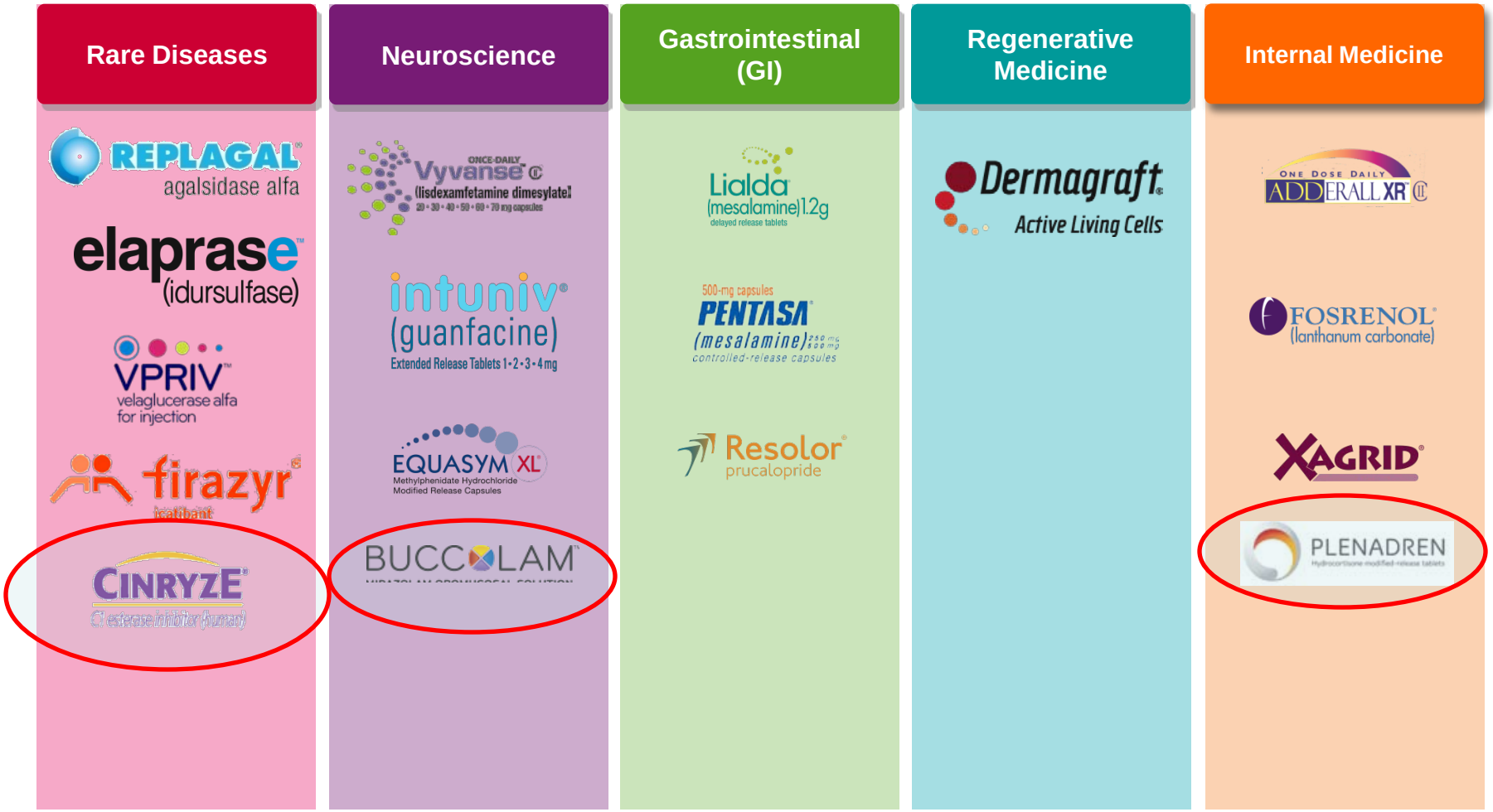



***Viropharma has guided to North American sales of $395m - $405m for 2013***

Shire To be as brave as the people we help.

(1) Shire consensus sales forecasts: based on the most recent consensus sales estimates compiled by Consensus Forecast Ltd, as of the date of this release for the year ending December 31, 2013, available on Shire's website
CINRYZE sales forecasts: based on FactSet consensus for year ended December 31, 2013 (accessed 4 November 2013)

# ViroPharma strengthens our growing In-Line portfolio




Shire To be as brave as the people we help.

# CINRYZE® (C1 esterase inhibitor [human])

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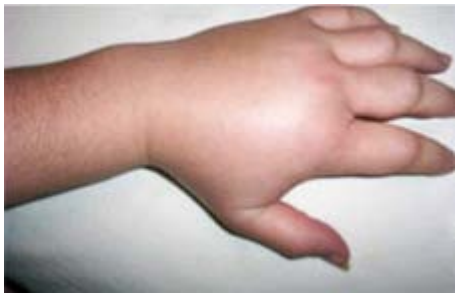
# Hereditary Angioedema (HAE)

**Edema attack**



*Source: US HAEA website*

- HAE is a very rare but debilitating genetic disorder characterized by unpredictable and recurring edema (swelling) attacks, of varying duration, severity, and frequency (see below)
- There are approximately 7,000 – 8,000* US HAE sufferers, of which an estimated 3,000 – 4,000 are treated**
- Many patients continue to be treated with androgens

**HAE is a variable condition that can be life threatening**
**Complementary treatment options are necessary**

| Infrequent symptoms | Frequent/moderate symptoms | Frequent/severe symptoms |
|---|---|---|
| Acute treatments - considered poor candidates for prophylaxis due to low disease burden | Prophylactic therapy may be added, depending on individual patient preferences/ characteristics. Patients still should have access to acute therapy | Severe patients have high need and generally receive prophylaxis and acute treatment for breakthrough attacks |



*Agostoni A, Aygoren-Pursun E, Binkley KE, et al. Hereditary and acquired angioedema: problems and progress: proceedings of the third C1 esterase inhibitor deficiency workshop and beyond. J Allergy Clin Immunol 2004;114(3 Suppl):S51-131

**Internal market research

# FIRAZYR and CINRYZE are complementary therapies

## Acute therapy

firazyr
icatibant

- Acute attacks of HAE in adults of 18 years and older
- >1,500 patients have tried Firazyr in the US, and > 2,500 in Europe
- Suitable for adult patients with acute episodes
  - On-demand, self-administered, portable, SQ
  - Monotherapy for patients with infrequent attacks
  - Adjunctive therapy to treat breakthrough attacks for patients using prophylaxis

## Prophylactic therapy

CINRYZE
C1 esterase inhibitor (human)

- Prophylaxis treatment of HAE in adolescents and adults
- ~ 1,000 patients on therapy in US and Europe
- Used in moderate to severe HAE patients
  - 2 infusions per week, IV
  - 75% of patients are treated through IV infusion at home
- Many patients still experience breakthrough attacks despite their prophylactic treatment and thus require acute treatment options

**CINRYZE and FIRAZYR occupy different market segments; where overlap in patients exists, the products are complementary**

# Delivering value from transaction

## Driving future CINRYZE growth

1. Leverage of Shire's infrastructure:
   - International commercial expertise and infrastructure
   - R&D expertise
   - Biologic manufacturing expertise

2. Expansion of patient outreach programs

## Additional In-Line products

## Synergies

## Pipeline optionality

# Transaction details

**Graham Hetherington**
**Chief Financial Officer**

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# Proposed transaction details

- Offer price of $50 per share in cash
- Total consideration of approximately $4.2 billion
- Pending anti-trust authority clearances, it is anticipated that the transaction will close in the last quarter of 2013, the first quarter of 2014 or as soon as possible thereafter
- The transaction is not subject to any financing contingency

# Financial benefits to Shire

- **Creates a Rare Disease business unit with a growing $2 billion revenue base(1)**
- **Enhances Shire's short and long term revenue growth**
- **Shire expects annual cost synergies of approximately $150 million by 2015**
- **Immediately accretive to Non-GAAP EPS and augments earnings growth profile in short and long term**
- **Shire expects transaction to deliver ROIC in excess of weighted average cost of capital**



(1) Shire consensus sales forecasts: based on the most recent consensus sales estimates compiled by Consensus Forecast Ltd, as of the date of this release for the year ending December 31, 2013, available on Shire's website
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# Financing

**Funded using:**
- **cash on hand**
- **existing $1.2bn committed bank facility**
- **newly arranged $2.6bn short term bank facility**

**Financing arranged also provides Shire with sufficient capacity to repay Shire's existing $1.1 billion convertible bond in May 2014 if required**

# Summary

**Excellent strategic fit**

**Increases rare disease portfolio which Shire is strategically committed to strengthen**

**Attractive financial profile**

# Questions and Answers

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# Appendix

# Two further marketed products

PLENADREN
Hydrocortisone modified-release tablets

BUCCOLAM
MIDAZOLAM OROMUCOSAL SOLUTION

## PLENADREN® for adrenal insufficiency in adults

- Modified release hydrocortisone for adrenal insufficiency in adults
- European approval received 2011, with launches underway
- Discussions with FDA ongoing regarding US regulatory path

## BUCCOLAM® for prolonged seizures in children and adolescents

- Oromucosal midazolam provided in an individual dose formulation for buccal delivery
- Portable, ready to use, pre-filled oral syringe containing an age-specific dose
- Approved in the EU in 2011
- Launched in seven EU countries plus one in the Middle East

# ViroPharma development pipeline (ex CINRYZE additional indications)

| | |
|---|---|
| **Subcutaneous CINRYZE (HAE)** | • Phase 3 ready<br>• An optimized, low volume version of CINRYZE for subcutaneous administration<br>• Discussions with FDA for pathway into Phase 3 planned for 1H 2014 |
| **Maribavir (CMV in transplant patients)** | • Phase 2 studies in refractory and treatment naïve CMV patients ongoing in US and EU respectively<br>• Unique mechanism of action<br>• Encouraging Ph2 data reported June 2013 with viral clearance observed<br>• Top line data expected 2014 |
| **VP20621 *(c. difficile)*** | • Phase 2 results reported April 2013<br>• A non-toxigenic spore based strain of *C. difficile* that helps to prevent recolonization with toxic strains<br>• Phase 2 studies showed a favourable tolerability profile with 98% having no recurrence of infection<br>• Further data evaluation underway to determine next steps |
| **Oral budesonide (eosinophilic esophagitis)** | • Phase 2 studies ongoing in eosinophilic esophagitis (EoE), a chronic inflammatory disorder of the esophagus affecting an estimated 160,000 patients in the US alone<br>• Being developed by Meritage Pharma – ViroPharma has an option to acquire<br>• A proprietary formulation of budesonide that acts topically on the esophagus<br>• Orphan Drug designation, no treatments currently available |
| **VP20629 (Friedreich's Ataxia)** | • Phase 1 currently enrolling<br>• A small molecule for the treatment of Friedreich's Ataxia, a life threatening, multi-system degenerative disorder<br>• Affects 1 in 50,000 people – no therapies available currently |

# ViroPharma development pipeline – CINRYZE additional indications

| | |
|---|---|
| **Antibody mediated rejection in renal transplant** | • Phase 2a<br>• ~1,600 transplant patients globally are positive cross match but therapy could expand number of potential transplant patients |
| **Autoimmune Hemolytic Anemia** | • Phase 1<br>• Target population of approximately 20,000 (the 10% of the 200,000 incident US & EU population that is not well managed by current therapies) |
| **Neuromyelitis Optica (Devic's syndrome)** | • Phase 1<br>• Target population of approximately 20,000 in US & EU |

# Financial outline of ViroPharma (in $m)

| | 2010A | 2011A | 2012A |
|---|---|---|---|
| Cinryze | 177 | 251 | 327 |
| Vancocin | 260 | 289 | 91 |
| Other | 3 | 5 | 10 |
| **Total Revenues** | **439** | **544** | **428** |
| *YoY growth* | | *24%* | *-21%* |
| Cost of Goods sold | (61) | (80) | (109) |
| **Gross Profit** | **378** | **464** | **319** |
| *Gross margin* | *86%* | *85%* | *75%* |
| R&D | (40) | (66) | (68) |
| SG&A | (96) | (128) | (174) |
| Amortisation | (29) | (31) | (35) |
| Other | (1) | (17) | (9) |
| **Operating income** | **212** | **222** | **33** |
| *Operating margin* | *48%* | *41%* | *8%* |

Outline prepared using historic company data under US GAAP

# About CINRYZE (C1 esterase inhibitor [human])

Cinryze is a highly purified, pasteurized and nanofiltered plasma-derived C1 esterase inhibitor product. In the U.S., Cinryze is approved by the FDA for routine prophylaxis against angioedema attacks in adolescent and adult patients with HAE. In the E.U., the product is approved by the EMA for the treatment and pre-procedure prevention of angioedema attacks in adults and adolescents with HAE, and routine prevention of angioedema attacks in adults and adolescents with severe and recurrent attacks of HAE, who are intolerant to or insufficiently protected by oral prevention treatments or patients who are inadequately managed with repeated acute treatment. Cinryze is for intravenous use only.

Severe hypersensitivity reactions to Cinryze may occur. Thrombotic events have occurred in patients receiving Cinryze, and in patients receiving off-label high dose C1 inhibitor therapy. Monitor patients with known risk factors for thrombotic events. With any blood or plasma derived product, there may be a risk of transmission of infectious agents, e.g. viruses and, theoretically, the CJD agent. The risk has been reduced by screening donors for prior exposure to certain virus infections and by manufacturing steps to reduce the risk of viral transmission including pasteurization and nanofiltration.

The most common adverse reactions in clinical trials associated with Cinryze were rash, headache, nausea, erythema, phlebitis and local reactions at the injection site. Adverse events of sinusitis and upper respiratory infection also were observed in clinical trials. No drug-related serious adverse events were reported in clinical trials. Please visit http://www.viropharma.com/products/cinryze.aspx for the full U.S. Prescribing Information; the prescribing information for other countries can be found at www.viropharma.com.

# About FIRAZYR

FIRAZYR is currently approved in 41 countries worldwide, including the countries of the European Union and the United States for the treatment of acute attacks of HAE in adults.

After injection training, patients may self-administer FIRAZYR. Most patients respond to a single dose of FIRAZYR. If response is inadequate or if symptoms recur, up to 2 additional doses may be administered within a 24 hour period at intervals of at least 6 hours.

**Important Safety Information**

Because laryngeal attacks may be fatal, patients with laryngeal symptoms should administer FIRAZYR and immediately seek medical attention. The most commonly reported adverse reactions were injection site reactions, which occurred in almost all patients (97%) in clinical trials. These most frequently included redness and swelling. Other common adverse reactions reported in at least 1% of patients included fever, transaminase increase, dizziness, and rash.

Full U.S. prescribing information for FIRAZYR is available at www.FIRAZYR.com. For more information about HAE visit www.haea.org. Prescribing information may differ between countries. Please consult your local prescribing information.