Spectrum Pharmaceuticals
Jefferies 2014 Global Healthcare Conference

June 3, 2014

Rajesh C. Shrotriya, MD
Chairman and Chief Executive Officer
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Risks that could cause actual results to differ include the possibility that our existing and new drug candidates may not prove safe or effective, the possibility that our existing and new drug candidates may not receive approval from the FDA and other regulatory agencies in a timely manner or at all, the possibility that our existing and new drug candidates, if approved, may not be more effective, safer or more cost efficient than competing drugs, the possibility that price and other competitive pressures may make the marketing and sale of our drugs not commercially feasible, the possibility that our efforts to acquire or in-license and develop additional drug candidates may fail, our lack of sustained revenue history, our limited experience in establishing strategic alliances, our limited marketing experience, our customer concentration, the possibility for fluctuations in customer orders, evolving market dynamics, our dependence on third parties for clinical trials, manufacturing, distribution, information and quality control and other risks that are described in further detail in the Company's reports filed with the Securities and Exchange Commission. We do not plan to update any such forward-looking statements and expressly disclaim any duty to update the information contained in this presentation except as required by law.
Spectrum Pharmaceuticals
NASDAQ: SPPI

- Overview/Focus - Hematology/Oncology
- FDA Approved Marketed Drugs
- Near Term Value Drivers (6-18 Months)
- Strong Maturing Pipeline
- Recent Acquisitions
- Financials
- Summary
Overview

Why Focus primarily in the Hematology/Oncology space?
- Cancer rates are increasing worldwide*
  - Only a fraction of patients respond to any treatment
  - Those who respond, often Relapse and become Refractory

- Rxs: Chemotherapy/Radiation/Surgery
  - Associated with Severe Toxicity
  - Dose limiting toxicity (DLT) limits the efficacy

*Global Cancer 2012
2013 Product sales $143.5 Million

- 4 oncology/hematology products on the market bringing in revenue
- Revenue pays for most of the operations of the company
Near Term Value Drivers (6-18 Months)

**BELEODAQ**
- NDA filed December 2013
- FDA Decision expected on August 9th, 2014

**CE Melphalan**
- Expect to file NDA in 3Q 2014

**Apaziquone**
- Expect to file NDA around near end 2014
# Strong Maturing Pipeline

## Approved Products

<table>
<thead>
<tr>
<th>DRUGS</th>
<th>Indication</th>
<th>Preclinical</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>NDA</th>
<th>Marketed</th>
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</thead>
<tbody>
<tr>
<td>FUSILEV® (evloleucovorin) for injection</td>
<td>Advanced Metastatic Colorectal Cancer • Rescue After High-Dose Methotrexate Therapy in Osteosarcoma</td>
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<tr>
<td>FOLOTYN® (pralatrexate injection)</td>
<td>Relapsed or Refractory Peripheral T-Cell Lymphoma</td>
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<tr>
<td>ZEVALIN® (ibrutinib-mab tuxetan) injection for intravenous use</td>
<td>Relapsed or Refractory, Low-grade or Follicular B-Cell NHL • Previously Untreated fNHL Who Achieve a PR or CR/CRu to First-line Chemotherapy</td>
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<tr>
<td>MARQIBO® (vinCrisline sulfate LIPOSOME) injection</td>
<td>Relapsed adult Ph(+) Acute Lymphoblastic Leukemia (ALL)</td>
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## Compounds in Development

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<th>DRUGS</th>
<th>Indication</th>
<th>Preclinical</th>
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<th>Phase 2</th>
<th>Phase 3</th>
<th>NDA</th>
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<tbody>
<tr>
<td>BELEODAQ™ (belinostat) for injection</td>
<td>Relapsed or Refractory Peripheral T-Cell Lymphoma</td>
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<tr>
<td>MARQIBO® (vinCrisline sulfate LIPOSOME) injection</td>
<td>Front-line Aggressive NHL</td>
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<td>MARQIBO® (vinCrisline sulfate LIPOSOME) injection</td>
<td>Front-line Elderly Ph(-) ALL</td>
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<tr>
<td>ZEVALIN® (ibrutinib-mab tuxetan) injection for intravenous use</td>
<td>ZEST: Diffuse Large B-Cell Lymphoma</td>
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<td>FOLOTYN® (pralatrexate injection)</td>
<td>Front-Line Peripheral T-Cell Lymphoma*</td>
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<td>Apaziquone/EOQuin®</td>
<td>Non-Muscle Invasive Bladder Cancer</td>
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<td>Captisol-enabled™ Melphalan</td>
<td>Multiple Myeloma Autologous Stem Cell Transplant</td>
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<td>Ozarelix</td>
<td>Hormone Dependent Prostate Cancer</td>
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<td>Menadione Topical Lotion</td>
<td>EGFR Inhibitor Rash Treatment and Prevention</td>
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<td>BELEODAQ™ (belinostat) for injection</td>
<td>Non Small Cell Lung Cancer (NSCLC)</td>
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<td>SPI-2012</td>
<td>Neutropenia: Breast Cancer</td>
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<td>SPI-1620</td>
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<td>SPI-1620</td>
<td>Biliary Cancer</td>
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<td>Renazorb®</td>
<td>Hyperphosphatemia in ESRD (Enrollment closed)</td>
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<tr>
<td>Brakiva™ (Vincristine Optisome™)</td>
<td>Small-Cell Lung Cancer and Ovarian Cancer</td>
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<tr>
<td>Alocrest™ (Topotecan Optisome™)</td>
<td>Breast and Lung Cancer</td>
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* Pivotal Trial under Special Protocol Assessment (SPA)

NHL - Non-Hodgkin's Lymphoma • fNHL - Follicular non-Hodgkin's Lymphoma • CR/CRu - Complete Response • PR - Partial Response • ALL - Acute Lymphoblastic Leukemia • EGFR - Epidermal Growth Factor Receptor • ESRD - End-stage Renal Disease

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Recent Acquisitions

**Companies**

- **Allos Therapeutics** 2012
- **Talon Therapeutics** 2013

**Compounds**

- **SPI-2012 (GCSF)** 2012
- **Captisol-enabled Melphalan** 2013
1Q Financial Highlights

- Product Revenue - $40.1 Million
  - Fusilev - $22.2 Million
  - Folotyn - $10.1 Million
  - Zevalin - $6.3 Million
  - Marqibo - $1.5 Million
- Non-GAAP EPS was $0.01, and GAAP EPS was ($0.44)
- $121 Million in cash/equivalents
Marqibo
Optimizes Vincristine to Create a Distinct Product

The Optisome encapsulation technology can be used to overcome the limitations of other chemical entities.
Periwinkle plant (Catharanthus roseus) has been used as a folk remedy for centuries. Studies in the 1950s revealed that it contains ~70 alkaloids, many of which are biologically active. Initial studies in diabetes mellitus were negative, however it was noted that one of the side effects in these studies was myelosuppression.

This observation led to studies in mice with leukemia, whose lifespan was prolonged by the use of a vinca preparation.
# Vincristine Clinical Use

<table>
<thead>
<tr>
<th>Hematologic Malignancy</th>
<th>Solid Tumors</th>
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<tbody>
<tr>
<td><strong>Adult</strong></td>
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<tr>
<td>Acute Lymphoblastic Leukemia (ALL)</td>
<td>Primary CNS Tumors</td>
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<tr>
<td>Non-Hodgkin’s Lymphoma (NHL)</td>
<td>Merkel Cell Carcinoma</td>
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<td>Peripheral T-Cell Lymphoma</td>
<td>Ovarian Cancer</td>
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<td>Angioimmunoblastic T-Cell Lymphoma</td>
<td>Small Cell Lung Cancer</td>
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<td>Anaplastic Large Cell Lymphoma</td>
<td>Thymic Malignancies</td>
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<td>Hodgkin’s Disease</td>
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<td>Multiple Myeloma</td>
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<td><strong>Pediatric</strong></td>
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<tr>
<td>Acute Lymphoblastic Leukemia (ALL)</td>
<td>Ewing’s Sarcoma</td>
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<td>Non-Hodgkin’s Lymphoma (NHL)</td>
<td>Chondrosarcoma</td>
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<td>Hodgkin’s Disease</td>
<td>Rhabdomyosarcoma</td>
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<td>Neuroblastoma</td>
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<td>Wilms’ Tumor</td>
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<td>Primary CNS Tumors</td>
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# Vincristine Sulfate
## A Foundational Chemotherapy

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\[ V = \text{vincristine} \quad O = \text{Oncovin}^\text{®} (\text{vincristine}) \]
Vincristine - Favorable Attributes

- Potent in vitro cancer cell killer
- Well-characterized MoA
- Minimally myelosuppressive
- Predictable toxicity profile
- Does not require premedication
- Can be combined with other chemotherapies and biologics
- Decades of clinical experience
Sphingosomes

- Liposomes made of sphingomyelin and cholesterol
- About 100 nm in size
- Less susceptible to degradation due to amide linkage in sphingomyelin
- Have improved vincristine retention characteristics
- Having no net charge, opsonize proteins to a lesser extent
- Less susceptible to uptake by the mononuclear phagocyte system
- Behave like stealth liposomes without surface modification
In a non-clinical study in Sprague-Dawley rats, MARQIBO Delivered More Drug To Critical Tissues

*Silverman and Deitcher, Cancer Chemother Pharmacol 71:555-564, 2013*
In a non-clinical study in mice, MARQIBO Reduced Tumor Volume More Than Vincristine

Namalwa tumors in female CB-17 SCID mice following IV administration on days 11, 18, and 25 post-implantation.

Silverman and Deitcher, Cancer Chemother Pharmacol 71:555-564, 2013
MARQIBO Had a Higher Plasma Exposure Profile Compared To Vincristine

Marqibo 2.25 mg/m²

Vincristine 1-1.6 mg/m²

Plasma concentration ng/mL

Marqibo Facilitates Dose Intensification and Individualized Dosing

Dosed at 2.25 mg/m²
- 1.6X to >2.5X Individual Dose Intensification Compared to Standard Vincristine Capped at 2 mg Regardless of Patient BSA
- Comparable Doses of Standard Vincristine Result in 100% Severe Neurotoxicity

Body Surface Area (m²)

Vincristine Dose (mg)

Marqibo (Red)

Standard Vincristine (Green)

90% of Adults
Activity of R-CHMP and Historical Data With R-CHOP

Activity of R-CHMP and Historical Data with R-CHOP

DLBCL Patients Over the Age of 60 and Unfavorable Prognosis (aaIPI 2-3)

- Median PFS: 1.9 vs. 9.8 years
- Median OS: 2.9 vs. 8.4 years

Historical data vs. Marqibo

Safety Data of R-CHMP and Historical Data with R-CHOP

- **Peripheral neuropathy**: 36% (Marqibo; R-CHMP; vincristine dose: 2mg/m²) vs. 0% (Historical data; Multi-drug regimen; vincristine dose: 1.4 mg/m²)
- **Paraesthesia**: 39% (Marqibo; R-CHMP; vincristine dose: 2mg/m²) vs. 10% (Historical data; Multi-drug regimen; vincristine dose: 1.4 mg/m²)
- **Grade 3/4 constipation**: 0% (Marqibo; R-CHMP; vincristine dose: 2mg/m²) vs. 16% (Historical data; Multi-drug regimen; vincristine dose: 1.4 mg/m²)
- **Grade 3 motor weakness**: 0% (Marqibo; R-CHMP; vincristine dose: 2mg/m²) vs. 16% (Historical data; Multi-drug regimen; vincristine dose: 1.4 mg/m²)

Ongoing Clinical Studies

Leukemia

ALL
Adult Ph- Relapsed/Refractory

ALL
Adult Ph- Frontline

ALL
Pediatric

NHL
Adult Frontline

Lymphoma

MARQibo

HALLMARQ Study
- Phase 3 Randomized Global Confirmatory Study
- SPA Received from FDA
- Active and Enrolling

HBS411 Study
- Phase 1 Dose-Finding Trial in Children and Adolescents with Refractory Cancers
- Enrolling at the US National Cancer Institute (NCI)
- Phase 2/3 ALL Program Being Planned with Leadership from St. Jude Children’s Research Hospital and NCI

OPTIMAL>60 Study
- Phase 3 Randomized Study Comparing R-CHMP to R-CHOP
- Lead by German High-Grade Lymphoma Group
- Active and Enrolling in Germany
- UK Sites Being Considered for Inclusion

Hyper-CMAD Study
- Phase 2 Study Sponsored by MD Anderson Cancer Center
SPI-2012
A Novel and Highly Potent Long-Acting Granulocyte Colony Stimulating Factor
Introduction to G-CSF
Neutrophils

1960’s Discovery of:

- Rapidity of turnover of neutrophils in blood
- The Myeloperoxidase in the killing of bacteria
- The importance of Integrins on the neutrophil for their migration to the inflammation site

- G-CSF is critical for maintaining blood neutrophil levels
- G-CSF can be used to increase neutrophil production and decrease susceptibility to infection.
LAPS-GCSF

- LAPS-GCSF, also called HM10460A, is based on a novel technology called LAPSCOVERY® [Long Acting Protein (peptide) Discovery Technology] developed by Hanmi Pharmaceuticals, Korea, to enhance the in vivo half life of therapeutic protein and peptides.

- LAPSCOVERY technology involves conjugation of a therapeutic protein or peptide to the Fc region of human IgG through a flexible non-peptidyl linker.

- Spectrum has been developing LAPS-GCSF in collaboration with Hanmi.
LAPS-GCSF Technology

LAPS-GCSF’s technology is next generation, enhanced long acting technology.

LAPS-GCSF Fc binds to the FcRn receptor, enhancing uptake and retention in the bone marrow thereby increasing potency.

Conjugation to Fc also increases the molecular size, avoiding elimination through kidney and extending the half-life of the GCSF analog.

LAPS allows minimum impairment to receptor surface allowing improved pharmacodynamics.

Traditional PEG technology adds mass to the GCSF to reduce clearance and allows it to stay in the bloodstream longer. However due to the added mass, it can impair the binding to the receptor.
LAPS-GCSF Pharmacology in Rats (BM distribution)

Higher distribution of LAPS-GCSF in bone marrow reduced DSN along with stronger stem cell proliferation and differentiation response

BM distribution in neutropenia rats (n=3)

ANC level (n=3)

** P<0.01
LAPS-GCSF Pharmacology

Potency of LAPS-GCSF and Neulasta® in Mice & Rats

Neutropenic Mouse Model (n=5)
3-fold higher activity compared to Neulasta

- Normal
- Vehicle (anti-cancer agent)
- HM10460A 30 mcg/kg (as G-CSF), Single
- HM10460A 100 mcg/kg (as G-CSF), Single
- HM10460A 300 mcg/kg (as G-CSF), Single
- Neulasta 100 mcg/kg (as G-CSF), Single
- Neulasta 300 mcg/kg (as G-CSF), Single

Neutropenic Rat Model (n=5)
10-fold higher activity compared to Neulasta

- Vehicle (CPA treat)
- Neulasta 100 mcg/kg (as G-CSF), Single
- HM10460A 10 mcg/kg (as G-CSF), Single
- HM10460A 30 mcg/kg (as G-CSF), Single
- HM10460A 60 mcg/kg (as G-CSF), Single
- HM10460A 100 mcg/kg (as G-CSF), Single
LAPS-GCSF Pharmacology

Pharmacodynamic effect of LAPS-GCSF and Neulasta® in Monkeys

PK/PD Study in Monkeys (n=3, sc)

- Neulasta 100 mcg/kg (as G-CSF)
- HM10460A 100 mcg/kg (as G-CSF)
- ANC level (Neulasta 100 mcg/kg as G-CSF)
- ANC level (HM10460A 100 mcg/kg as G-CSF)

G-CSF concentration (ng/mL) vs. Time (day)

ANC level (10^6/mL) vs. Time (day)
LAPS-GCSF – Phase 1 studies (PK)

Once every three week administration potential

PK Profiles from Phase I Study (KR)

PK Profiles of Phase I Study (US)
LAPS-G-CSF: Phase 1 studies (PD)

Neutrophil Profiles of LAPS-GCSF and Neulasta®

PD Profiles of Ph I study (KR)

PD Profiles of Ph I study (US)

ANC (cells x 10⁹/L)

Time (day)

HM 350 µg/kg (n=6)
HM 135 µg/kg (n=6)
HM 45 µg/kg (n=6)
HM 15 µg/kg (n=6)
HM 5 µg/kg (n=6)
Placebo (n=10)_KR

KR 350 µg/kg (5.2 mg as G-CSF)
KR 135 µg/kg (2 mg as G-CSF)

270 µg/kg (4 mg as G-CSF)
Neulasta® 6mg (as G-CSF)

expected therapeutic dosage amount

HM 270 µg/kg (n=12)_US
HM 135 µg/kg (n=12)_US
HM 45 µg/kg (n=12)_US
HM 10 µg/kg (n=6)_US
HM 3.3 µg/kg (n=6)_US
Neulasta 6mg (n=10)_US
Placebo (n=10)_US
GCSFs have important clinical applications in:
- the prevention and treatment of neutropenia
- mobilization of stem cells for transplantation

Long-acting GCSF avoids the need for daily injections

Spectrum has been developing a novel long-acting GCSF called LAPS-GCSF in collaboration with Hanmi

LAPS-GCSF is a conjugated form of GCSF wherein a human GCSF analog is conjugated to the Fc region of human IgG through a flexible non-Peptidyl linker

In animal studies, LAPS-GCSF showed pharmacodynamic effect comparable to that of pegfilgrastim at one-third the dose

In a Phase 1 study in Healthy volunteers, LAPS-GCSF showed comparable safety profile and pharmacodynamic effect at one-third the dose when compared to pegfilgrastim

LAPS-GCSF is currently undergoing a Phase 2 study in cancer patients in comparison with pegfilgrastim
Summary Highlights

Long Term Catalysts
1. Marqibo® in NHL (Phase 3)
2. Marqibo ALL (Phase 3)
3. Zevalin® in DLBCL (Phase 3)
4. SPI-2012 (Phase 2)

Development Drugs Targeting Significant Unmet Need

Attractive Near Term Catalysts
1. Beleodaq™
2. Captisol-enabled™ Melphalan
3. Apaziquone

FDA Grants Priority Review Designation
Potential NDA Filing Expected in 3Q14
Potential NDA Filing Expected to file around near end 2014

Sustainable, Stable Base Business
1. Fusilev®
2. Folotyn®
3. Zevalin®
4. Marqibo®

Approved Drugs Fund Development

Existing Commercial Infrastructure can be Leveraged as New Products are Approved