AST-OPC1 Development Program for Spinal Cord Injury

Asterias Biotherapeutics Inc.
NYSE MKT: AST

Investor Day
May 8, 2015
Forward Looking Statements

Statements pertaining to future financial and/or operating results, future growth in research, technology, clinical development, and potential opportunities for Asterias, along with other statements about the future expectations, beliefs, goals, plans, or prospects expressed by management constitute forward-looking statements. Any statements that are not historical fact (including, but not limited to statements that contain words such as “will,” “believes,” “plans,” “anticipates,” “expects,” “estimates”) should also be considered to be forward-looking statements. Forward-looking statements involve risks and uncertainties, including, without limitation, risks inherent in the development and/or commercialization of potential products, uncertainty in the results of clinical trials or regulatory approvals, need and ability to obtain future capital, and maintenance of intellectual property rights. Actual results may differ materially from the results anticipated in these forward-looking statements and as such should be evaluated together with the many uncertainties that affect the businesses of Asterias, particularly those mentioned in the cautionary statements found in Asterias’ Registration Statement on Form S-3 and Prospectus, as well as its other periodic reports, filed with the Securities and Exchange Commission. Asterias disclaims any intent or obligation to update these forward-looking statements.
# Asterias Biotherapeutics, Inc

**Issuer:** Asterias Biotherapeutics, Inc.

<table>
<thead>
<tr>
<th>Exchange / Tickers:</th>
<th>NYSE MKT / AST</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shares outstanding:</td>
<td>32.3 M</td>
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<tr>
<td>Market cap:</td>
<td>$341M (based on share price of $10.54 as of May 1, 2015)</td>
</tr>
<tr>
<td>Major institutional holders:</td>
<td>Romulus, Fidelity, Scarsdale Equities, First Eagle</td>
</tr>
</tbody>
</table>

**Key financials (as of February 2015):**

- ~$7.4M cash
- ~$19M marketable securities
- Potential near-term proceeds of $11.7M from 5M “in the money” warrants at $2.34 which expire June 15, 2015

**Guidance for 2015:** Expected net cash burn of $15-17M

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1 $4.1M (unaudited) as of January 31, 2015 plus estimated $5.3M net proceeds from financing closed February 5, 2015

2 3.8M shares of BioTime (NYSE MKT: BTX) as of Mar 31, 2015
Key Highlights of Asterias

• **Two transformative platforms:**
  – Industry-leading Pluripotent Stem Cells
  – Dendritic Cell Immunotherapy

• **Both lead products entering the clinic**
  – Clinical development focused on de-risked indications with robust proof-of-concept data

• **Partnerships with leading institutions**
  – $14.3mm in non-dilutive funding from California Institute of Regenerative Medicine (CIRM) to launch AST-OPC1 Phase 1/2a for spinal cord injury
  – Partnered with Cancer Research UK (CRUK) to conduct AST-VAC2 Phase 1/2a for lung cancer with ~$20-30mm funded by CRUK

• **Addressing large markets with significant unmet medical needs – multiple milestones over the next 24 months**
  – AST-OPC1 Phase 1/2a trial and FDA pending potential expansion cohort may result in path to registration study
Today’s Agenda: AST-OPC1 Development Program for SCI

9:30AM: Welcome and Introduction to Asterias: Pedro Lichtinger (10’)

9:40AM: Introduction to Spinal Cord Injury and AST-OPC1: Jane Lebkowski (25’)

10:05AM: Design, Objectives and Status of Asterias’ Current Spinal Cord Injury Clinical Trial: Ed Wirth (25’)

10:30AM: Clinical Foundations for the Endpoints and Outcome Measures in Asterias’ Spinal Cord Injury Trials: John Steeves. (30’)

11:00AM: Future Clinical Development Plan for AST-OPC1: Ed Wirth (30’)

11:30AM: Summary and Questions: Jane Lebkowski: Moderator (30’)

ASTERIAS BIOOTHERAPEUTICS
Introduction to Spinal Cord Injury and AST-OPC1

Jane Lebkowski Ph.D.
President of R&D

Investor Day
May 8, 2015
Spinal Cord Injury: Multiple Devastating Life-Changing Effects

• Loss of limb function
• Impaired cardiovascular control
• Impaired bowel and bladder control
• Chronic neurgenic pain
• Increase pain sensation
• Decreased sexual function
• Increased frequency of pressure sores
• Urinary tract infections
• Spasticity
• Debilitating burning/tingling sensations
Spinal Cord Injury: Incidence and Costs

### Devastating Condition with High Unmet Medical Need and High Costs to the System

- Affects 12,000 patients per year in US alone
- Primarily affects young and previously healthy males in their 20s and 30s at time of injury
- No currently approved therapies
- Lifetime cost of care per patient of $2-4mm
- Healthcare costs to system of $14.5bn per year in US alone, plus $5.5bn in lost productivity
- Multi-billion dollar annual market opportunity

### Cervical Spinal Cord injury is a High Priority Target

- Cervical SCI has highest incidence and is most prevalent SCI type
- First year cost of care is ~$1 million for cervical complete SCI and ongoing care and support thereafter exceeds $150,000/year
- Integration back into a work environment for patients with cervical complete injuries is rare.
- Average life expectancy is now 75% of able bodied population, which means a person injured as a young adult could live with SCI for ~ 50 years
- Lifetime costs for ongoing care and support for a severe cervical injury can exceed $8.5 million/person

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1 National Spinal Cord Injury Statistical Center, Facts and Figures 2013
3 Internal estimates
Human Spinal Cord Injury Causes Tissue Destruction and Ectopic Tissue Formation in the Spinal Cord

- Trauma to the spinal cord causes hemorrhagic necrosis
- Secondary damage includes cell death, cavity formation, demyelination, and scarring
- Chronic stage: gray matter replaced by either a lesion cavity or collagenous scar
- Typical spared rim of white matter

Kakulas, Paraplegia, 25:212-216, 1987

Cervical SCI at C5; 10 days post-injury

Rationale for Oligodendrocyte Progenitor Cells

Pathology of the lesion provides rationale for oligodendrocyte progenitor transplantation

Aubourg, P., Nature Genetics 2007
Obermair, Schröter and Thallmair, Physiology 2008
AST-OPC1: hESC-Derived Oligodendrocyte Progenitor Cells (OPCs)

AST-OPC1

- Cryopreserved Allogeneic Cell Population
- Derived from Human Embryonic Stem Cells (hESCs)
- Characterized Composition of Cells:
  - Oligodendrocyte progenitors
  - Neural progenitors
  - Infrequent mature neural cells and
  - Rare other characterized cell types
- Three identified functions
  - Produces neurotrophic factors
  - Induces remyelination
  - Induces vascularization
- “Off the shelf” administration
- First indication: spinal cord injury
- Potential line extensions in other neurodegenerative diseases
AST-OPC1: Three Major Physiologically Relevant Functional Activities

1. Wraps host neurons and forms compact myelin sheaths

2. Produces neurotrophic factors and stimulates neurite outgrowth

3. Stimulates neovascularization
Models of Spinal Cord Injury Used to Evaluate Safety/Activity of AST-OPC1

- Midline Contusion Injury at T10
- Unilateral Contusion Injury at C5/C6

Transplant AST-OPC1 7 days post-injury at injury site

Evaluate
- Efficacy & Activity
- Histological Effects
- Cell Survival
- Cell Phenotype
- Cell Migration
- Toxicity
AST-OPC1 Improves Locomotor Recovery When Transplanted in Rats with Sub-acute Thoracic and Cervical SCI

Locomotor Improvement in Thoracic SCI

- Increased Weight Bearing
- Improved HL-FL Coordination
- Improved Hind Paw Clearance
- Improved Trunk Stability
- Decreased Tail Drag

Locomotor Improvement in Cervical SCI

- Increased Running Speed
- Increased Right Forelimb Stride Length
- Increased Right Forelimb Maximal Longitudinal Deviation
- Increased Right Rear Stride Frequency
AST-OPC1: Improved Locomotor Activity

Control (no cells) .

AST-OPC1 Treated
AST-OPC1 Decreases Parenchymal Cavitation In Injured Rats

Area of Parenchymal Cavitation (mm$^2$)

- AST-OPC1
- HBSS

p<0.05

**
AST-OFC1 Reduces SCI Cavity Formation and Induces Persistent Myelination

Rat Thoracic Spinal Cord Injury Model

9 months vehicle

Cavity forms in untreated SCI lesion

Myelinated axons do not extend across cavity

9 months post-transplant with AST-OFC1

AST-OFC1 in SCI lesion; Significantly Reduced Cavity Formation

Robust AST-OFC1 survival (brown)

Myelinated Fibers (blue)

Brown: antibody to human nuclear antigen labels AST-OFC1; Blue: Eriochrome Cyanine stains myelin
28 Animal Studies
>3000 Rodents and Pigs

- Activity/ Efficacy
- Biodistribution
- Dosing/Delivery
- Toxicity
- Tumorigenicity
- Ectopic Tissue
- Immune Rejection

- Survives in the Spinal Cord
- Predominantly Neural Cell Types
- Greatest Activity in Subacute Injury
- Improves Locomotor Activity
- Reduces Parenchymal Cavitation
- Active Doses Established
- Migrates Up 5cm in Spinal Cord
- No Distribution Outside CNS
- Does Not Increase Mortality
- Does Not Induce Allodynia
- Does Not Induce Systemic Toxicity
- Does Not Produce Teratomas
- Produces Low Frequency (1-2%) Small Ectopic Tissue at Injury Site
- Not Highly Susceptible to Direct Immune Responses
Overall Development Path for AST-OPC1 and Regulatory Status

Potential for:
- Orphan Drug Status
- Breakthrough Designation
Partnership with CIRM Provides Project Validation and Non-dilutive Funding

$14.3 Million Grant

Includes funding for:
- Execution of Phase 1/2a study
- Process and assay development activities to prepare for pivotal trials and commercialization
- Facilities and indirect costs

Potential follow-on grants to expand and accelerate trial
Design, Objectives, and Status of Asterias’ Current Spinal Cord Injury Clinical Trial

Edward Wirth, III, M.D., Ph.D.
Chief Medical Officer

Investor Day
May 8, 2015
AST-OFC1: Phase 1 Safety Study in Complete Thoracic SCI

- Open Label Trial
- Multi-Center (7 sites)
- 8-10 Subjects
- Subacute, Neurologically Complete T3-T11 Lesions
- 2x10^6 Cells
- Transplant 7-14 Days Post Injury
- Temporary Immunosuppression

Primary Assessment: Safety
Secondary Assessment: ISNCSCI exams
Exploratory Assessments
- UAB-IMR
- SCIM
- SCI Pain Basic Data Set
- Bowel and Bladder Basic Data Set
## AST-OPC1: Subject Demographics

### Demographic and Baseline Disease Characteristics – All Treated Subjects

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Sex</th>
<th>Level of Injury</th>
<th>Cause of Injury</th>
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<tbody>
<tr>
<td>21</td>
<td>Male</td>
<td>T6</td>
<td>Motor vehicle accident</td>
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<tr>
<td>23</td>
<td>Male</td>
<td>T8</td>
<td>Restrained driver in rollover motor vehicle collision with ejection</td>
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<tr>
<td>32</td>
<td>Male</td>
<td>T6</td>
<td>Motorcross</td>
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<tr>
<td>31</td>
<td>Male</td>
<td>T7</td>
<td>Fell 30 feet down rock embankment</td>
</tr>
<tr>
<td>23</td>
<td>Female</td>
<td>T3</td>
<td>Car accident</td>
</tr>
</tbody>
</table>

### Enrolling Sites

- **Shepherd Center**
  - Dr. David Apple
- **Rehabilitation Institute of Chicago**
  - Dr. Richard Fessler
  - Dr. David Chen
- **Santa Clara Valley Medical Center**
  - Dr. Gary Steinberg
  - Dr. Steve McKenna
Delivery of AST-OPC1 in Complete Thoracic SCI Was Feasible and Safe

- All Subjects Received AST-OPC1 (2 x 10^6 cells) at 1-2 weeks of post-injury
- Injections performed using a Syringe Positioning Device (SPD)
- No intraoperative complications
- No SAEs Associated with Delivery of Cells
- 9 Adverse Events Possibly Related to Injection Procedure
  - All Grade 1 or 2: Post-Operative Pain, Transient Fever (1) or Urinary Tract Infection (1)
Immunosuppression Regimen Was Well-Tolerated

- All Subjects Completed Tacrolimus Immunosuppression Regimen
- No SAE’s Associated with Immunosuppression
- 16 Grade 1 or 2 Adverse Events Possibly Associated with Immunosuppression
- Nausea, Urinary Tract Infection, Low Magnesium Blood Levels
No Evidence of AST-OPC1 Directed Immune Responses One Year After Administration

- Immune monitoring shows no evidence of antibodies or cellular immune responses to AST-OPC1 through 1 year in all subjects
- Some subjects complete mismatch with AST-OPC1: Closest match was 5 of 10 alleles

**PRA Assay**

**ELISpot Assay**
AST-OPC1 Was Well Tolerated

- No SAE’s Associated with AST-OPC1
- No Evidence of adverse findings on MRI scans
- 5 Adverse Events Possibly Associated with AST-OPC1
  - Transient Low Grade Fever (1)
  - Burning Sensation in Trunk and Lower Extremities (4 in one subject)

### Three SAEs to date

<table>
<thead>
<tr>
<th>Subject</th>
<th>SAE</th>
<th>Timeframe</th>
<th>Related to AST-OPC1</th>
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<tr>
<td>1101</td>
<td>Pyelonephritis: Grade 2</td>
<td>Day 215</td>
<td>Not Related</td>
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<tr>
<td>1204</td>
<td>Urinary tract infection: Grade 3</td>
<td>Day 325</td>
<td>Not Related</td>
</tr>
<tr>
<td>1204</td>
<td>Autonomic Dysreflexia/Dyspnea: Grade 3</td>
<td>Year 2</td>
<td>Not Related</td>
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No Major Sensory Neurological Changes Observed

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<td>T6</td>
<td>T7</td>
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<td>T8</td>
<td>T10*</td>
<td>T10*</td>
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<td>Year 2</td>
<td>T8</td>
<td>T9</td>
<td>T10*</td>
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<td>T5</td>
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<td>Year 2</td>
<td>T4</td>
<td>T4</td>
<td>T6</td>
<td>T5</td>
</tr>
</tbody>
</table>

* Day 270
MRI Results: Evidence Consistent with Prevention of Lesion Cavity Formation

- No adverse findings on primary MRI safety reads
- In 4 of 5 subjects, graft sites are hyperintense on T2, but signal intensity is < CSF
- Suggests lesion cavity formation may have been prevented by formation of a tissue matrix

Image on right is axial T2 at 3 years post-grafting through center of lesion/graft site – Slice 22 on sagittal image above)
Summary of Findings from First in Man Study of AST-OPC1

- AST-OPC1 is extremely well tolerated, with no SAEs to date deemed related to the cells, delivery method, or immunosuppressive regimen
  - 4 of 5 patients have completed 3 year follow up visit, one has completed 4 years of follow-up
  - 5th patient will complete 3 year follow up in early November

- Immune response monitoring shows no evidence of rejection of AST-OPC1, even 10 months after removal of all immunosuppression
  - Despite significant HLA mismatches between AST-OPC1 and subjects
  - Suggests well tolerated low dose, transient immunosuppressive regimen likely sufficient to enable long term engraftment of cells

- MRI results consistent with continued, stable engraftment in 4 of 5 subjects at 2-3 years post-transplant

- No evidence of significant changes in neurological function
  - No evidence for ascending loss of function from cells or delivery
  - Efficacy not anticipated in this study due to low dose (5-10x below predicted efficacious range) and suboptimal patient population (complete thoracic injuries)
AST-OPC1: Scientific Rationale for Evaluation in Cervical SCI Patients

- Repair/regeneration of axons only required over a short distance to reinnervate motor neurons for arms & hands
- For example, with an SCI at C6 (last intact motor level at C5), repair of axons to C7 could yield return of 2 motor levels
- Few complete cervical SCI patients recover \( \geq 2 \) motor levels with current standard of care
- Recovery of \( \geq 2 \) motor levels leads to significant improvement in self-care ability
- Self-care ability could be a clinically meaningful endpoint for a pivotal trial and BLA approval

Design of Phase 1/2a Study of AST-OPC1 in Complete Cervical SCI

Key Design Elements
- AST-OPC1 Injection 14-30 days post-injury
- 10 day stagger within cohorts
- DMC review prior to dose escalation

Efficacy Target
- Recovery of >= 2 motor levels at 6 months or 12 months
AST-OFC1 Phase 1/2a Study Schema

- Open Label Trial
- Multi-Center (8 sites)
- Complete cervical SCI (C5-C7)
- Temporary Immunosuppression

Primary Assessment: Safety
Secondary Assessment: ISNCSCI exams
Exploratory Assessments: SCIM, GRASSP

Protocol AST-OFC1-01

Protocol AST-OFC1-02

Acute complete cervical SCI

Day -11
Day -3
Day -1
Day 0
Day 7
Day 30
Day 60
Day 90
Day 180
1 Year
5 Years
15 Years

Screening
Baseline
AST-OFC1 Injection 14-30 Days Post-SCI

Days 46-60 Immunosuppression Taper

Discontinue Immunosuppression

In person visits
Phone f/u
Operational Update

• First two clinical sites are open for enrollment (Shepherd Center, Atlanta; Rush University, Chicago)

• Third clinical site expected to open in May (Stanford/Santa Clara Valley Medical Center)

• Patient recruitment efforts initiated
  – Study website landing page to go live in May
  – Branding and messaging for health care providers developed
  – Outreach to referral centers for open sites has begun
AST-OPC1 Phase 1/2a Trial: Design and Milestones

Cohort 1:
- 3 subjects
- 2 million cells

Cohort 2:
- 5 subjects
- 10 million cells

Cohort 3:
- 5 subjects
- 20 million cells

Q1’15: Study initiates
Q3’15: Dose escalation
Q1’16: Dose escalation
1H’16: 6 mo efficacy, cohort 2
• Appointed University of British Columbia (UBC) since 1979
• Founded ICORD in 1995, generated $50 million for Blusson Spinal Cord Center
• ICORD is engaged in all aspects of SCI research (~35 faculty + 150 trainees)
• President of NeuroTherapeutics Inc. (1999-2002)
• ISCoS Scientific Chair and ISCoS Executive
• ASIA Board Member and ASIA Program Committee Chair
• International Neurological Standards Committee
• Distinguished Scholar, Peter Wall Institute of Advanced Studies, UBC
• Founded and Co-Chair of SCOPE (2006 - )
The industry, academic and community roundtable for spinal cord injury research

www.scopesci.org

Co-Chairs
Dr. John Steeves (ICORD at UBC & VGH)
Dr. Andy Blight (Acorda Therapeutics)

Mission:

Enhance the development of clinical trial and human study protocols that will accurately validate therapeutic interventions for spinal cord injury (SCI) and facilitate improved best practices.
Origins of SCOPE

- SCOPE arose out of an initial effort (started in 2004) from a concerned group of international scientists and clinicians to establish a set of valid guidelines for the conduct of spinal cord injury (SCI) clinical trials. A series of meetings was supported by a coalition of SCI Foundations.
- After extensive meetings, a series of 4 peer-reviewed papers was published in 2006 and they have become the fundamental basis for all SCI clinical trials.
- Several regulatory agencies, including the FDA have used these guidelines for protocol reviews. The FDA has also participated in SCOPE sponsored workshops.
- Industry and foundations recognized the efforts as valuable and joined with the clinical investigators in 2006 to elaborate further understanding of SCI protocols and outcomes.
Past Activities:

• Since 2006, SCOPE has hosted annual international workshops addressing SCI outcome choices in human studies.
• Select articles on spontaneous recovery of sensory & motor function after sensorimotor complete (AIS-A) SCI.

  Steeves et al. *Topics Spinal Cord Injury Rehabilitation* 2012;18:1
  Kramer et al. *NeuroRehabil & Neural Repair* 2012; 26:1064
  Tanadini et al. *NeuroRehabil & Neural Repair* 2014; 28:507
Present Activities:

- Examine feasibility for greater participation in early clinical studies by correctly enrolling and accurately measuring outcomes of individuals with incomplete SCI (iSCI) in clinical studies (peer-reviewed publications 2014)
- Discuss and define appropriate functional outcomes (clinical endpoints) for pivotal Phase III SCI trials.

Current and Past Contributing Partners:
SCOPE participation is from industry, basic scientists, clinical researchers, academic institutions, health care centers, government agencies, not-for-profit foundations, and the SCI community.
Cervical spinal cord motor functions

Breathing and neck movement
Shoulder and elbow movement
Elbow and Wrist movement
Hand finger Movement

C5 – elbow flexors
C6 – wrist extensors
C7 – elbow extensors
C8 – hand finger flexors
T1 – small finger abductor
Movements of the forearm and hand

**C5 Elbow flexors**
- Biceps brachii
- Brachialis
- Brachial artery
- Medial epicondyle of humerus
- Median nerve
- Tendon of biceps brachii
- Pronator teres
- Brachioradialis
- Palmaris longus
- Flexor carpi radialis
- Flexor carpi ulnaris

**C6 Wrist extensors**
- Extensor carpi radialis longus
- Medial epicondyle of humerus
- Lateral epicondyle of humerus
- Olecranon of ulna
- Extensor carpi ulnaris
- Extensor digitorum
- Flexor carpi ulnaris

**C7 Elbow extensors**
- Triceps brachii
- Brachioradialis

**C8 Finger flexors**

**T1 Small finger abductor**
- Abductor digiti minimi
- Tendons of extensor digitorum
- Extensor retinaculum
- Flexor retinaculum
- Metacarpals
- Tendon of flexor digitorum superficialis
- Tendon of flexor digitorum profundus
Functional Recovery Requires Return of Motor Activity
(ISNCSCI motor scores evaluates strength of contraction by “key” muscles)

- C5 ------ • Elbow flexors
- C6 ------ • Wrist extensors
- C7 ------ • Elbow extensors
- C8 ------ • Finger flexors
- T1 ------ • Finger abduction

Upper Extremity Motor Score (UEMS):
5 muscles × max. strength score of 5 × 2 sides = maximum 50 points

Muscle Strength Scores for Key Limb Muscles

0 = total paralysis
1 = palpable or visible contraction
2 = active movement, gravity eliminated
3 = active movement, against gravity
4 = active movement, against some resistance
5 = active movement (normal)

Motor Level: Defined by
The key muscle for the most caudal (lowest) spinal segment having a muscle strength score of at least 3/5 (contraction against gravity alone) while all key muscles above this level are normal (5/5).
Outcome challenges:
Link neurological changes to functional improvements

- Neurology (impairment)
- Function (activities of daily living)
Outcome challenges:
Link neurological changes to functional improvements

International Standards for the Neurological Classification of Spinal Cord Injury (ISNCSCI)

Magnetic Resonance Imaging

Electrophysiology

Spinal Cord Independence Measure (SCIM)

Function (activities of daily living)

Neurology (impairment)

Graded Redefined Assessment of Strength, Sensibility and Prehension
Outcome challenges:
Link neurological changes
to functional improvements

Neurology (impairment) vs. Function (activities of daily living)

Functional

Neurological
Spinal Cord Independence Measure (SCIM)

- SCIM is a “global” functional activities exam within the activity/function domain (does not cover pain, spasticity, or autonomic functions)

- Maximum score of 100 comes from 3 sub-scales within SCIM (self-care = 20 points, respiration and sphincter management = 40, mobility = 20)

- SCIM Self-care sub-score focuses on upper extremity activities and is therefore linked to assessments of cervical SCI
SCIM Self-care sub-score

• Self-care
  – Feeding (3 pts)
  – Bathing
    • Upper body (3 pts)
    • Lower body (3 pts)
  – Dressing
    • Upper body (4 pts)
    • Lower body (4 pts)
  – Grooming (3 pts)
Activities of daily living (ADLs) for individuals with different levels of motor function after cervical complete SCI
(modified from Whiteneck et al. 1999)

<table>
<thead>
<tr>
<th>Function</th>
<th>C1-C3</th>
<th>C4</th>
<th>C5</th>
<th>C6</th>
<th>C7-C8</th>
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<td></td>
<td></td>
<td></td>
<td>total assist</td>
<td>partial assist</td>
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<tr>
<td>Bladder</td>
<td></td>
<td></td>
<td>total assist</td>
<td>partial assist</td>
<td>independent</td>
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<tr>
<td>Bed Mobility</td>
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<td></td>
<td>total assist</td>
<td>partial assist</td>
</tr>
<tr>
<td>Transfers</td>
<td></td>
<td></td>
<td></td>
<td>total assist</td>
<td>partial assist</td>
</tr>
<tr>
<td>Pressure Relief</td>
<td></td>
<td></td>
<td></td>
<td>total assist</td>
<td>partial assist</td>
</tr>
<tr>
<td>Eating</td>
<td></td>
<td></td>
<td></td>
<td>total assist</td>
<td>partial assist</td>
</tr>
<tr>
<td>Dressing</td>
<td></td>
<td></td>
<td></td>
<td>total assist</td>
<td>partial assist</td>
</tr>
<tr>
<td>Grooming</td>
<td></td>
<td></td>
<td></td>
<td>total assist</td>
<td>partial assist</td>
</tr>
<tr>
<td>Bathing</td>
<td></td>
<td></td>
<td></td>
<td>total assist</td>
<td>partial assist</td>
</tr>
<tr>
<td>Wheelchair</td>
<td></td>
<td></td>
<td></td>
<td>total assist</td>
<td>partial assist</td>
</tr>
<tr>
<td>Car transport</td>
<td></td>
<td></td>
<td></td>
<td>total assist</td>
<td>partial assist</td>
</tr>
<tr>
<td>Daily Home Care</td>
<td>24 hr attendant</td>
<td>18-24 hr attendant</td>
<td>6-12 hr assistance</td>
<td>4 hr housework</td>
<td>1 hr housework</td>
</tr>
</tbody>
</table>
Upper Extremity Motor Score (UEMS) recovery after cervical sensorimotor complete SCI (AIS-A)

Phases of recovery by rate:
- Rapid
- Slower
- Plateau

Similar number of motor points (~10) recovered in the upper extremities (independent of cervical level SCI)

Comparable results obtained using another dataset from Sygen clinical trial

(Steeves et al., 2011. *Spinal Cord* 49: 257)
There were no significant differences between the recovery of SCIM self-care subscore when 0 and 1 motor level was recovered (right panel), despite a significant increase in motor points (left panel).

There was no significant difference between 1 and 2 motor-level recovery with regard to the total SCIM score.

Proportion of People with Cervical complete SCI recovering motor levels at 6 months after injury

<table>
<thead>
<tr>
<th>Type of Cervical SCI</th>
<th>0-1 motor level</th>
<th>&gt;2 motor levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensorimotor Complete</td>
<td>79%</td>
<td>21%</td>
</tr>
<tr>
<td>Sensorimotor Incomplete</td>
<td>77%</td>
<td>23%</td>
</tr>
</tbody>
</table>

**Motor level** = most caudal spinal segment, as indexed by key muscle group for that segment, having a muscle strength score of at least 3/5 (contraction against gravity alone) while all more rostral key muscles are normal (5/5).
Sample Power Calculations for Cervical Sensorimotor Complete SCI

- Example of sample size calculations to demonstrate a significant change in either UEMS (A) or recovery of two motor levels (B) from baseline to approximately one year after SCI ($\beta=0.2$, $\alpha=0.05$, equal allocation of subjects to treatment and control groups)

- Effect size based on the mean spontaneous UEMS increase or two motor level improvement approximately one year after SCI in combined databases and cervical motor levels (C5-C7).

SUMMARY

- SCOPE has established peer-reviewed, published guidelines for SCI clinical trials that have had a significant impact on FDA guidance for industry sponsors.

- SCOPE has identified outcome measures (UEMS, Motor Level, SCIM Self-Care) for complete cervical SCI that link recovery of neurological function to improvements in functional ability.

- This work by SCOPE provides a path to pivotal SCI trials in which both clinical and statistical significance could be demonstrated with manageable numbers of patients.
Future Clinical Development Plan for AST-OPC1

Edward Wirth, III, M.D., Ph.D.
Chief Medical Officer

Investor Day
May 8, 2015
Target Product Profile for AST-OPC1 in Complete Cervical SCI:

- Increase of ≥20% in the percentage of patients regaining two or more motor levels of function
- Enables powering of trial with only ~200 subjects
- Translates into clinically significant improvements in ability to self-care, significant reductions in cost of care

AST-OFC1 Phase 1/2a Trial: Expansion Cohort

**Cohort 1:**
- 3 subjects
- 2 million cells

**Cohort 2:**
- 5 subjects
- 10 million cells

**Cohort 3:**
- 5 subjects
- 20 million cells

**Q1’15:**
Study initiates

**Q3’15:**
Dose escalation

**Q1’16:**
Dose escalation

**1H’16:**
6 mo efficacy, cohort 2

File IND amendment for study expansion based on initial safety data in Cohort 2

---

**Expansion Cohort**
- Up to 27 additional patients
- 10 and/or 20 million cells
- Adaptive Design

---

- Open label trial enables use of adaptive design for selection of dose in expansion cohort
- Work of SCOPE enables comparison to robust historical outcomes databases

*Subject to FDA clearance for expansion from 13 to 40 subjects*
AST-OPC1 Future Clinical Development Plan in Complete Cervical SCI

Cohort 1
- 3 subjects with C5-C7 cervical SCI
  - Dose $2 \times 10^6$ AST-OPC1

Cohort 2
- 5 subjects with C5-C7 cervical SCI
  - Dose $1 \times 10^7$ AST-OPC1

Cohort 3
- 5 subjects with C5-C7 cervical SCI
  - Dose $2 \times 10^7$ AST-OPC1

Results from Phase 1/2 Clinical Trial Could Enable:
- Breakthrough therapy designation
- Phase 2 expansion cohort
- Randomized pivotal trial in cervical complete SCI
- Trials in additional indications (e.g., MS, Stroke)

Objectives of Trial
- Establish safety of AST-OPC1 in cervical sensorimotor complete SCI
- Assess effects on upper extremity motor function
- Investigate effects on additional measures of neurological function
A Pivotal Randomized Trial Could be Feasible with 200 Total Subjects

Analysis: A 200 patient pivotal trial (100 per arm) could show a statistically significant difference in self-care ability (functional endpoint) if >40% of AST-OPC1 recipients recover >= 2 motor levels at 6 months post-injection.
## AST-OPC1: Follow-on Indications in Other Neurodegenerative Diseases

<table>
<thead>
<tr>
<th>Indication</th>
<th>Rationale</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple Sclerosis</td>
<td>• Remyelination of axons in lesion site could restore function</td>
<td>• POC in primate model of chemical demyelination (Jeff Kocsis, Yale)</td>
</tr>
<tr>
<td></td>
<td>• Leverage safety data &amp; delivery system for OPC1 transplantation in spinal cord</td>
<td>• Clinical advisory panel held</td>
</tr>
<tr>
<td>White Matter Stroke</td>
<td>• Oligodendroglial dysfunction prominent in white matter (subcortical) stroke</td>
<td>• Preclinical collaboration underway to test AST-OPC1 in a white matter stroke model (Tom Carmichael, UCLA)</td>
</tr>
</tbody>
</table>
## Asterias 24 Month Milestone and Catalyst Outlook

<table>
<thead>
<tr>
<th>Timing</th>
<th>Milestone / Catalyst / Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q4’14 - completed</td>
<td>• Sign CIRM grant – triggers disbursement of CIRM funds</td>
</tr>
<tr>
<td>Q1’15 – completed</td>
<td>• Initiate AST-OPC1 Phase 1/2a clinical trial</td>
</tr>
<tr>
<td><strong>AST-OPC1</strong></td>
<td></td>
</tr>
</tbody>
</table>
| Q3’15        | • Safety readout from 2M cell cohort  
• Initiation of 10M cell cohort                                                              |
| H1’16        | • 6 month efficacy data from 10M cell cohort                                                |
| H2’16        | • 12 month efficacy data from 10M cell cohort  
• 6 month efficacy data from 20M cell cohort                                                 |