



# **Initial Clinical Trials of hESC-Derived Oligodendrocyte Progenitor Cells in Subacute Spinal Cord Injury**

ISCoS Meeting  
September 14, 2016

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



# AST-OPC1: hESC-Derived Oligodendrocyte Progenitor Cells (OPCs)



## AST-OPC1 (formerly GRNOPC1)

- 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: Phase 1 Safety Study in Complete Thoracic SCI

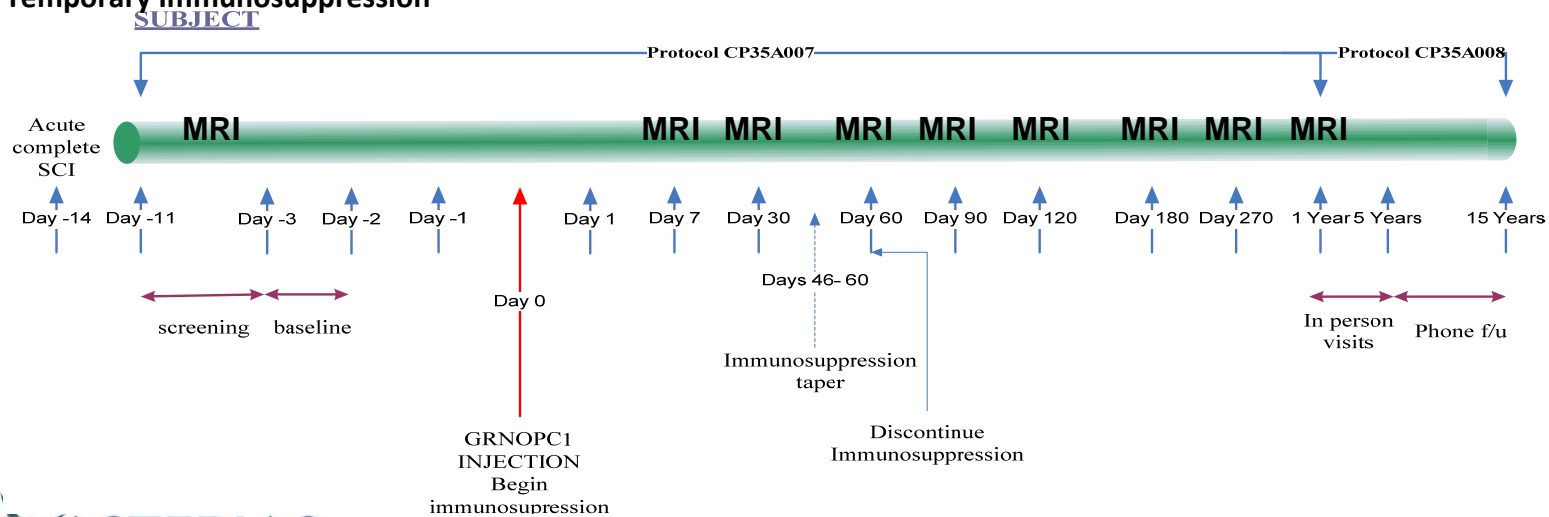
- Open Label Trial
- Multi-Center (7 sites)
- 5 Subjects received AST-OPC1
- Neurologically Complete T3-T11 Lesions
- $2 \times 10^6$  Cells
- Transplant 7-14 Days Post Injury
- Temporary Immunosuppression

Primary Assessment: Safety

Secondary Assessment: ISNCSCI exams

Exploratory Assessments

- UAB-IMR / SCIM
- SCI Pain Basic Data Set
- Bowel and Bladder Basic Data Set



# Summary of Phase 1 Thoracic Safety Study of AST-OPC1

## Well Tolerated

- ❖ AST-OPC1 well tolerated, with no SAEs to date deemed related to the cells, delivery method, or immunosuppressive regimen

## No Immune Responses

- ❖ No evidence of immune responses to AST-OPC1, even 10 months after removal of all immunosuppression
  - Despite significant HLA mismatches between AST-OPC1 and subjects

## Activity

- ❖ MRI results consistent with activity in injection site in 4 of 5 subjects at 4-5 years post-transplant

## No Changes Neurological Function

- ❖ 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)

# Evaluation of AST-OPC1 in Subacute Cervical SCI

## **A Phase 1/2a Dose Escalation Study of AST-OPC1 in Subjects With Subacute Cervical Spinal Cord Injury**

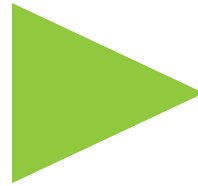
**Six Sites Currently Enrolling**

**ClinicalTrials.gov: [NCT02302157](https://clinicaltrials.gov/ct2/show/study/NCT02302157)**

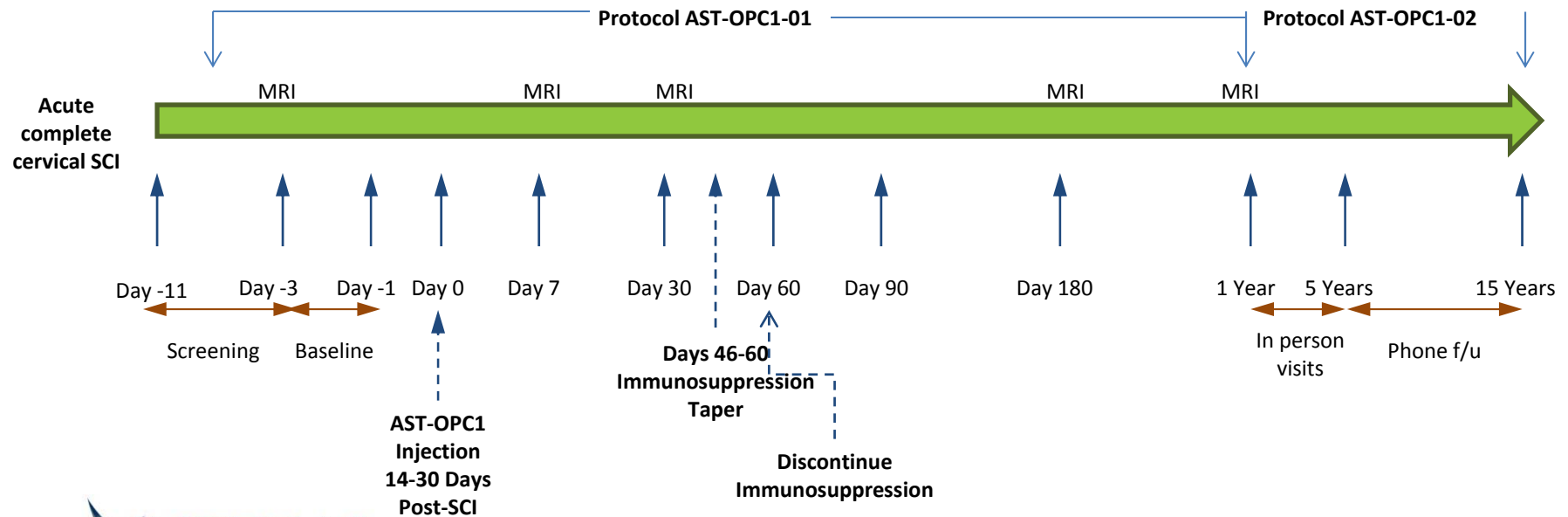


# AST-OPC1 Phase 1/2a Study Schema

- Open Label Trial
- Multi-Center (8-12 sites)
- Complete cervical SCI (C5-C7)
- Temporary Immunosuppression

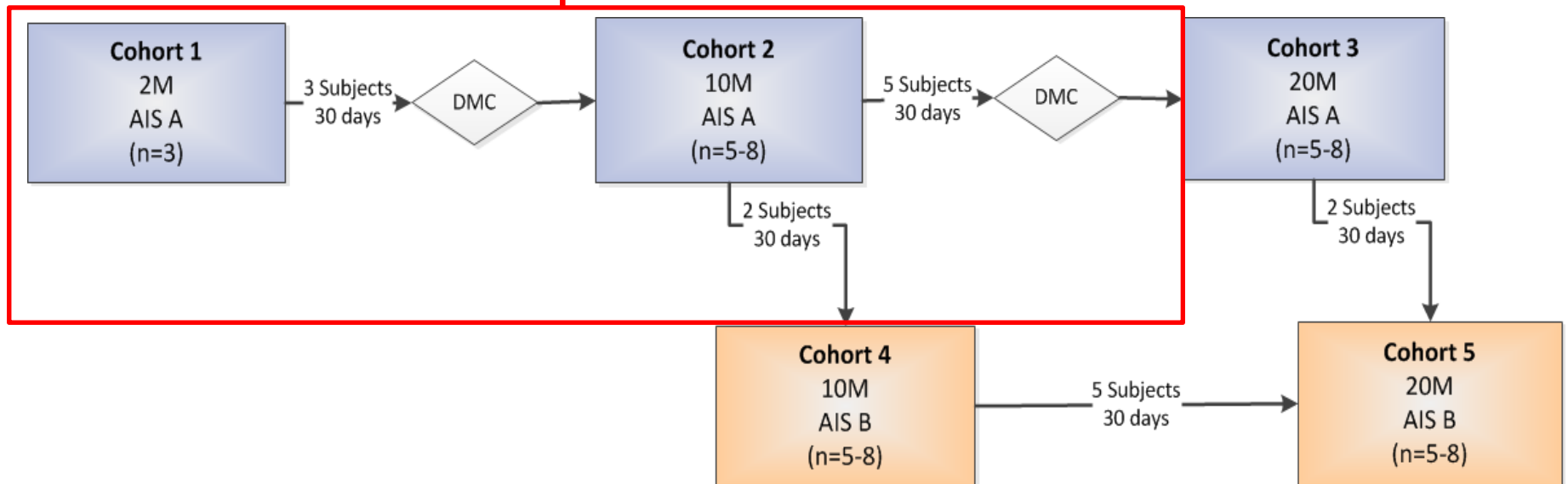


**Primary Assessment: Safety**  
**Secondary Assessment: ISNCSCI exams**  
**Exploratory Assessments: SCIM, GRASSP**



# AST-OPC1 Current Study Design

Completed

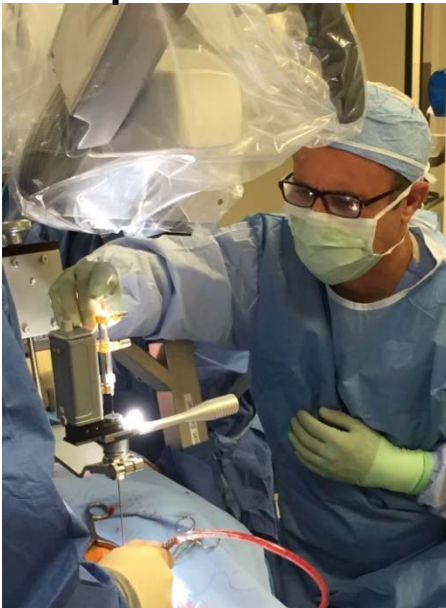


Currently recruiting patients for both Cohorts 3 & 4



# AST-OPC1 Injection Procedure

Shepherd Center



Rush University

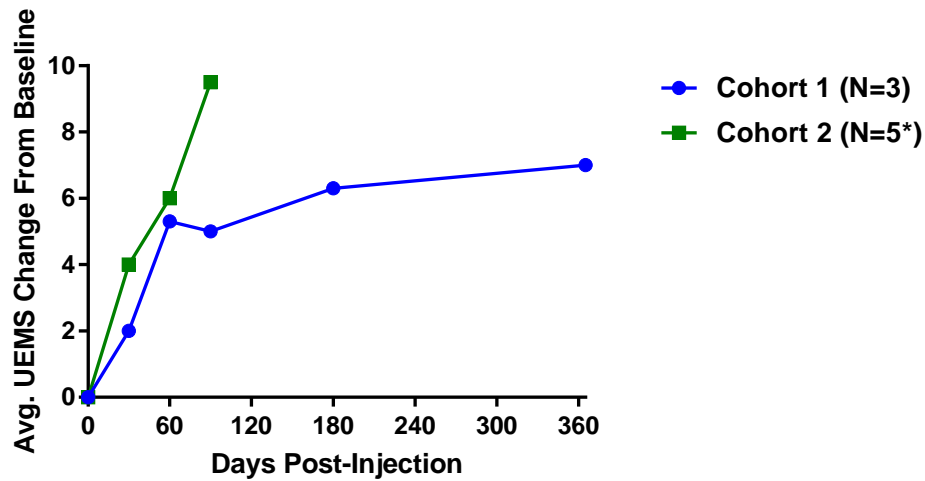


- Injections performed using a table-mounted syringe positioning device (SPD)
- Direct intra-parenchymal injection into the spinal cord lesion
- Single 50 $\mu$ L injection for both the 2M & 10M doses
- No intraoperative complications to date

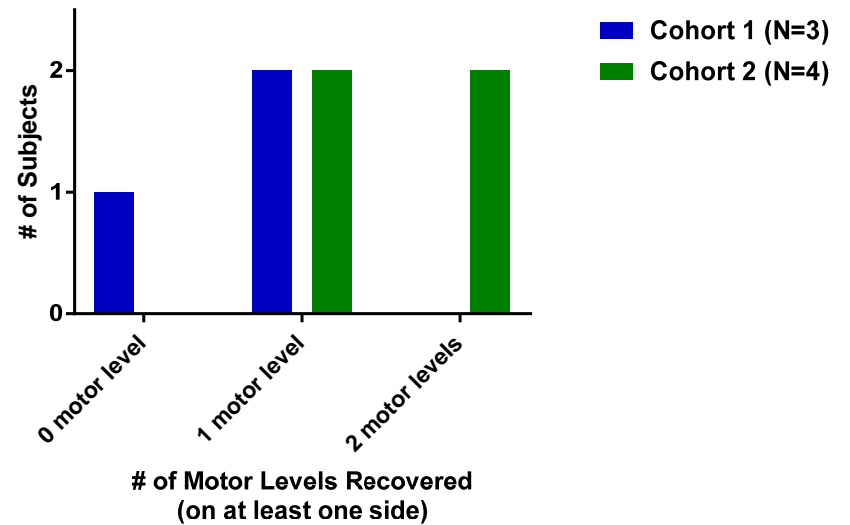


# Upper Extremity Motor Recovery to Date

Upper Extremity Motor Score (UEMS)



Motor Level Recovery at Day 90 Follow Up



\* N=4 at Day 90 (fifth subject has only reached Day 60)  
 Cohort 1: 2 million AST-OPC1 cells  
 Cohort 2: 10 million AST-OPC1 cells



# Upper Extremity Motor Score (UEMS) – Per Subject Data to Date

Cohort 1

Subject	Baseline	Day 90	Day 365
2001	24	26	28
2101	20	24	27
2102	8	17	18

Avg. time from SCI  
to AST-OPC1 Injection  
Cohort 1: 27 days  
Cohort 2: 28 days

Cohort 2

Subject	Baseline	Day 90
2501	30	41
2003	20	26
2301	24	38
2502	32	39
2202	15	---

No correlation  
between degree of  
recovery and baseline  
UEMS

Has not reached Day 90



# Motor Recovery Summary

- All subjects in Cohorts 1 & 2 have exhibited improved upper extremity motor scores (UEMS) relative to baseline
- The average UEMS improvement at Day 90 was 5.0 points in Cohort 1 (N=3) and 9.5 points in Cohort 2 (N=4)
- At 1-year of follow up, all subjects in Cohort 1 have improved one motor level on at least one side
- At Day 90 of follow up, 2 of 4 subjects in Cohort 2 have improved one motor level and 2 of 4 have improved two motor levels on at least one side (one patient has improved two motor levels on both sides)
- Cohort efficacy target of 2 of 5 patients improving two motor levels within 6-12 months post-administration has already been met, despite 4 patients only at Day 90 and 1 patient not yet even at Day 90

# Conclusions

- AST-OPC1 can be safely administered to patients in the subacute period after severe cervical SCI
- There have been no serious adverse events related to AST-OPC1, the injection procedure, or immunosuppression with low-dose tacrolimus
- A dose response effect on upper extremity motor recovery appears to be emerging by Day 90 of follow up, much earlier than we expected
- These data are early, but very encouraging; We look forward to the UEMS & motor level 6-month readouts in Cohort 2 in January 2017
- Concurrent enrollment of both AIS-B patients with 10M cells and AIS-A patients with 20M cells is in progress to further elucidate the dose response of OPC1

# Acknowledgments

## Asterias

Jane Lebkowski  
Cathy Priest  
Linda Jones  
Maria Schaefer  
Susy Chen  
Anthony Davies  
Jerrod Denham  
Katy Spink  
Nate Manley  
Kevin Nishimoto  
Naomi Kautz  
AST-OPC1 Team



## The Trial Participants

### Pre-Clinical Collaborators

Hans Keirstead  
Gabriel Nistor

### Committees

Steering Committee  
Data Monitoring Committee  
Radiology Committee  
Outcomes Committee

### Funding

California Institute of Regenerative Medicine (CIRM)

## Clinical Investigators

Richard Fessler  
James Young  
Don Leslie  
David Apple  
Gary Steinberg  
Steve McKenna  
Charles Liu  
Shekar Kurpad  
Eric Horn  
Jim Harrop  
Mary Schmidt Read  
David Chen