

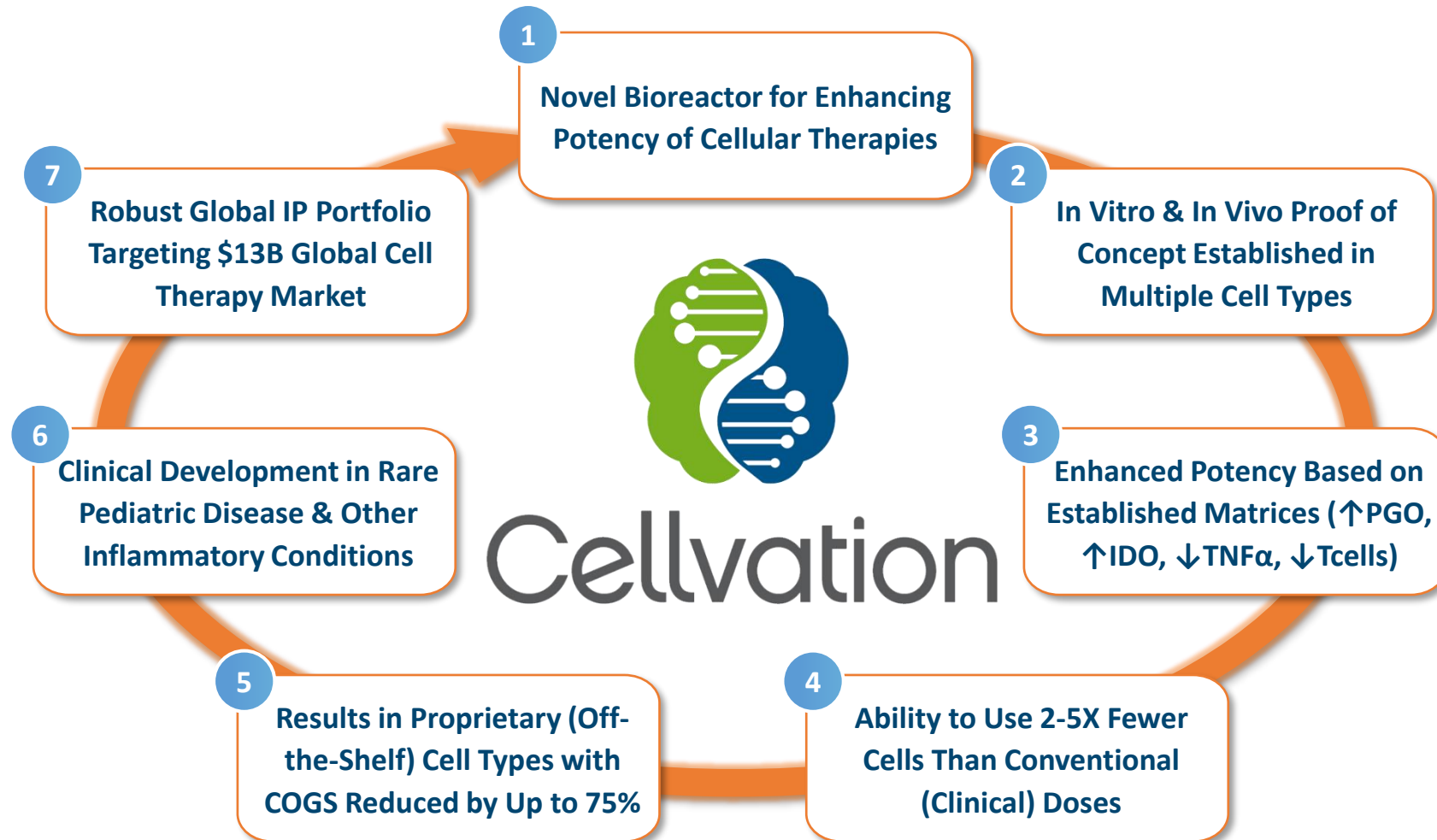


Cellvation

A Majority-Owned Subsidiary of Fortress Biotech

May 2025

Investment Highlights



Novel Cellular Therapeutics for Inflammatory Conditions

- Based on Research from University of Texas Health Science Center (Houston)

CEVA-D (Mechano-Transduction Device)

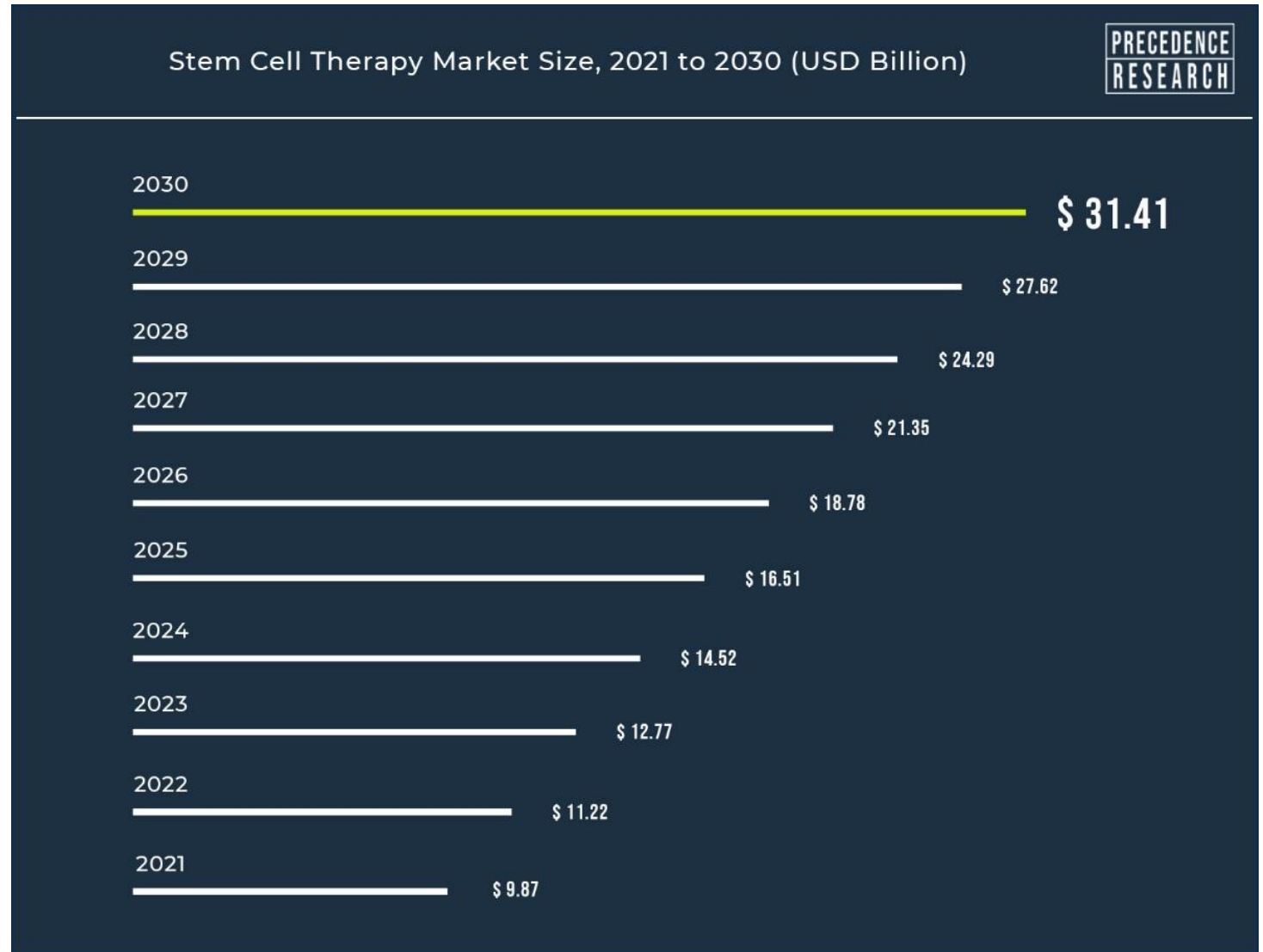
- Shear Stress Up-Regulates Anti-Inflammatory Gene Programs
 - Ability to use fewer, more potent cells for *any* cell therapy
 - Substantially reduces COGS (vs. conventional MSCs)
- Proof of Concept Completed *In Vitro*, *In Vivo*
 - Tested with Adipose, Amniotic Fluid, Bone Marrow
 - Mechano-Transduced Cells More Effective at Lower Dose

CEVA101 (Next Gen Cell Product)

- “Off-the-Shelf” Mechano-Transduced MSCs
- Upregulated Anti-Inflammatory Gene Programs
 - More Effective @ Substantially Lower Dose
- Initial Indication(s): rGVHD, Crohn’s, ARDS, CHF

Global Stem Cell Market

- 🌐 Global Stem Cell Therapy Market Estimated at \$11B in 2022, Expected to Reach \$31.5B by 2030
- 🌐 Pharma with Increased Interest In Stem Cell Therapy Based on Number and Size of Biotech Deals
- 🌐 Expanding Clinical Applications in Cardiac, Neurological and Autoimmune Disorders
- 🌐 Increased Adoption, Growing Investment in R&D, Favorable (Global) Regulatory Environment



Development Pipeline

CEVA-101 (Mechano-Transduced Cells)	Pre-Clinical	Phase 1	Phase 2	Phase 3	Market Potential
<i>Steroid-Refractory Pediatric Graft Versus Host Disease</i>					\$2.7B Global Market in 2023
<i>Crohn's Disease</i>					\$10B Global Market in 2023
<i>Acute Respiratory Distress Syndrome</i>					\$3B Global Market in 2023
<i>Congestive Heart Failure</i>					\$7B Global Market in 2023
<i>Chronic Low Back Pain</i>					\$10B Global Market in 2023
<i>Other Inflammatory Conditions</i>					>\$5B Potential

CEVA-D: Enhanced Potency Reduces COGS

- 🌐 Enhanced potency based on established matrix
 - PGE2 production
 - IDO production
 - TNF α suppression
 - T cell proliferation suppression
- 🌐 Increased potency translates into
 - Decreased COGS based on lower dosing requirements
 - Potential to expand into other indications
- 🌐 Dosing of MSCs typically in the 2-10 million cells / kilogram range
- 🌐 Data generated to-date demonstrates a 2-5X dose reduction
 - Using potency assays of PGE2 production and/or TNF α suppression
- 🌐 COGS of ~US\$20,000 per billion cells (or 10M cells per kilogram for 100 kilograms)
 - Based on estimated cost of cells from major supplier (Rooster Bio)
 - COGS could conservatively be reduced to \$4,000 per dose

CEVA-101: Proprietary Cell Product

Initial Indication: Refractory Pediatric Acute GvHD

 Children with steroid-refractory acute graft versus host disease (SR-aGVHD)

Treatment Options

- Corticosteroids are first-line therapy for aGVHD
- Only one approved treatment for disease refractory to steroids
- No approved treatment in the US for children under 12 years old

Burden of Illness

- Acute GVHD is a life-threatening complication
- Occurs in ~50% of patients receiving allogeneic bone marrow transplants (BMTs)
- Acute GVHD primarily affects skin, GI tract, and liver
- Steroid-refractory aGVHD is associated with mortality rates as high as 90%
- Significant costs associated with extended hospital stays

Market Opportunity

- More than 30,000 allogeneic BMTs performed globally (>20K US/EU) annually, ~20% pediatric
- >4,000 allogeneic BMTs in children and adolescents in US
- >5,000 allogeneic BMTs in children and adolescents in China

CEVA-101: Proprietary Cell Product

Initial Indication: Refractory Pediatric Acute GvHD (cont.)

Initial Clinical Design

Inclusion Criteria

- Male and female, ages of 2 months and 17 years
- Confirmed aGVHD following BMT
- Failed to respond to treatment with systemic corticosteroid therapy
- Grades C and D aGVHD involving the skin, liver and/or gastrointestinal (GI) tract OR
- Grade B aGVHD involving the liver and/or GI tract, with or without concomitant skin disease

Number of Patients & Design

- Single Arm (Open Label) Trial in ~20 patients
- Initial Therapy: IV CEVA-101 at dose TBD twice per week, for each of four consecutive weeks
- Continued Therapy: eligible participants to receive add'l once per week infusion for four weeks
 - Twice per week for four consecutive weeks if aGVHD persists or flares

Endpoints

- Primary Outcome: Overall Response Rate 28 Days after Initiation of Therapy
 - Complete Response: resolution of aGVHD in all organs
 - Partial Response: organ improvement of at least one stage w/o worsening of other organs
- Secondary Outcome: Overall Survival at Day 100

Proprietary Bioreactor and Novel Cells

Key Data & Technical Details



REGENERATIVE MEDICINE

Biomechanical Forces Promote Immune Regulatory Function of Bone Marrow Mesenchymal Stromal Cells

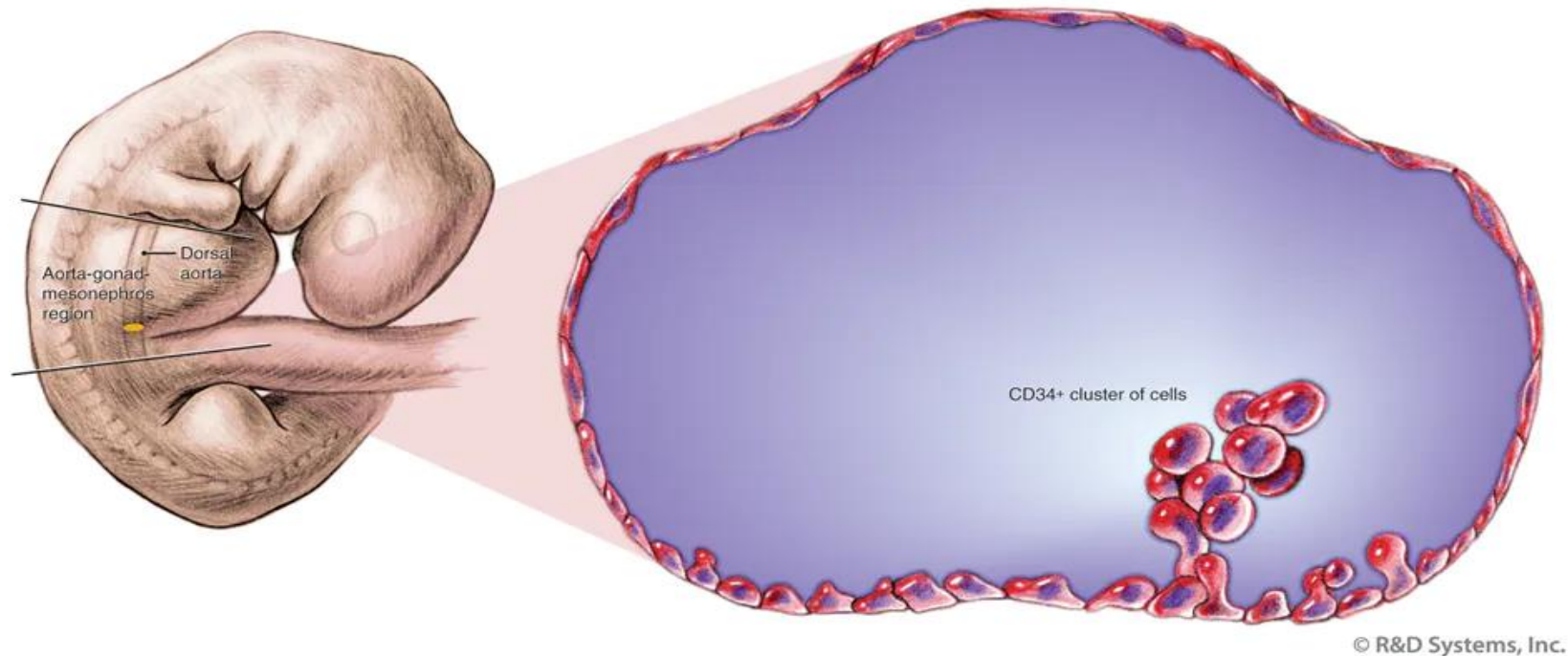
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BENJAMIN M. AERTKER,^a ALEXANDER J. ALEXANDER,^{a,b,c} KATHERINE M. PRICE,^{a,b,c}
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-  Wall Shear Stress (WSS) Stimulates Anti-Inflammatory Mediators
 - Promotes Signaling To Suppress TNF- α
 - Improves Therapeutic Efficacy of MSCs in Rat Model of TBI

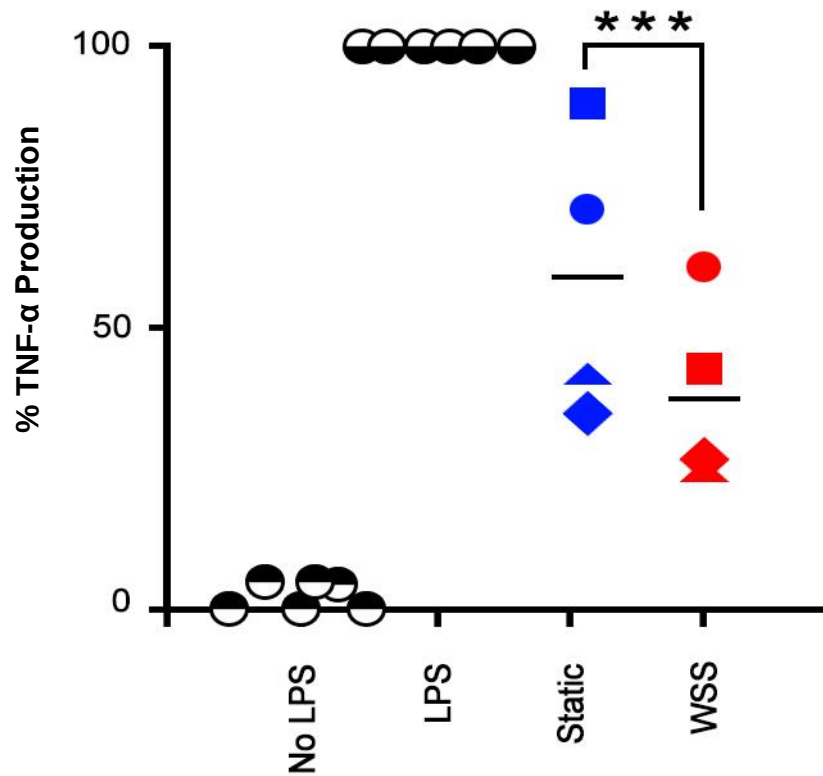
CEVA-D: Rationale

- 🌐 Create a biological enhancement during the manufacturing process
- 🌐 Stem cells start out in embryologic aorta-gonad-mesonephros
- 🌐 Subjected to shear stress that up-regulates specific gene programs

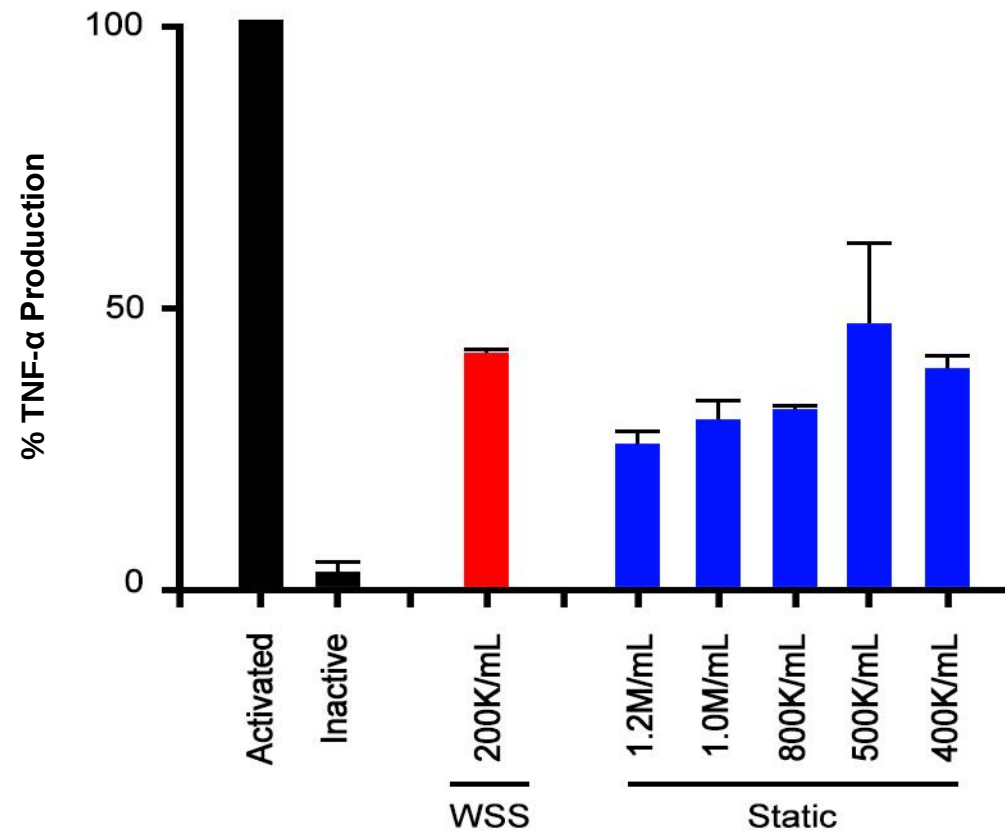


CEVA-D: Conditioned Cells More Effective @ Lower Dose (published)

A Suppression of TNF- α

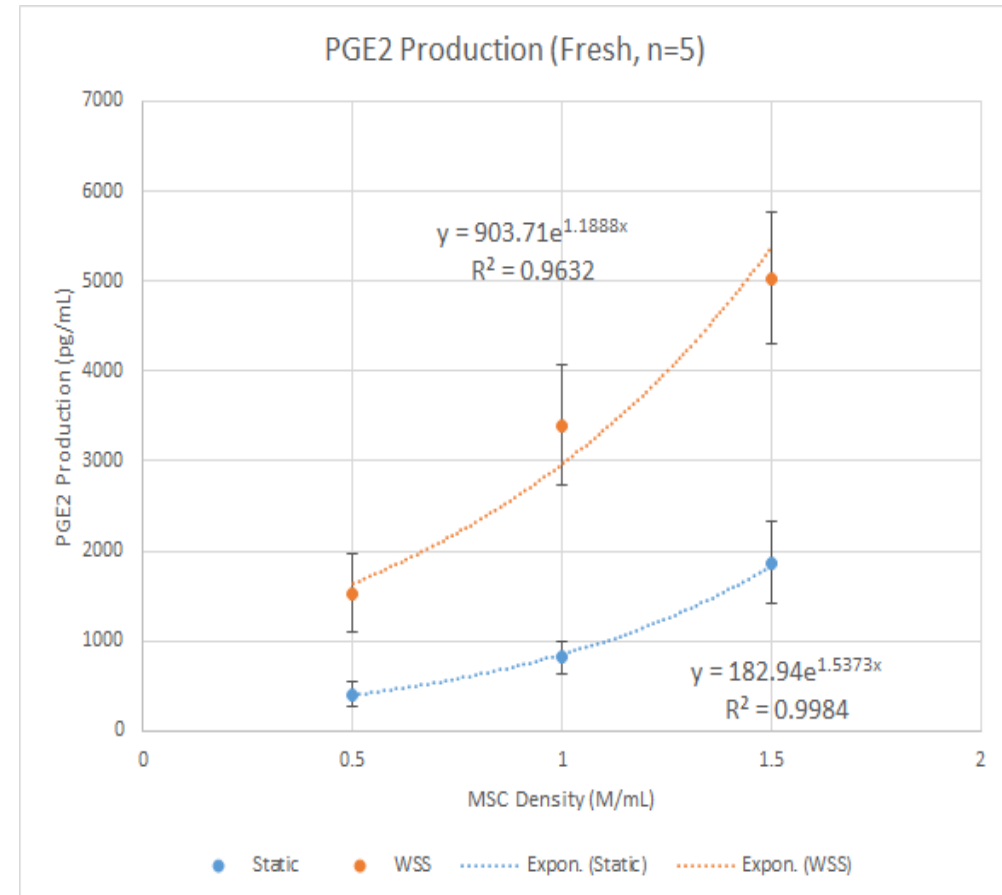
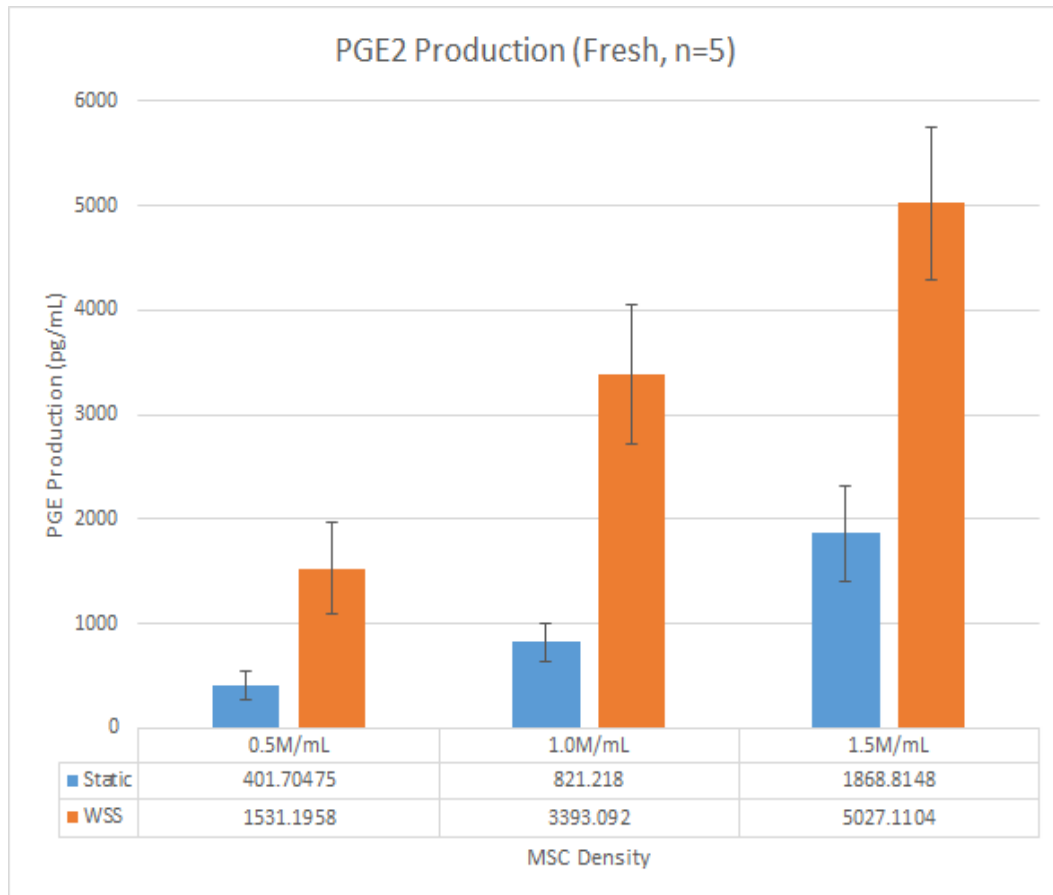


B Dosing for Equivalence of TNF- α Suppression

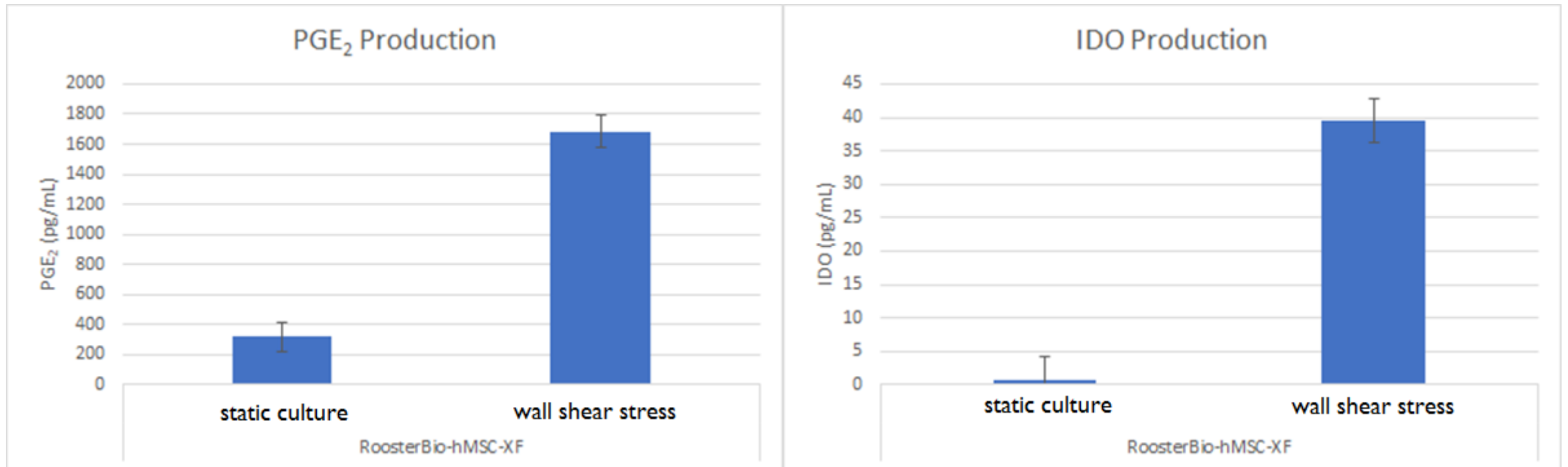


CEVA-D: Increases PGE₂ Production

- 3x Increase in PGE₂ Production
 - Cells treated for three hours in CEVA-D bioreactor
 - PGE₂: established marker for MSCs efficacy

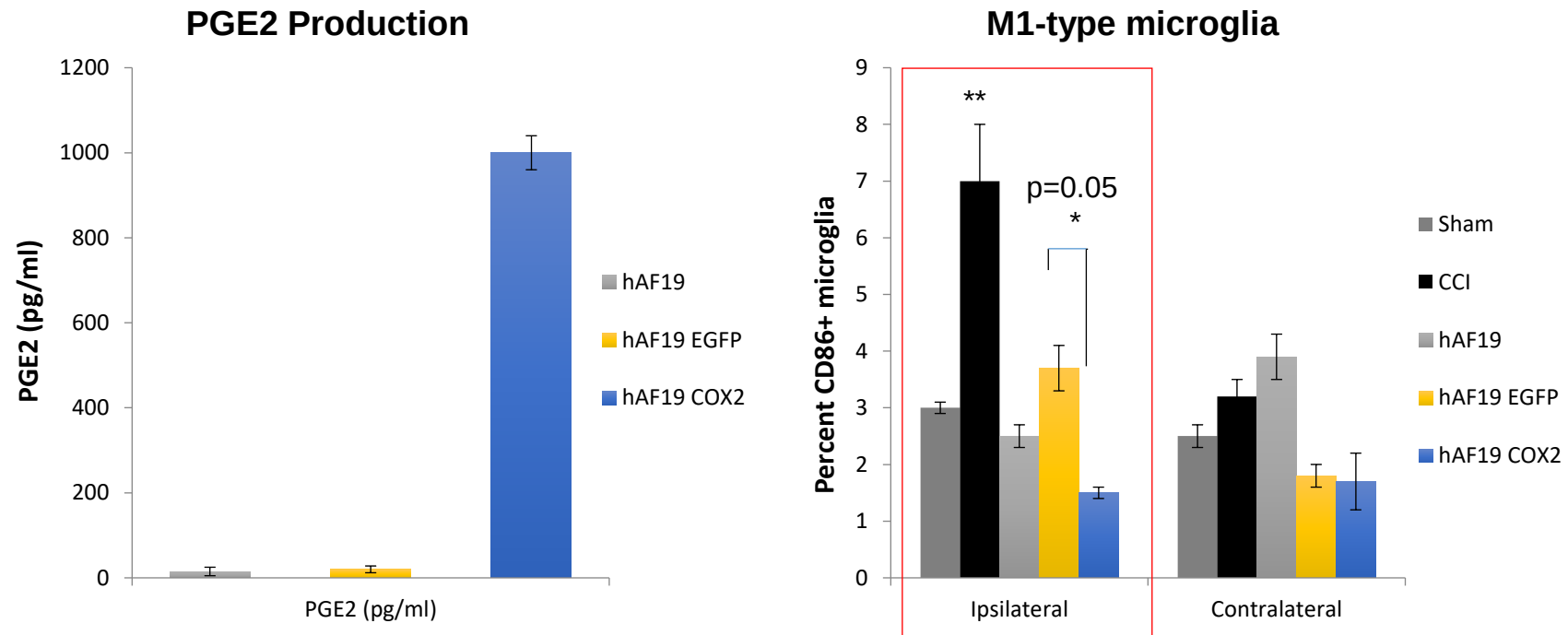


CEVA-D: Increases PGE₂ and IDO Production



Importance of PGE₂ Expression

- Genetically engineered MSCs expressing PGE₂ better suppress microglial M1 polarization
- MAPCs suppress GVHD via PGE₂ synthesis (Highfill et al, *Blood* 2009)



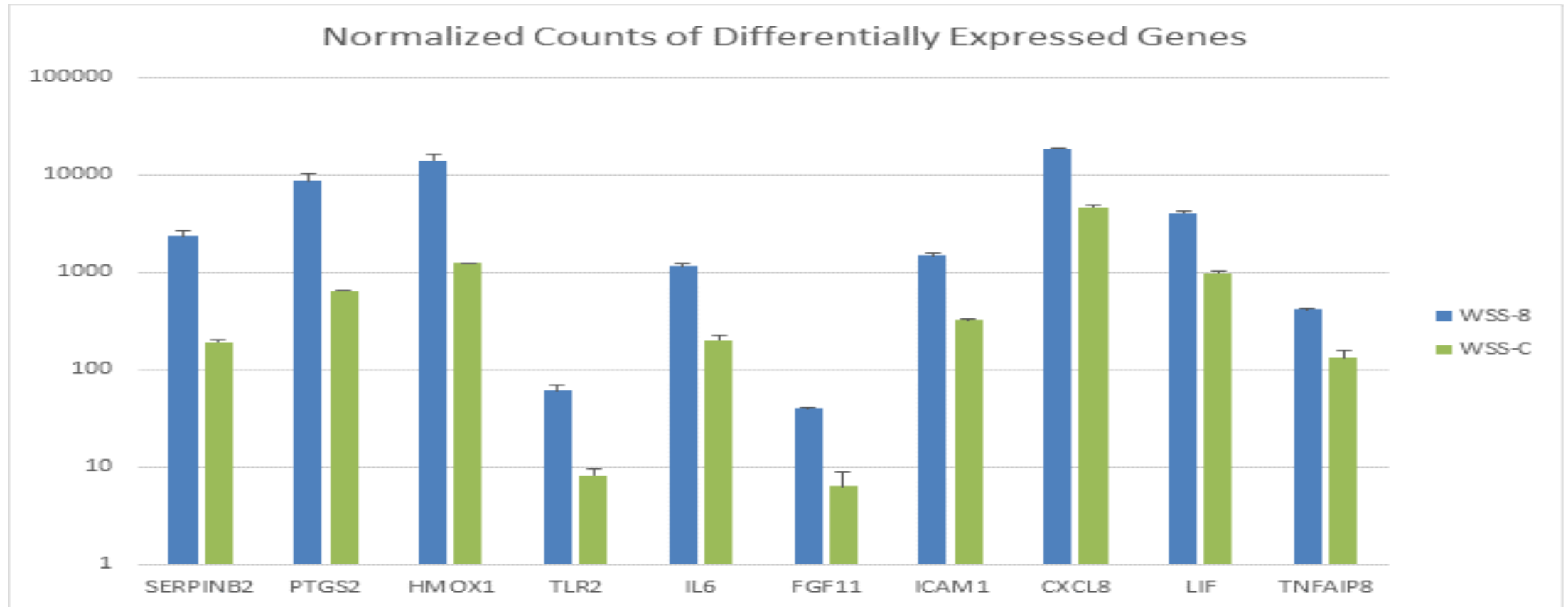
CEVA-101 vs. Static MSC

	Static-MSC					WSS-MSC				
	Media	TNF- α	IFN- γ	IL-1b	Combo	Media	TNF- α	IFN- γ	IL-1b	Combo
PGE ₂ (pg/mL)	302.55 $\pm$ 55.33	459.61 $\pm$ 258.39	317.42 $\pm$ 19.93	331.33 $\pm$ 48.32	647.18 $\pm$ 290.60	1038.14 $\pm$ 336.90*	1351.23 $\pm$ 520.99*	1381.71 $\pm$ 680.51*	2427.72 $\pm$ 311.15*	1610.97 $\pm$ 272.09*
HO-1 (pg/mL)	201.31 $\pm$ 29.73	151.49 $\pm$ 3.59	161.61 $\pm$ 10.29	172.55 $\pm$ 17.22	153.51 $\pm$ 29.77	3855.85 $\pm$ 158.00*	3967.68 $\pm$ 215.73*	4055.52 $\pm$ 275.17*	4428.55 $\pm$ 290.26*	3303.80 $\pm$ 238.97*
Rel. TNF- α Prod.	0.53 $\pm$ 0.23	N.D.	N.D.	N.D.	N.D.	0.17 $\pm$ 0.06*	N.D.	N.D.	N.D.	N.D.
Rel. IFN- γ Prod.	0.58 $\pm$ 0.03	N.D.	N.D.	N.D.	N.D.	0.59 $\pm$ 0.12	N.D.	N.D.	N.D.	N.D.

* Denotes significant difference from Static-MSC:Media

Data derived using cGMP compliant WJ-derived MSCs

CEVA-D Cells: Potency



RNA-Seq Demonstrates Enhanced Potency of CEVA101 Versus Static Cells

- Log-fold increases in key anti-inflammatory signals
- Confirms published pre-clinical data with cGMP compliant cell line

*PTGS2 is COX2

**TNFAIP8 is TSG6

CEVA-D Cells: Characterization

- Consistent Expression of Key Cell Surface Markers After Mechano-Transduction
 - Repeated passages & differentiation often reduce anti-inflammatory potency

Sample	CD34	CD73	CD90	CD105	CD146
<i>hBM-MSC 5204 (Research Grade Control) [p3]</i>	0.17	99.99	99.93	99.08	100
<i>RoosterBio hBM- MSC (GMP Grade Control) [p4]</i>	0.06	100	99.89	99.72	99.86
<i>RoosterBio hBM- MSC (CEVA-101) [p4]</i>	0.11	99.93	99.79	99.58	99.89

Viability

- ▷ Release Criteria: >70.0%
- ▷ Lot Average: 90.80%

Endotoxin Testing

- ▷ Release Criteria: <5.00 EU/mL
- ▷ Lot Average: <1.00EU

14 Day Sterility Culture

- ▷ Release Criteria: Negative
- ▷ Lot Average: Negative

Viable Cell Yield

- ▷ Release Criteria: >80.0%

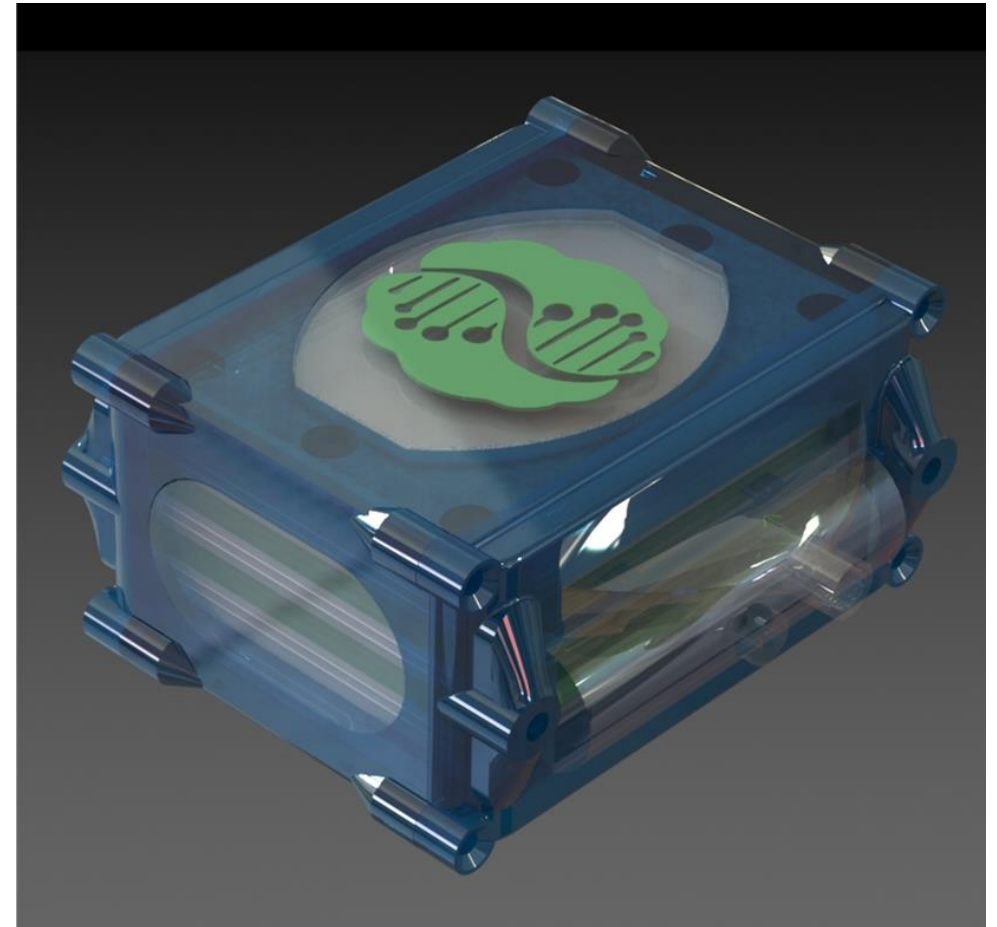
CEVA-D: Biology of Mechano-Transduced Cells

-  Enhanced anti-inflammatory activity (Potency)
 - Broad set of gene programs up-regulated
 - Gain and loss of function of PGE2 confirms importance
-  MSC Source Agnostic
-  Reproduced under cGMP conditions, release
-  Potency assays linked to outcomes in *in vivo models*

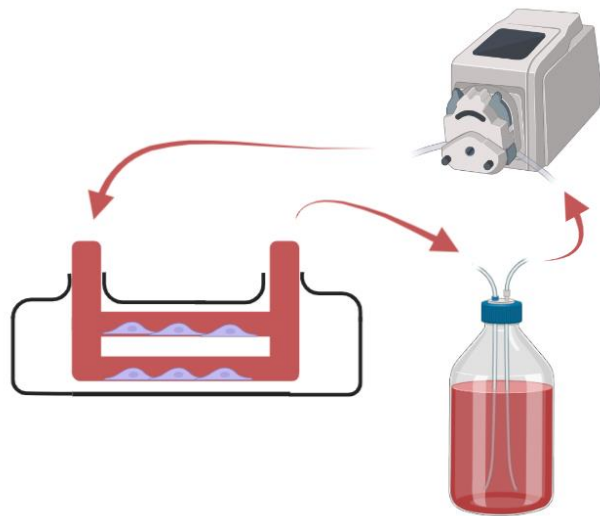
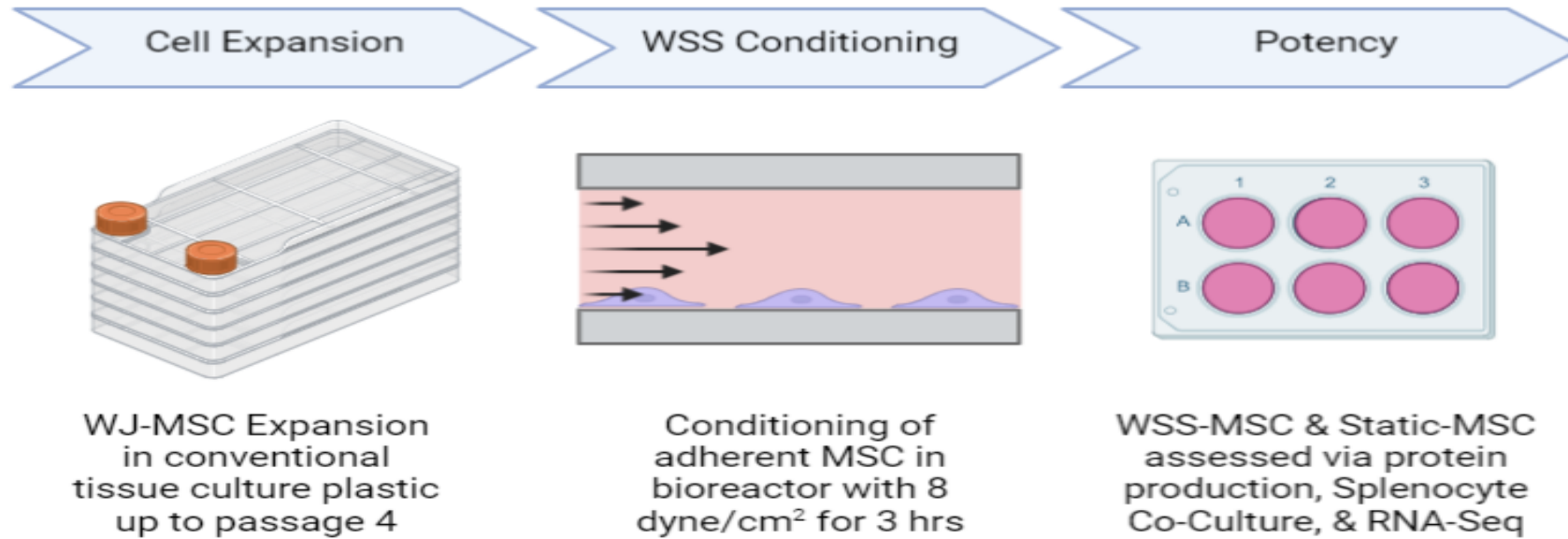
CEVA-D: Development Status and Intellectual Property

-  2D Device: functioning with defined manufacturing process
-  3D Device: in prototype development phase
-  All devices and methods backed by robust IP protection
 - Methods & Apparatus for Conditioning Cell Populations
 - Issued / Allowed: Australia, China, Japan, Russia, US
 - Pending: Brazil, Canada, EP, Hong Kong, Israel, Korea
 - Earliest Expiration Date: 06/23/2036
 - *Broadest Claim: An apparatus comprising: an inlet fluid feed plate; a base plate; and a plurality of intermediate plates positioned between the inlet fluid feed plate and the base plate, wherein each of the plurality of intermediate plates comprises: a first end, a second end, a first side, and a second side; a distribution channel proximal to the first end; and a gathering channel proximal to the second end, wherein: the distribution channel extends between the first side and the second side of the intermediate plate; and the gathering channel extends between the first side and the second side of the intermediate plate.*

- 🌐 Production of Single Dose (CEVA101)
- 🌐 Channel Dimensions: 7.50 x 8.00 x 0.04 cm
 - $\sim \frac{1}{5}$ Clinical-scale
 - Seeding Density: 60k MSC / cm²
- 🌐 All parts designed for injection molding

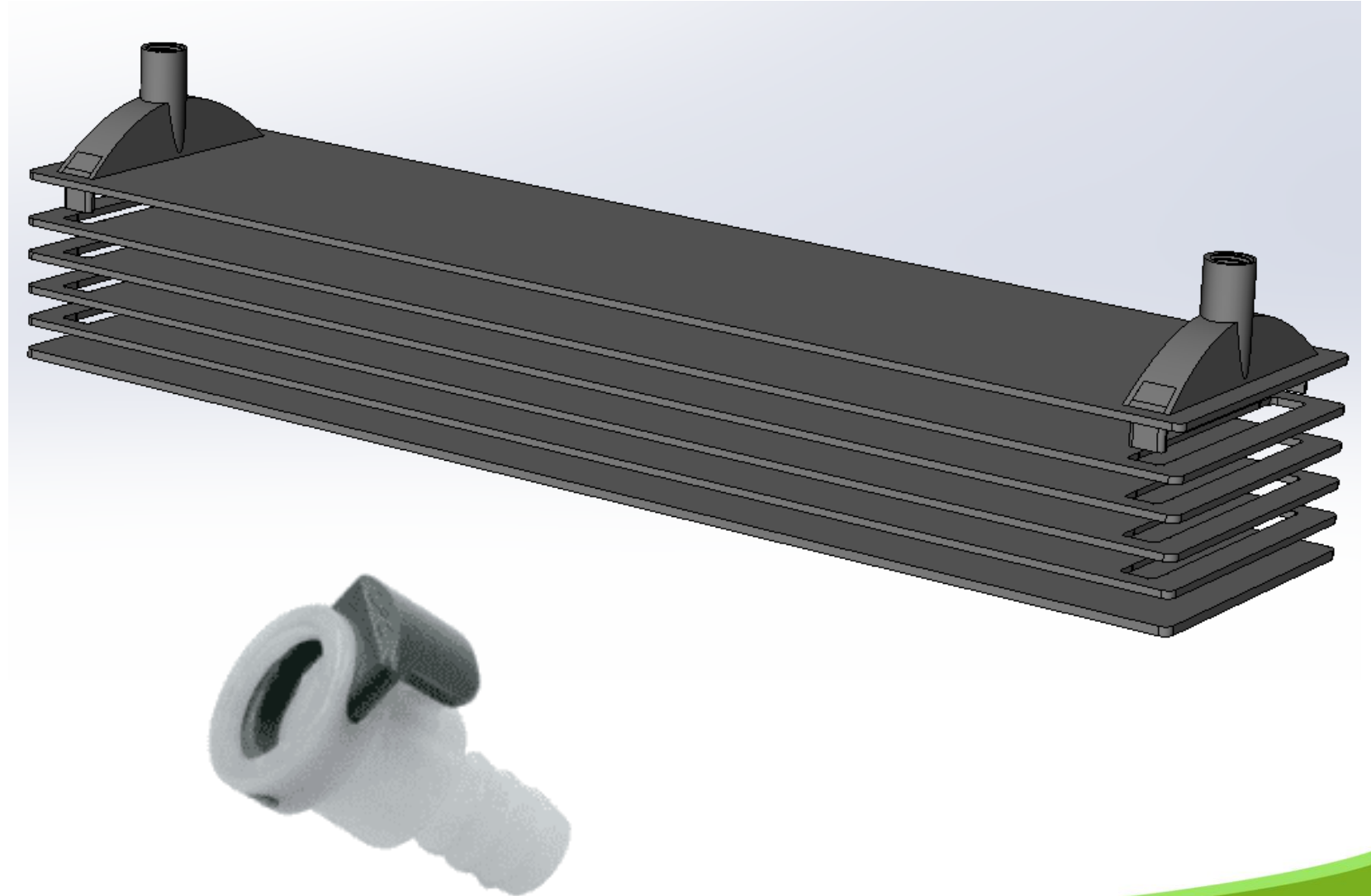


CEVA-D: Manufacturing Work-Flow

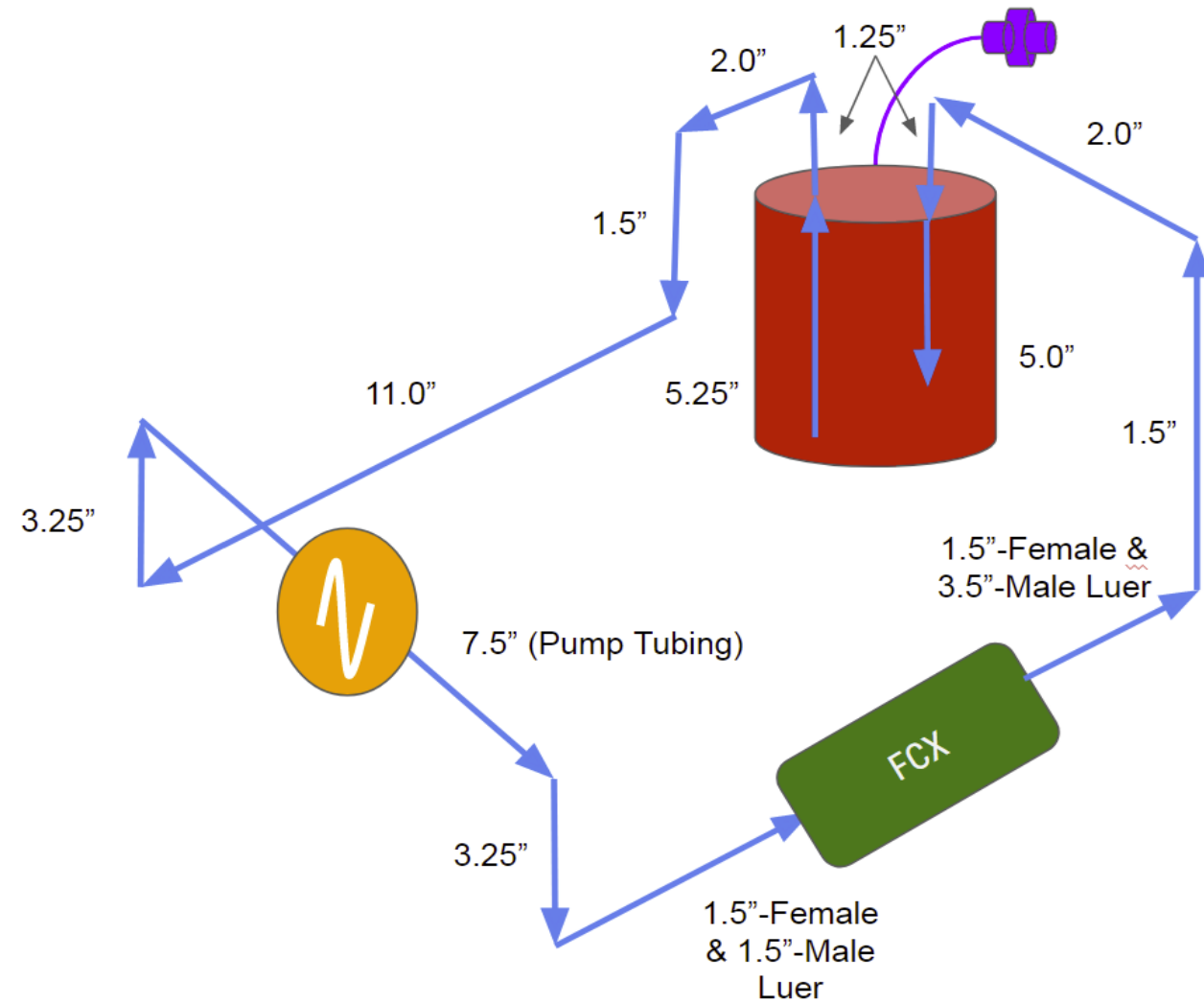
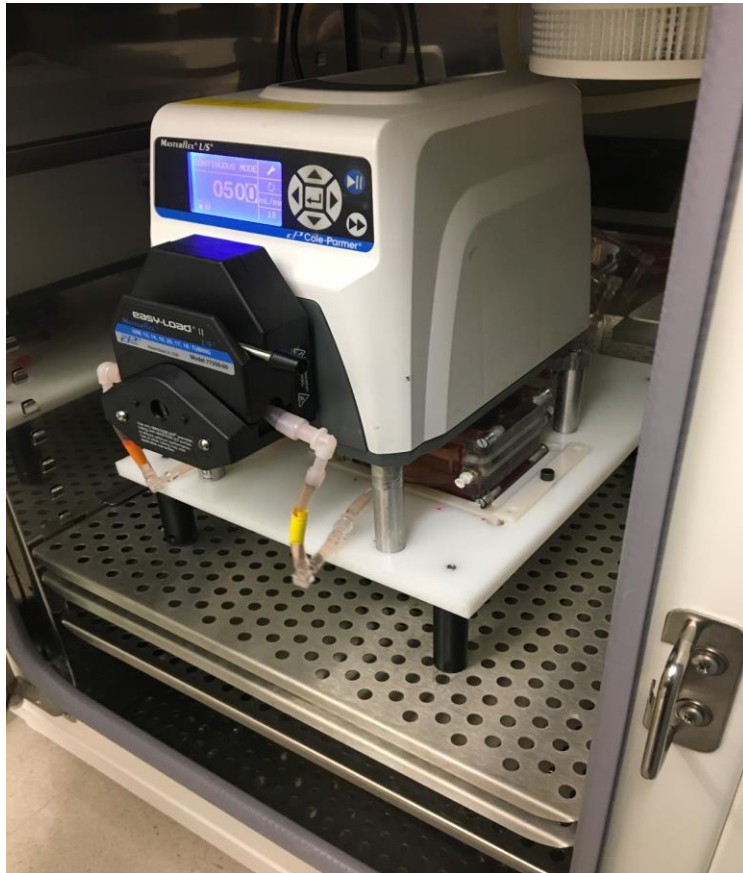


CEVA-D: Production Model

- Quick Connects
- Run 8X per pump
- 50 million cells @ 25k/cm²
- 45 x 10 cm size



CEVA-D: Flow Loop

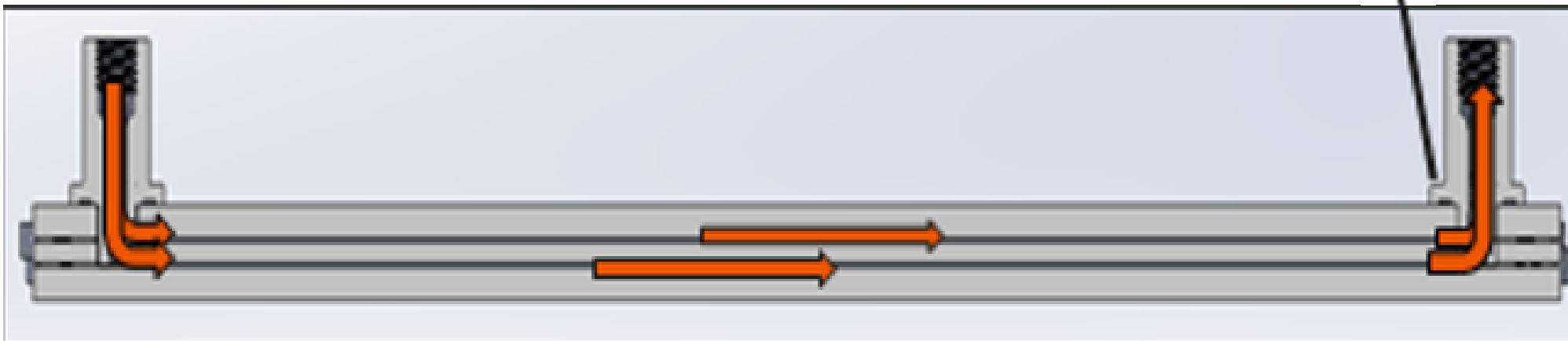
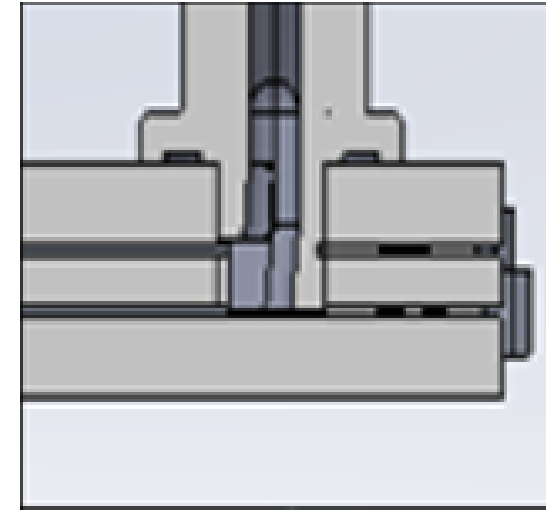


CEVA-D: Conditioning Schedule



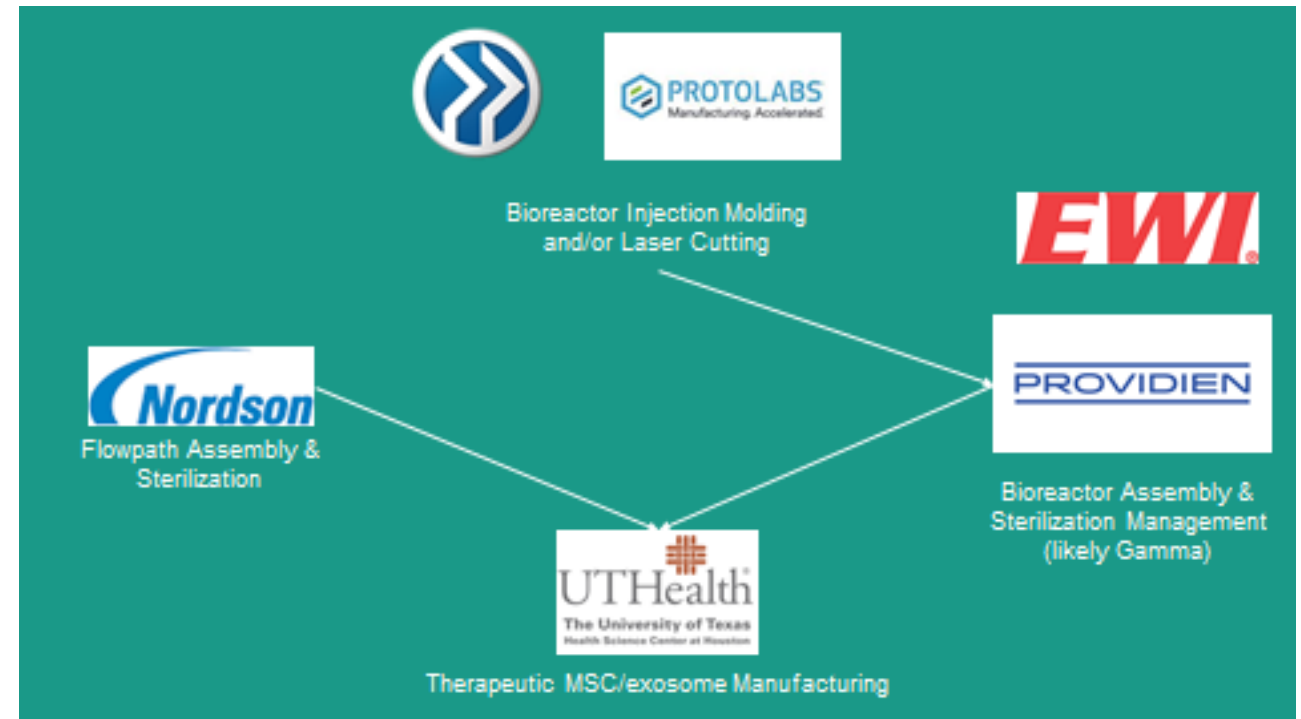
Conditioning Schedule

- Fibronectin Coating: 12 hours
 - 10 ug/mL
- Seeding: 4 hours
 - Can optimize for chosen cell line
- Incubation: 15 hours
- Flow Loop: 3 hours
- TrypLE™ Harvest: 15 minutes



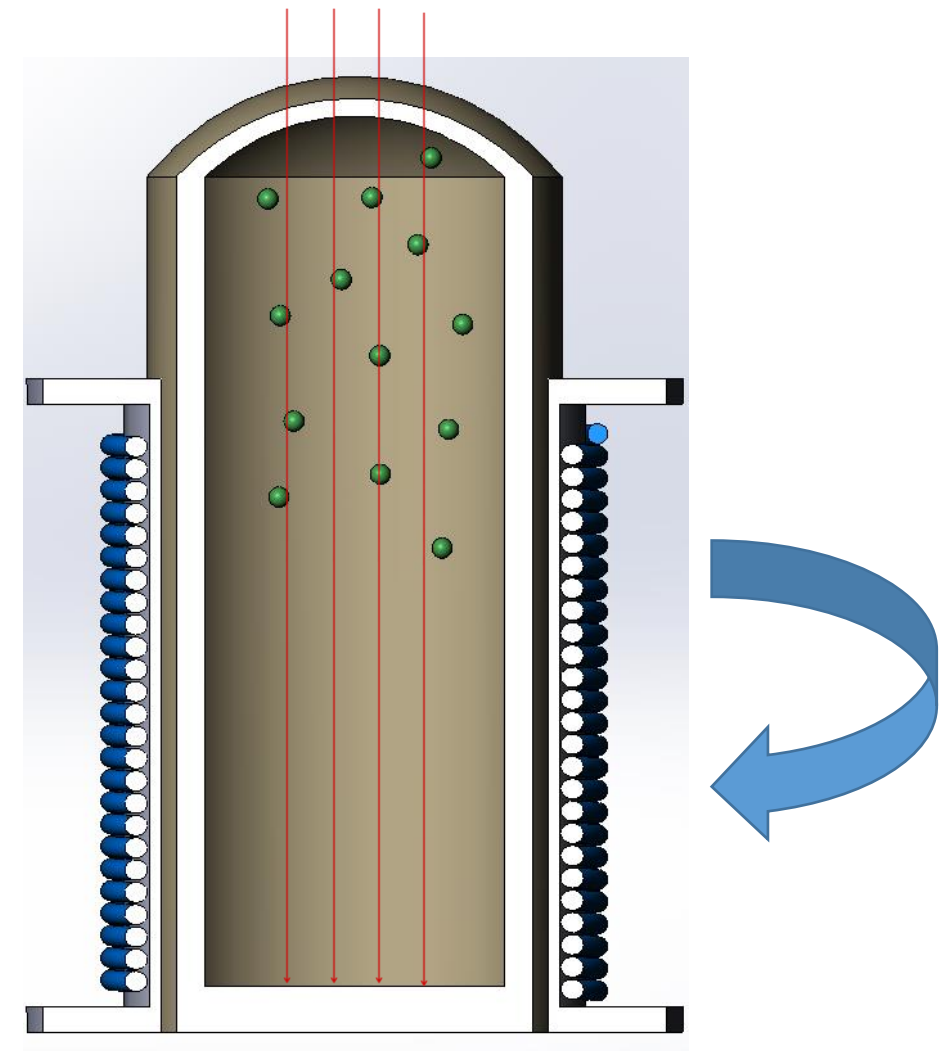
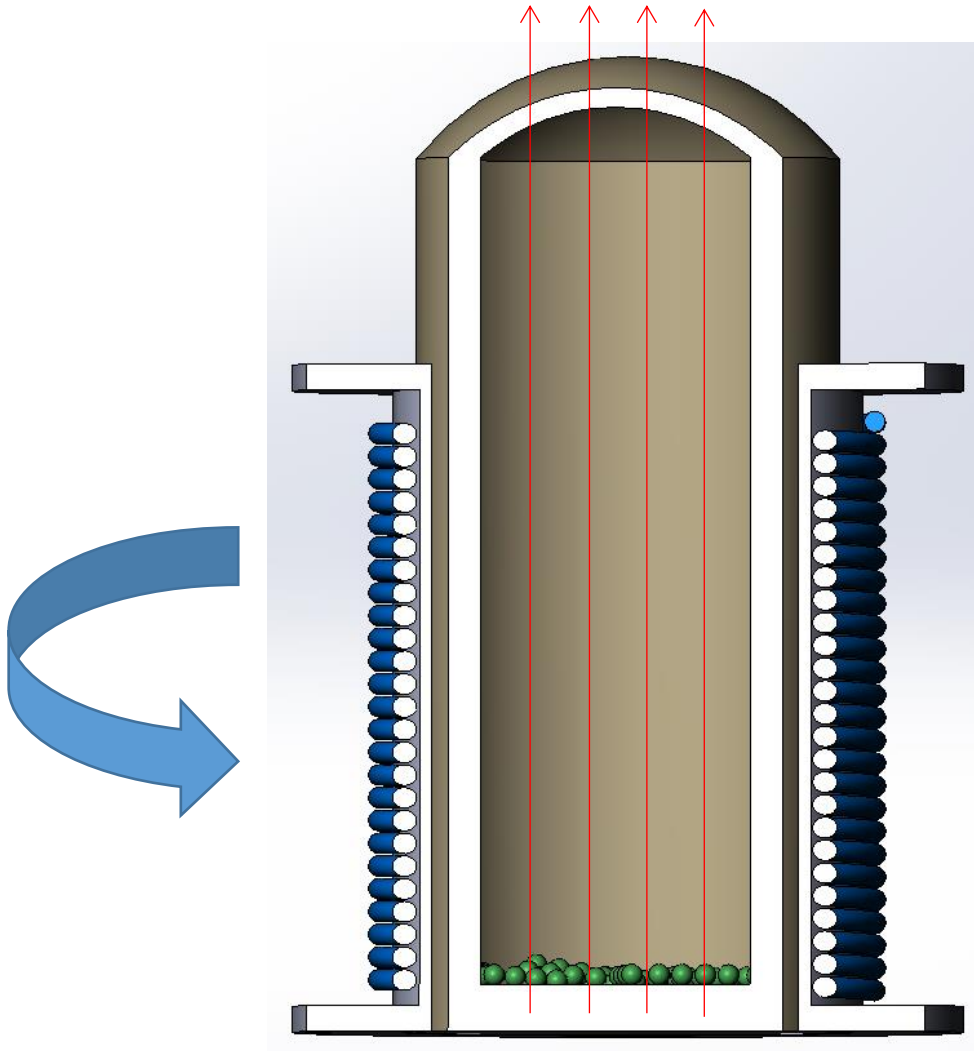
CEVA-D: Process for 2D Production

- Injection molding of casing
- Laser cutting of plates
- Laser welding
- Cleaning
- Sterilization (gamma, EtO)
- Packaging



- 🌐 Rather than keeping cells still and moving fluid (2D), the opposite is done for 3D
- 🌐 3D cannot be accomplished with stirrer tank as beads and cells move with fluid
- 🌐 Strategy based on use of magnetic beads with pulsatile current
 - Produces cell movement through the fluid
 - Generates shear stress in large-volume bioreactor
- 🌐 No moving parts
- 🌐 No cleaning or disinfection (simply discard canister after use)
- 🌐 Programmable shear profiles

CEVA-D: 3D Process Rendering



-  Magnetic beads (depicted in green) are coated with cells
-  Spiral current (see blue arrows) creates magnetic field
-  Magnetic field accelerates movement of beads and produces shear stress

Investment Highlights

