Issuer Free Writing Prospectus Filed pursuant to Rule 433 Registration Statement No. 333-224502 June 12, 2018



### **Forward-Looking Statements & Disclaimers**

The forward-looking statements included in this presentation, involve known and unknown risks that relate to future events or our future financial performance and the actual results could differ materially from those discussed in this presentation. Some of those forwardlooking statements include statements regarding: our financial condition and prospects; the expected reduction in operating expenses following our restructuring; our commercialized and pipeline products and technologies; the timing and conduct of our clinical trials and other parties' clinical trials involving Cytori Cell Therapy™ and Cytori Nanomedicine, including associated financial, clinical and regulatory burdens and projected timing for trial approval, enrollment and completion; the various medical indications and markets that may be addressed by Cytori Cell Therapy and Cytori Nanomedicine; the potential benefits of our strategic initiatives in Japan; the potential effectiveness of Cytori Cell Therapy and Cytori Nanomedicine, including clinical outcomes; conduct of our European managed access program; anticipated uses of clinical trial data; regulatory, reimbursement and commercial strategies and pathways; potential costs and other adverse effects of diseases targeted for treatment by our products, including the Celution System; and anticipated future funding and contract revenues. Some risks and uncertainties related to such forward looking statements include risks and uncertainties regarding: the funding, conduct and completion of our clinical trials and other parties' clinical trials involving Cytori Cell Therapy and Cytori Nanomedicine; our ability to successfully execute our managed access program; uncertain clinical outcomes, including the possibility that we may determine that there is not a viable continued development path for one or more of our product candidates; regulatory uncertainties (including potentially adverse decisions regarding our existing and expected regulatory registrations, approvals and authorizations); unfavorable reimbursement outcomes; inability to access sufficient capital on acceptable terms (including inability to fund, or find third party sources to fund, our proposed clinical trials or continued development of our technologies); the risk that the cost and other negative effects related to our workforce reduction may be greater than anticipated; the risk that we may not realize the benefits expected from our workforce reduction or other cost control measures; our ability to retain our existing employees and effectively operate our business with our reduced workforce; failure to maintain our substantially reduced cash burn; failure to achieve projected product revenue and contract revenue growth; our and our partners' failure to launch products and grow revenues in markets where we currently forecast sales; our ability to service, pay and/or refinance our corporate debt and the potential that our secured lender, which has a lien on all of our assets, including our intellectual property, may accelerate our indebtedness and/or foreclose on our assets; availability of future government funding and changes in government procurement priorities; the U.S. federal government's ability to reduce, modify or terminate the BARDA contract if it determines it is in its best interests to do so; increasing or unanticipated competitive pressures; potential performance issues with our products and technologies; lack of customer acceptance of our technologies; inability to find commercial partners for our therapies; risks related to our dependence on third party performance; the potential for litigation or other disagreements with third parties; and other risks and uncertainties described under the "Risk Factors" section in our filings with the U.S. Securities and Exchange Commission. These risks and uncertainties may cause our actual results to differ materially from those discussed in this presentation. We advise reading our most recent annual report on Form 10-K and subsequent quarterly reports on Form 10-Q filed with the U.S. Securities and Exchange Commission for a more detailed description of these risks. Disclaimers

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- This presentation highlights basic information about us and the offering. Being a summary document, this slide does not contain all the information that you should consider before investing.
- We have filed a registration statement (including a preliminary prospectus) with the SEC for the offering to which this presentation relates. The registration statement has not yet become effective. Before you invest, you should read the preliminary prospectus in the registration statement (including but not limited to the risk factors described therein) and other documents, including our Form 10-Ks and Form 10-Qs, that we have filed with the SEC for more complete information about us and the offering.
- You may get these documents for free by visiting the "Search EDGAR" section on the SEC web site at <u>http://www.sec.gov</u>. The preliminary prospectus, dated June 6, 2018, is available on the SEC website. Alternatively, we or the dealer-manager for this offering, Maxim Group LLC will arrange to send you a preliminary prospectus of you contact Maxim Group LLC, Prospectus Department, 405 Lexington Ave., New York, NY, 10174; Telephone: (212) 895-3745; Email: syndicate@maximgrp.com.



## About Cytori

Cytori Therapeutics, Inc. is a U.S. headquartered company with global operations.

We are committed to providing meaningful and quality therapeutic options with broad utility that benefit patients and healthcare providers around the world. Whether it's advancing our product and technology pipeline, performing clinical trials, or commercializing approved therapies, we believe that every day, every trial and every patient matters.



### Cytori Nanomedicine & Cell Therapy Platforms







- Lead: ATI-0918 potential 1<sup>st</sup> EU generic of market leading oncology drug
- ATI-0918 potential positive cash flow by 2020
- Pipeline: ATI-1123 phase II ready oncology drug
- Anticipate Phase III trial read out in urinary incontinence indication
- Double-digit consumable growth in lead market- Japan\*
- BARDA contract with financial offsets

\*Based on 2016/2017 year-over-year consumable growth



Bcytori nanomedicine



# **Oncology Pipeline**

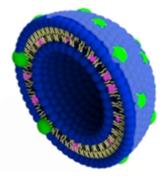
Therapeutic	Market	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Anticipated Milestone
ATI-0918	$\odot$	Breast, Ovarian, MM, Kaposi's					Launch 2020 w/ partner
ATI-0918		Ovarian, MM, Kaposi's					BE 2018, need partner
ATI-0918	*2	Breast, Ovarian, MM, Kaposi's	reast, Ovarian, MM, Kaposi's			BE 2018, need partner	
ATI-1123		Small Cell Lung Cancer		>			Phase 2 2018

BE = bioequivalence



### Nanomedicine Encapsulation Platform

- Lead: ATI-0918, liposomal doxorubicin, generic formulation of market leader Doxil/Caelyx.
- Pipeline: ATI-1123, liposomal docetaxelready for Phase II, proprietary technology for lipophilic compounds.
- Cytori operates dedicated liposomal manufacturing plant in Texas.
- Proprietary manufacturing know-how & test methods with 10+ years experience





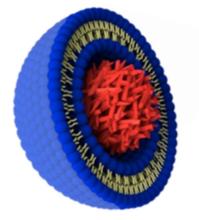


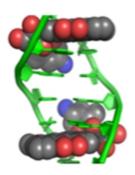
## 'The Liposomal Doxorubicin Story'

- Doxorubicin- highly effective chemotherapeutic
- Liposomal encapsulation substantially lowers cardiotoxity of doxorubicin
- Widely used & profitable oncology drug as a branded therapeutic
- Therapy for advanced breast & ovarian cancer, multiple myeloma & Kaposi's sarcoma
- Production process complex- more of a biosimilar
- Global supply plagued by manufacturing, scalability and quality issues
- Pricing analogous to branded drugs
- Cytori well positioned to compete in largest doxorubicin market segment as U.S.-manufactured, high quality, complex generic



### Lead-ATI-0918 Liposomal Doxorubicin





### Doxorubicin

Anthracycline topoisomerase inhibitor

- · Liposomal formulation superior to Doxorubicin alone
- Generic formulation of market leader, Caelyx, Doxil
- · Primary indications: advanced breast & ovarian cancer
- Primary target markets: Europe, China, MENA
- Challenging manufacturing process, global shortages



# ATI-0918 Clinical Bioequivalence

DIZ Descent as	LS	GM	0/D-4-			
PK Parameter	CAELYX	ATI-0918	%Ratio	CI 90% Lower	CI 90% Upper	
Encapsulated Doxorubicin						
C <sub>max</sub> , ng/mL	47,200	42,400	89.85	85.36	94.57	
AUC <sub>0-t</sub> , ng*h/mL	4,280,000	3,690,000	86.21	82.96	89.59	
AUC <sub>0-inf</sub> ng*h/mL	5,040,000	4,400,000	87.21	81.43	93.41	
Free Doxorubicin						
C <sub>max</sub> , ng/mL	3,090	3,120	100.88	86.21	118.04	
AUC <sub>0-t</sub> , ng*h/mL	180,000	176,000	98.20	92.39	104.38	
AUC <sub>0-inf</sub> ng*h/mL	230,000	226,000	98.01	89.22	107.67	
Doxorubicinol						
C <sub>max</sub> , ng/mL	3.36	2.99	88.94	81.32	97.27	
AUC <sub>0-t</sub> , ng*h/mL	489	442	90.26	83.02	98.13	



## ATI-0918 Liposomal Doxorubicin

### Well Positioned to Compete in Largest Doxorubicin Market Segment As U.S.-Manufactured, High Quality, Complex Generic\*

Pegylated Liposomal Doxorubicin	Europe	China	US
Estimated Market Segment Size	\$120-\$160M	\$110-\$130M	\$180-\$220M
Reference Listed Drug / Reference Standard	Janssen Caelyx	-	Janssen Doxil / Sun Lipodox
Marketing Authorization – Brand	Janssen Caelyx	Janssen Caelyx (withdrawn)	Janssen Doxil
Marketing Authorization – Generic	Sun (denied approval)	CSPC† Fudan-Zhanjiang† Changzhou Jinyuan†	Sun Dr Reddys Patriot
BE Study Complete	Cytori + 1 other	-	1 other
BE Study Pending Initiation / In Progress	4 others	Cytori‡	Cytori‡ + 7 others

\* Referred to as 'Hybrid Generic' by EMA

† BE studies not required for CFDA approvals ‡ Partner-dependent

# Partner-dependent

Source: IQVIA, Company Press Releases and Reports, Internal Estimates, FDA Orange Book, clinicaltrials.gov, ctri.nic.in

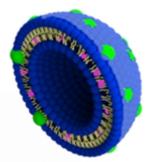


# ATI-0918 Liposomal Doxorubicin

Milestone	Target Completion Date
EU Bioequivalence Trial	Complete
Registration Lots & Stability Testing	H2 2018
Partnering	2018
EMA MAA Submission	1H 2019
EMA MAA Approval	1H 2020
EU Launch	1H 2020

		2018			2019		2020
EU	Facility	Fabricate	Stability	EMA Submission	12 Month	EMA Submission	EMA Approval &
	Validation	Stability Lots	Testing	(6 Month Stability)	Stability Complete	(12 Month Stability)	EU Launch





New Chemical Entity Pegylated & Protein Stabilized

### Docetaxel

**Highly Lipophillic Taxane** 

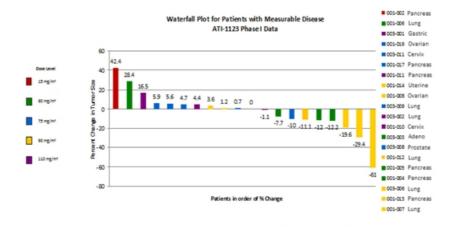
- Mitotic inhibitor
- Apoptosis via Bcl-2 phosphorylator
- Protein stabilization overcomes liposomal instability with lipophilic compounds (USPTO #7179484)
- 14 preclinical studies indicate:
  - ATI-1123 serum AUC 4-5x higher than Docetaxel alone
  - · Better tissue distribution and greater activity in key tumors
  - · Potentially greater efficacy than docetaxel alone
  - · Potential reduction of side effect profile

\*Mahalingam et al (2014) Cancer Chemother Pharmacol. 74(6):1241-50



### ATI-1123 Phase I Clinical Trial Summary

- 29 patients, dosing range from 15-110mg/m<sup>2</sup>
- ATI-1123 achieved 20% increase in MTD vs. standard docetaxel & demonstrated signs of efficacy with 1 partial responder
- 16/26 evaluable patients (62%) had stable disease, with toxicity profile comparable to or better than docetaxel alone
- · 82% pts. had clinical benefit



\*Mahalingam et al (2014) Cancer Chemother Pharmacol. 74(6):1241-50



### Initial Clinical Target- Small Cell Lung Cancer, Highly Aggressive Rare Disease

- Small Cell Lung Cancer (SCLC)
  - 30,000 adults in the U.S.
  - 15% of total lung cancer cases
  - 93% of patients relapse/refractory to 1<sup>st</sup> line therapy
  - 68% of relapse/refractory patients receive 2<sup>nd</sup> line therapy
- Topotecan- only FDA-approved drug for SCLC 2<sup>nd</sup> line therapy
- Generates \$70M in annual sales U.S., top 5 EU markets, and Japan
- Standard docetaxel is used off-label for SCLC, included in MD Anderson practice algorithm as 2<sup>nd</sup> line therapy
- Patented, protein-stabilized liposomal docetaxel (ATI-1123)- 3 part positioning: less toxicity, similar or improved efficacy, and more patientfriendly dosing schedule vs. Topotecan
- Company intends to expand clinical indications beyond SCLC in subsequent trials



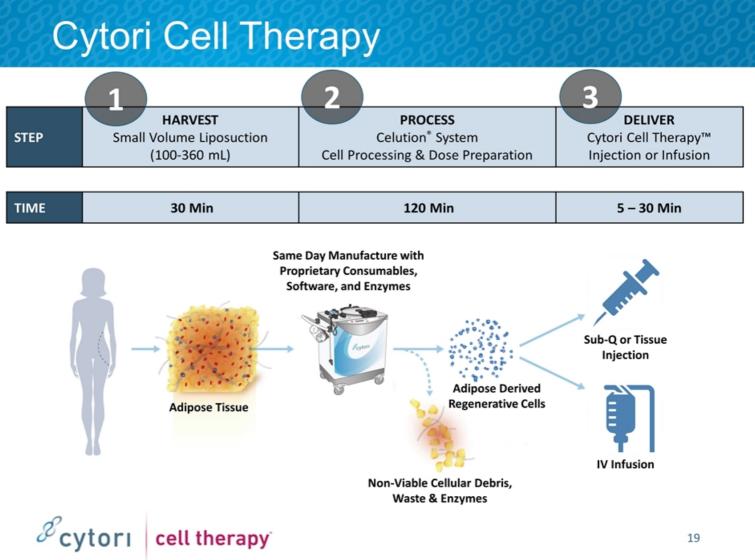
- Regulatory Strategy-
  - SCLC initial indication
  - Potential eligibility for orphan status and US FDA 505(b)(2) pathway
  - SPA
- Clinical Development Plan-
  - Open label, single dose study of ATI-1123
  - Dosage of 90 mg/m<sup>2</sup> on an every 3 week schedule. In phase 1 trial, doses of 75 90 mg/m<sup>2</sup> would be clinically appropriate.
  - Enrollment of up to 40 subjects at approximately 8 clinical centers.
  - Primary end point- objective response rate at up to 30 weeks for each subject.
  - Key secondary end points- duration of response, overall survival and progressionfree survival (PFS) (each assessed at up to 30 weeks for each subject)
- Business Development Plan-
  - Seek partner for non small cell lung cancer and pancreatic indications





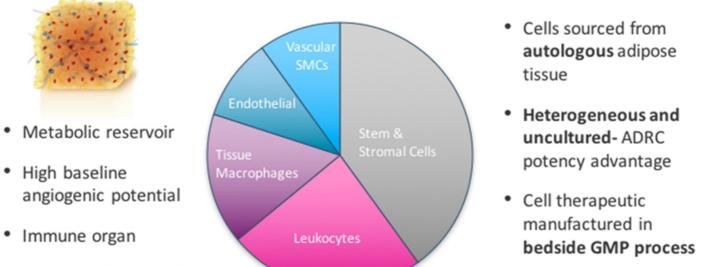
# Scytori cell therapy





# Cytori Cell Therapy

Adipose-derived regenerative cells- Clinical grade, heterogeneous cell population highly-enriched for adipose-derived stem, stromal, vascular, and immunoregulatory cell types



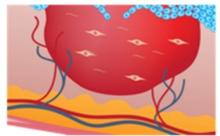
Stem cells & progenitors



# Cytori Cell Therapy

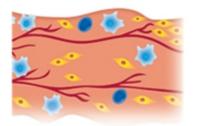
Cytori Cell Therapy is being developed with the goal of beneficially modulating multiple key pathologic processes which are anticipated to reduce pain and disability and improve quality of life

### Angiogenesis/Vasculopathy



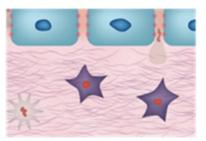
- · Promotes angiogenesis
- Normalization of vessel architecture
- Improved vasomotor function<sup>1-5</sup>

### Inflammation



- Modulates expression of proand anti-inflammatory factors
- Modulates the function of proand anti-inflammatory cells<sup>3, 6-9,</sup>

### Fibrosis/Wound Remodeling



- Reduces development of fibrosis
  Remodels existing
- fibrosis<sup>2,10,11</sup>

Foulsert et al (2015); 2. Kdn et al (2014); 3. Premaratine (2011); 4. Morris et al (2015); 5. Eguchi et al (2015); 6. Feng et al (2010); 7. Hao et al (2014); 8. Dong et al (2013);
 9. Data on file (Cytori); 10. Sematrice et al (2014); 11. Data on file (Cytori)



# **Cell Therapy Pipeline**

Therapeutic	Market	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Status/Anticipated Milestone
Habeo™		Scleroderma					Phase III required in Diffuse subset
Habeo™	$\odot$	Scleroderma/Cryopreserved *					Data in 2H 2018
Habeo™	٠	Scleroderma					Planned, funds permitting
ECCO-50		Knee Osteoarthritis					Planned, funds permitting
ECCI-50	•	Male SUI *					Fully enrolled
DCCI-10		Thermal Burn/Radiation #					Phase 1 2018
Kerastem		Alopecia †					Potential Phase 3 2018

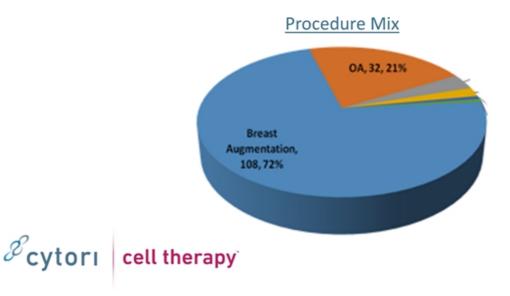
- Breast surgery & osteoarthritis indications approved in Japan under Japanese Regenerative Medicine Law
- Other investigator initiated trials underway in US, Europe & Japan



\*Substantial third-party financial support or investigator initiated trial \*BARDA funded program † Licensee funded program <sup>††</sup>Regenerative Medicine Law

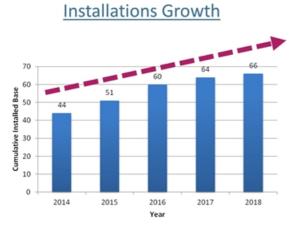
## **Commercial Performance in Japan**

- Japan Regenerative Medicine Law- early market access in 2015
- Full medical device commercial team in Tokyo
- Leverage safety & efficacy data from US & EU clinical trials
- Targeting historically self pay or 'lifestyle' procedures
- Expanded device approval- applied for class III approval



# **Commercial Performance Japan**

- Steady growth in Installations and Procedures since 2015
- Preservation of ASP
- Building foundation for launch in Stress Incontinence







## **Urinary Incontinence Opportunity**

- Stress urinary incontinence (SUI), the 2<sup>nd</sup> most common type of incontinence in elderly, is caused by a loss of strength in pelvic floor muscles and urinary sphincter following childbirth and prostate surgery
- Published clinical data (n=20 patients) in Japan indicates that Cytori Cell Therapy may benefit both men and women with SUI
- In Japan, no treatments available for 820K+ men with mildmoderate SUI
- · Estimated global urinary incontinence market by 2022
  - Asia Pacific: \$5.9B, 4.2% CAGR → Japan has largest market share
  - Europe: \$6.7B, 4.1% CAGR
  - North America: \$12.6B, 4.2% CAGR

Source: Market Research Future; M Gotoh Presentation at Japan Society of Regenerative Medicine



## **Cell Therapy in Urinary Incontinence**

Phase	Approach	Status	Key Findings
Preclinical (human) <sup>1</sup>	Demonstration of in vitro differentiation towards smooth muscle	Complete	Expression of multiple markers consistent with smooth muscle
Preclinical (porcine) <sup>2</sup>	Injection into the rhabdosphincter immediately following injury	Complete	Reduced fibrosis
Preclinical (porcine) <sup>2</sup>	Injection into the rhabdosphincter 30 days following injury	Complete	Reduced fibrosis
Pilot Clinical Trial <sup>3</sup>	11 patient, single arm, OUS (Japan)	Complete	No significant reported adverse events Improved continence
Independent Case Series <sup>4</sup>	6 patient, single center, OUS	Complete	No significant reported adverse events Improved continence
Pivotal Clinical Trial <sup>5</sup>	45 patient, multi-center, single arm, OUS	Enrollment complete	Last patient, last visit Jan 2019
			guez et al (2006) Proc Natl Acad Sci U S A. 103(32):12167-72 er et al (2016) J Urol. 196 (3):934-42

3. Gotoh et al (2014) Int. J. Urol. 21, 294–300

4. Choi et al (2016) Yonsei Med J 57 (5). 1152-8

5. Shimizu et al 2017 BMC Urol 17(1):89. doi: 10.1186/s12894-017-0282-7



### Initial Clinical Data in Urinary Incontinence

### **Pilot Trial**

- Single center, open label study
- Patients with mild-to-moderate urine leakage persisting more than 2 years after prostatectomy
- 11 subjects enrolled and followed-up for 12 months

### **Results**<sup>1</sup>

- · No serious adverse events reported
- 55% (6/11) of patients exhibited >50% improvement in 24 hour leakage at 1 year
  - Anticipated incidence of spontaneous improvement with standard care is 10%
- 41% mean improvement in 24 hour urinary leakage volume (p=0.01)

#### Benefit sustained for several years<sup>2</sup>

- 14 patients with median follow-up >4yrs
- Retention of efficacy
  - 39% mean improvement in 24 hour urinary leakage volume
  - 79% (11/14) of patients exhibited improvement
    - 56% mean reduction in daily leakage volume
- 1. Gotoh et al (2014) Int. J. Urol. 21, 294–300
- 2. Gotoh et al (2017) International Continence Society: Abst 489
- 3. Gotoh et al. Int J Urology 2014



### Persistence of Effect in Urinary Incontinence



# **Pivotal Trial Design**

### Status: Enrollment complete; last subject will complete 12 month visit in Q1 2019

#### Indication

· Stress urinary incontinence following prostatectomy

#### **Study Design**

• Multi-center, single arm, open label

#### **Primary Endpoint**

- Percentage of subjects with >50% reduction in urinary leakage at 1 year
  - Anticipated percentage with spontaneous improvement with standard care is 10%
  - Observed rate of improvement in pilot study =55%
  - ADRESU powered for statistical significance at 30% rate of improvement

#### **Secondary Endpoints**

- Percentage of subjects with >50% reduction in urinary leakage at other time points
- · Urine leakage volume per day
- Number of incontinence episodes per day
- · Incontinence-related Quality of Life
- · Urodynamics (maximum urethral closing pressure)

Shimizu et al 2017 BMC Urol 17(1):89. doi: 10.1186/s12894-017-0282-7.









### Anticipated Urinary Incontinence Timeline

	2018		2019		2020	
	<u>1<sup>st</sup> Half</u>	2 <sup>nd</sup> Half	<u>1<sup>st</sup> Half</u>	<u>2<sup>nd</sup> Half</u>	<u>1<sup>st</sup> Half</u>	2 <sup>nd</sup> Half
Base enario	Complete Enrollment	Class III device Approval	Analyze Data/ File for MHLW Approval		Japan Approval	Japan Launch
edited enario	Complete Enrollment	Class III device Approval Analyze Data/ File for MHLW Expedited Approval		Japan Approval	Japan Launch	Japan Reimbursement



## **BARDA** Contract

#### Goal

- Medical countermeasure for use in thermal burn injury ± concomitant radiation exposure
- · Government acquisition contract for use of the countermeasure in burn mass casualty event

#### **Research and Development Contract**

- Contract value up to \$106MM
- ~\$34MM awarded to date
  - ~\$20MM for preclinical activities in Contract Base and Option 1
  - \$13.4MM awarded 2017 for execution of Pilot Clinical Trial (Contract Option 2)
- ~70MM of additional contract options available at BARDA's discretion for clinical trials leading to FDA approval and for preclinical work in burn injury complicated by radiation exposure

#### Work Completed

- Demonstration of improved healing of thermal burn wounds following treatment with ADRCs
   Efficacy also evident in context of concomitant radiation and burn injury
- Preclinical development needed for FDA approval of pilot clinical trial under Investigational Device Exemption (IDE) pathway

#### Status

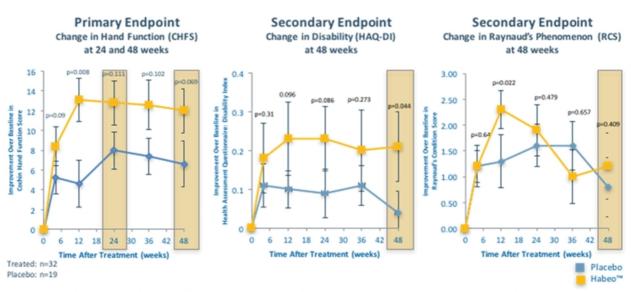
- IDE approved
- Pilot clinical trial recruiting
- Additional clinical sites being added (target 6 sites active by end 2018)

### Cytori cell therapy





## Scleroderma



- Clinically meaningful efficacy trends noted early and sustained for hand function and disability in the diffuse subgroup at 24 & 48 weeks that approached statistical significance
- · At or near statistically significant benefit in all key endpoints @ 12 weeks in diffuse group

Data presented as mean ± sem Other than the 24 & 48 week time for CHFS, p values are not corrected for multiple comparisons

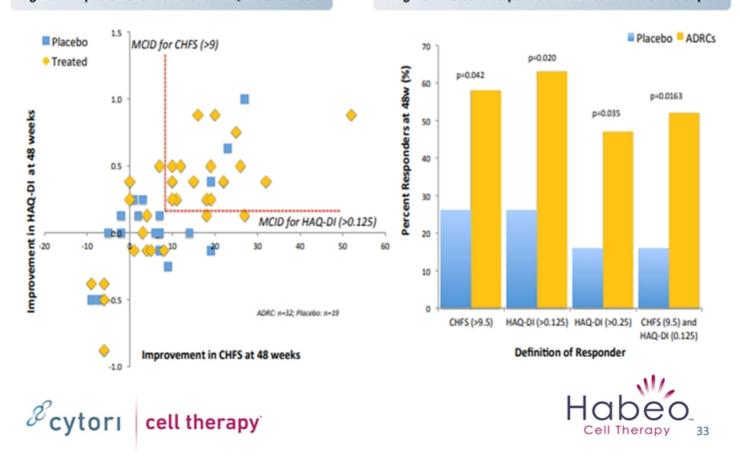




## Scleroderma

Figure 3: Improvement in CHFS and HAQ-DI at 48 weeks

Figure 4: Percent Responders in ADRC and Placebo Groups



## Scleroderma

Market	Agency	Product Designation	Orphan Designation
U.S.	FDA CBER	Habeo <sup>™</sup> Fresh: Device (Class III)	No
	FDA CBER	Habeo <sup>™</sup> Cryopreserved: Drug	Yes
Japan	PMDA MHLW	Celution <sup>®</sup> System • Device = Class I • Consumables = Class I → Class III	Yes with application
Europe	BSI	Celution <sup>®</sup> System: Device (Class II/III)	No
	EMA	Habeo <sup>™</sup> Fresh: ATMP	Yes
	EMA	Habeo <sup>™</sup> Cryopreserved: ATMP	Yes





# **Intellectual Property**

### **Global Patent Estate**

- 102 issued patents and with 45 pending applications
- 15 issued patents in Japan (several pending)



### **Trade Secrets and Know-how**

- Celase® proprietary enzyme blend supplied exclusively to Cytori by Roche
- Cytori cell processing systems embody tissue collection, processing, and handling parameters resulting from >15 years of experience optimizing tissue processing, cell extraction and delivery

### **Brand recognition and Trademarks**



Select Data – as of 3/31/18					
Cash	~ \$5.9MM				
Senior term loan	~ \$13MM				
Common Shares outstanding	~ 6.2MM				
Options, Series B, RSAs and warrants	~ 2.6MM				
Fully diluted share count	~ 8.8MM				



## **Anticipated Milestones**

- SCLERADEC-II trial readout
- First enrolled partient for US RELIEF trial funded by BARDA
- Identify commercial partner for ATI-0918
- ATI-0918- complete manufacturing validation and production of stability lots
- ATI-0918- file for EMA approval following 6 months stability
- ATI-1123 development & Phase II- Decisions on orphan designation, viability of 505(b)2 pathway & SPA
- ADRESU trial readout & file for approval
- · Begin Japanese scleroderma trial- pending funding
- Puregraft royalty milestone
- · Japan Class III device approval
- · Decision on expedited review for incontinence trial



