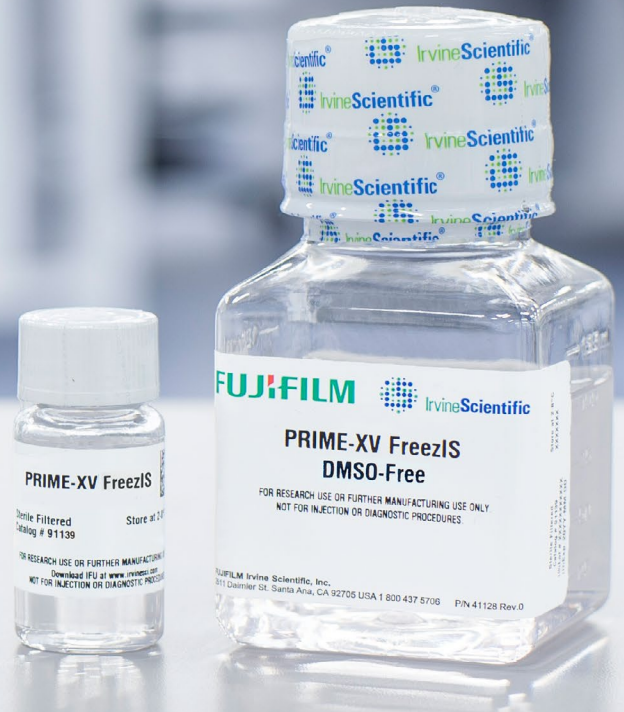


Freeze Cells—Not the Transition
from Research to Clinical



High Performing PRIME-XV FreezIS Cryopreservation Media Solutions

Preserve Viable Cells with Scalable Cryopreservation Media Solutions

Protein-free, animal component-free, chemically defined cryopreservation media

Maintain viability and maximize efficiency for preserving cells in today's advanced applications. Whether it's regenerative medicine, drug discovery, or biobanking, PRIME-XV FreezIS offers DMSO-containing and DMSO-free formulations to accelerate time-to-market.

Faster to market. *Faster to patients.*

PRIME-XV FreezIS Cryopreservation Solutions are the go-to cryoprotectants that scale through every stage of development. With the flexibility of using non-excipient media for research needs and a seamless transition to excipient* for clinical trials, we are dedicated to therapeutic success throughout your workflow.

Choosing the right PRIME-XV formulation

Our exceptional team of cell culture media experts offer support in determining the right PRIME-XV FreezIS formulation for process needs.



Product	Contains DMSO	DMSO-free	Ancillary	Excipient	Post-thaw wash step	Reduce vein-to-vein time
PRIME-XV FreezIS	●		●		●	
PRIME-XV DMSO-Free		●	●			●
PRIME-XV FreezIS (EX)	●			●	●	
PRIME-XV FreezIS DMSO-Free (EX)		●		●		●

*Excipient products are not for injection as standalone product. Testing for individual applications is the responsibility of the customer.

Excipient and Ancillary Product Details

The cutting-edge formulations of PRIME-XV FreezIS Cryopreservation Media Portfolio are optimized to protect and preserve cells without compromising functionality—all while providing the options to get therapies to patients, faster.

Ancillary Material

Finished product: Starting material, Drug

Use of cryomedia:

Further manufacturing use:

- Used in starting material
- Used in finished product. Washed out prior to administration

Cryomedia washed out? Yes

Cryomedia active ingredient: N/A

Safety evaluation: Residuals risk assessment

Regulations, standards, and guidances:

- Public Health Service Act 361 (minimally processed): CBER, 21 CFR 1271
- Public Health Service Act 351: CBER, 21 CFR 210 and 211(drug), 600s (biologics)
- USP <1043> Ancillary Materials for Cell, Gene, and Tissue-Engineered Products
- USP <1044> Cryopreservation of Cells
- ISO 20399:2022 Biotechnology – Ancillary Materials Present during the Production of Cellular Therapeutic Products and Gene Therapy Products
- EP 5.2.12 Raw Materials for the Production of Cell-Based and Gene Therapy Medicinal Products
- EMA 410/01 Note for Guidance on Minimizing the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products
- FDA-2021-D-0404 Considerations for the Development of Chimeric Antigen Receptor (CAR) T Cell Products

Raw material supplier quality system:

- No standard. Should follow relevant sections of FDA 21 CFR 820/211.
- EXCiPACT for PAMs
- ISO 9001
- ISO 13485

Excipient

Finished product: Drug

Use of cryomedia:

Excipient for further manufacturing use

Cryomedia washed out? No

Cryomedia active ingredient: No

Safety evaluation: Toxicological/Pharmacokinetic testing

Regulations, standards, and guidances:

Ancillary material guidelines PLUS:

- FDA-2002-D-0188 Nonclinical Studies for the Safety Evaluation of Pharmaceutical Excipients
- USP <1046> Cell-Based Advanced Therapies and Tissue-based Products
- EMEA/CHMP/QWP/396951/2006 Guideline on Excipients in the Dossier for Application for Marketing Authorization of a Medicinal Product
- FDA media Defining Excipients in the Substance Registration System

Raw material supplier quality system:

- No standard. Should follow relevant sections of FDA 21 CFR 820/211.
- EXCiPACT/ NSF/IPEC/ANSI 363
- ISO 9001
- ISO 13485
- 21 CFR 211/820



The information above is not intended to provide regulatory advice or be all inclusive. Regulations, standards, and guidance are subject to change.

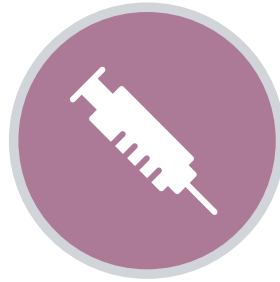
PRIME-XV FreezIS DMSO-Free

Ensure Potency That Therapies Require Without the Toxicity Risk



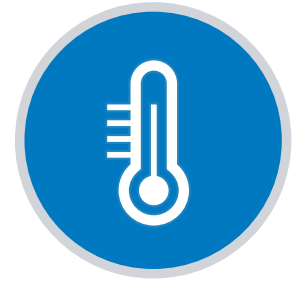
Low Toxicity

Eliminate the risk of DMSO toxicity and maintain potency of human mesenchymal stromal/stem cells (MSCs), PBMC, T cells, and hematopoietic stem cells (HSCs)*



High Cell Viability

Produce therapies using a complete, ready to-use medium with 90% post-thaw cell viability comparable to solutions containing DMSO



Maximum Protection

Enable cell preservation for short-term storage at -80°C** and long-term storage in liquid nitrogen to -196°C

Supports Comparable MSC Viable Cell Density and Percent Viability with DMSO-free and DMSO-containing Media

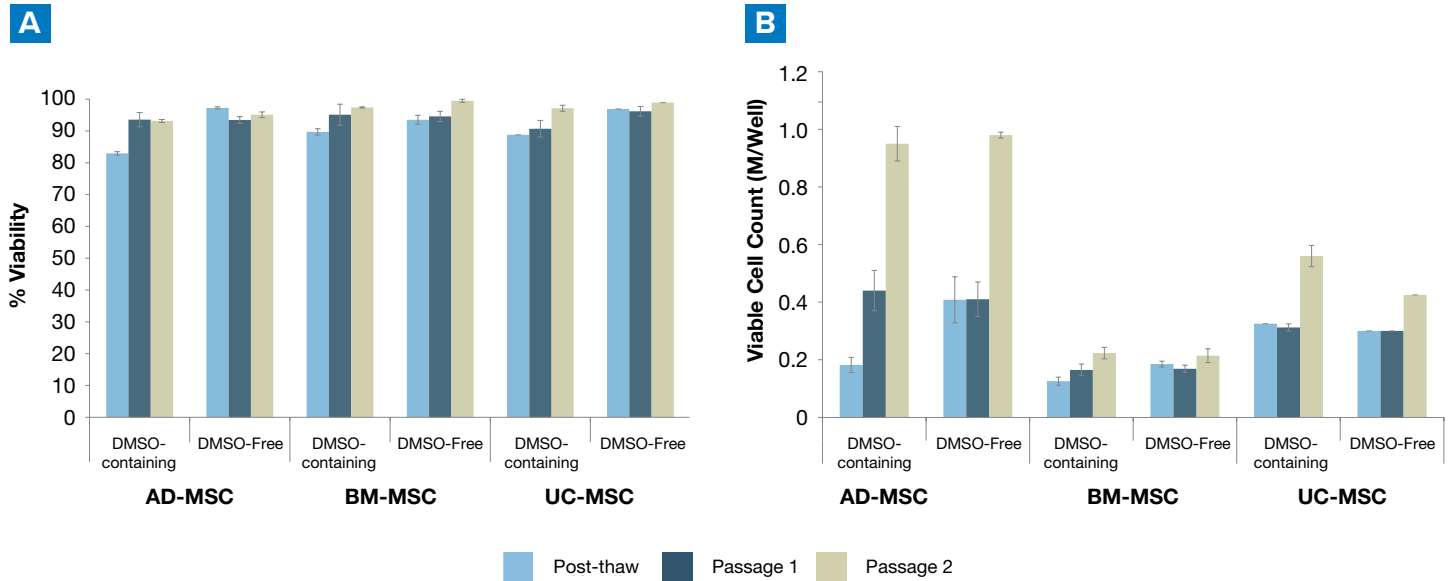


Figure 1. PRIME-XV FreezIS DMSO-Free retains comparable MSC viable cell density and percent viability after cryopreservation compared to DMSO-containing solution. Human adipose-derived MSCs were frozen in PRIME-XV FreezIS DMSO-Free and in PRIME-XV FreezIS. The cells were stored in liquid nitrogen for 2 days before they were thawed and cultured through 2 passages until 80% confluent. The viable cell density (A) and percent viability (B) were assessed with trypan blue staining in a Vi-CELL Cell Viability Analyzer at thaw and 2 passages post-thaw. Viable cell density was calculated using the cell count multiplied by the volume.

*Nontoxic when injected in animal models.

**Human MSC and PBMC (T cell) data available for short-term storage. Human HSC data is not available.

PRIME-XV FreezIS DMSO-Free Successfully Protects Human T Cells Potency and Viability

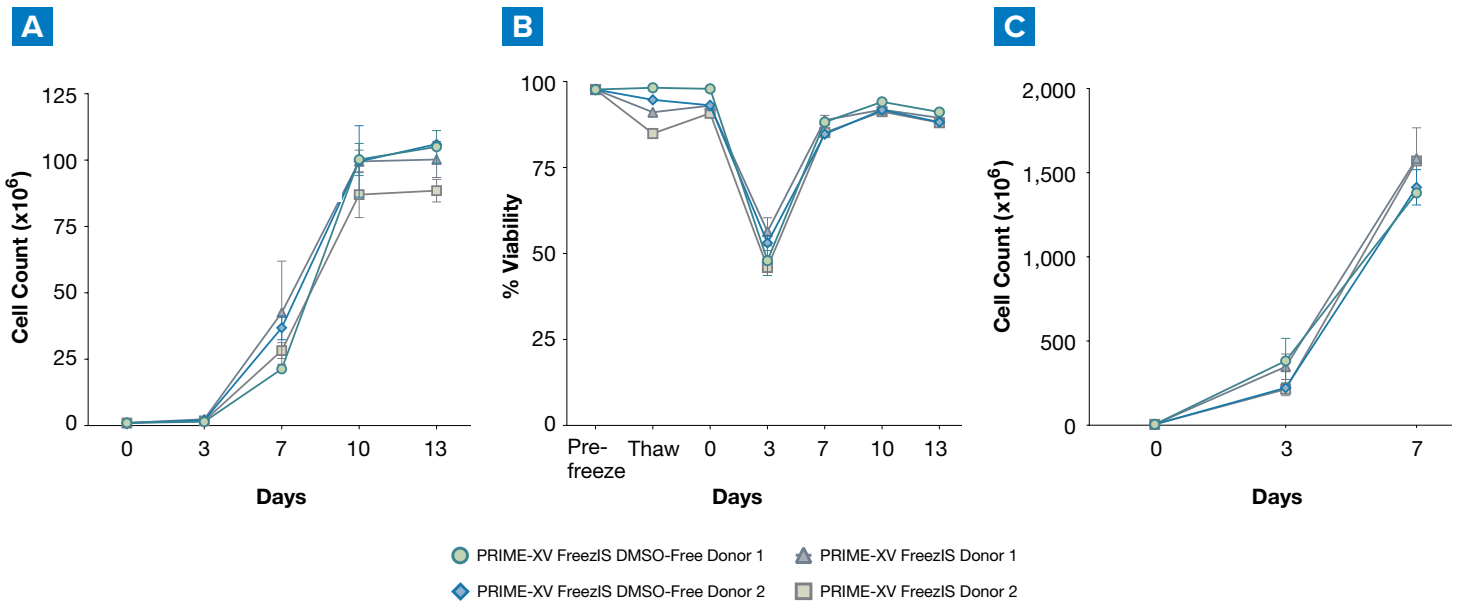


Figure 2. Cells frozen in PRIME-XV FreezIS DMSO-Free show robust expansion if plated directly into culture medium after thaw, without washing out the cryopreservation medium. Cells cultured in 24-well R-series G-Rex plates (A) and 6-well M-series G-Rex plates (C) recovered well from cryopreservation when plated directly into cell culture media post-thaw. Cells thawed from PRIME-XV FreezIS DMSO-Free media best maintained pre-freeze viability in the first 24 hours post-thaw (B). Data is representative of 3 donors.

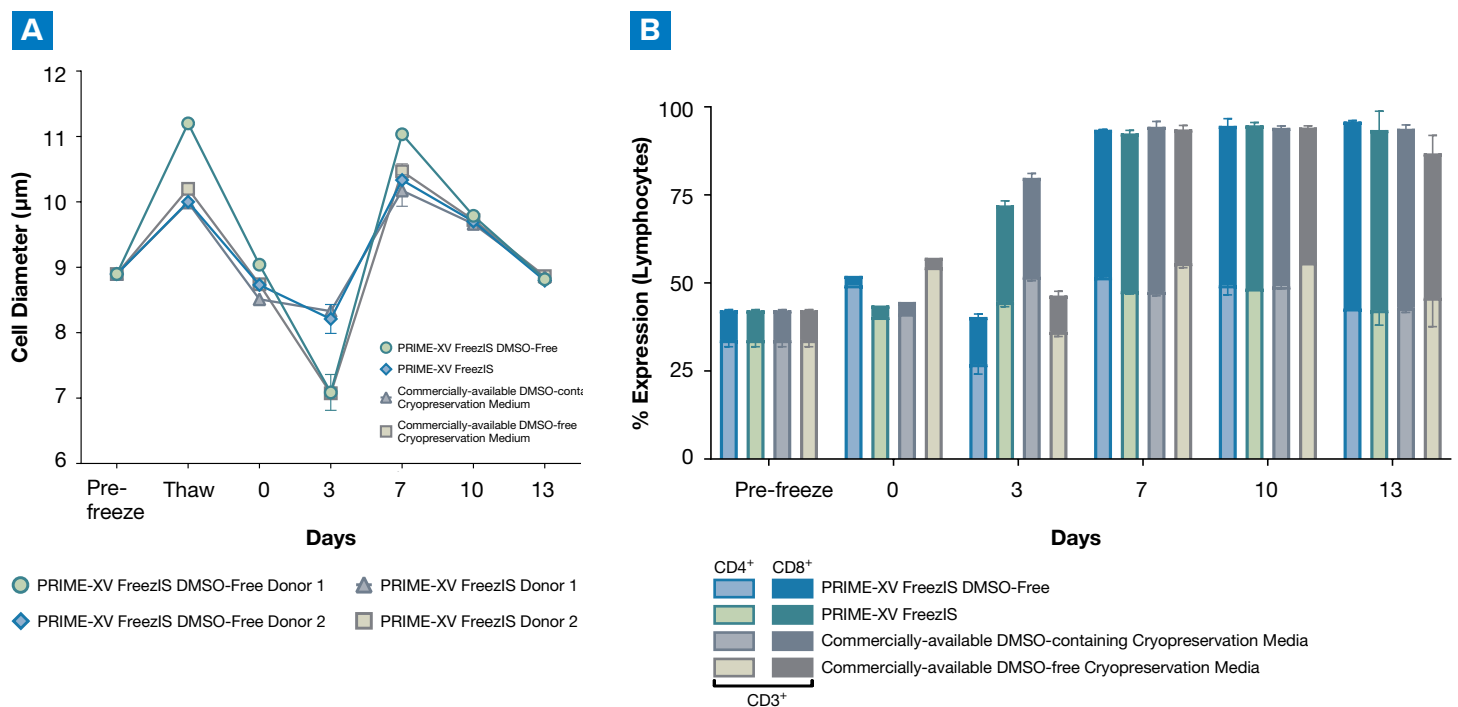


Figure 3. Cells thawed directly into cell culture media show similar trends in cell diameter and distribution of CD4⁺ and CD8⁺ cells with minor differences between DMSO-containing and DMSO-free groups. (A) Cells thawed directly into cell culture media exhibit an increase in diameter immediately post-thaw, returning to baseline after a 24-hour rest period. Cell diameter increased following cell activation using αCD3 and αCD28-conjugated beads, though was delayed slightly in DMSO-free conditions, recovering by Day 7. **(B)** Distribution of CD4⁺ and CD8⁺ cells were comparable across all conditions from day to day; however, total CD3⁺ cell proportion among DMSO-free conditions was lower on Day 3, recovering by Day 7. Data is representative of 3 donors.

Nonclinical Cryopreservation Toxicology

Study 1: Investigate the Effects of PRIME-XV FreezIS DMSO-Free via Different Administration Route

Table 1. Treatment and testing regiment via different route of administration.

Nr.	Test Compound	Route	Volume / 25 g (Body Weight)	Dosing at Day 0	N Mice	Sacrifice Timepoint
1	PRIME-XV FreezIS DMSO-Free medium	IP	1 mL	Single dose	3	Day 28
2	Negative control (PBS)					
3	PRIME-XV FreezIS DMSO-Free medium	IV	0.2 mL			
4	Negative control (PBS)					
5	PRIME-XV FreezIS DMSO-Free medium	SC	1 mL			
6	Negative control (PBS)					
7	PRIME-XV FreezIS DMSO-Free medium	PO	0.5 mL			
8	Negative control (PBS)					

Weaned mice were administered with one injection of PRIME-XV FreezIS DMSO-Free, set as Day 0. Intermediate blood samples and body weight measurements were taken on Days -2, 0, 7, 14, and 21. Upon sacrifice on Day 28, organs were processed for weight and general histopathology.

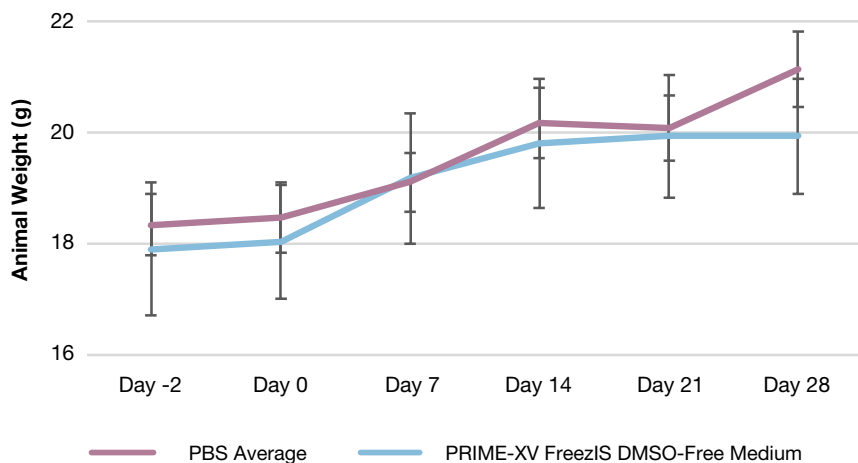


Figure 4. Normal growth following IV injection of PRIME-XV FreezIS DMSO-Free. Intravenous (IV) injection of PRIME-XV FreezIS DMSO-Free does not affect growth, in terms of body weight, of mice over the 28-day period of the study. Error bars are SEM. Similarly, intraperitoneal (IP), subcutaneous (SC), and per os/oral (PO) administration did not impact body weight either (data not shown).

PRIME-XV FreezIS DMSO-Free injected via different routes does not affect growth progression in mice. No abnormalities in growth progression were observed between control and compound-treated mice for any dosing routes. Analysis of the organs showed no adverse toxicity effects after injection.

Study 2: Compared the Effects of IV-injected Stem Cells in PRIME-XV FreezIS DMSO-Free to Those in DMSO-containing Cryomedium or PBS

Table 2. Animal models were administered one injection of PRIME-XV FreezIS DMSO-Free.

Tab	Route/Dose	Test Material	Number per Group	Post-inoculation Observation Period
Guinea pigs	IV = 0.5 mL	AlloRX stem cells in DMSO-containing cryomedia	3	7 days
		AlloRX stem cells in PRIME-XV FreezIS DMSO-Free	3	
		AlloRX stem cells in PBS	3	
		PRIME-XV FreezIS DMSO-Free	3	
		PBS	2	
Mice	IV = 0.2 mL	AlloRX stem cells in DMSO-containing cryomedia	5	7 days
		AlloRX stem cells in PRIME-XV FreezIS DMSO-Free	5	
		AlloRX stem cells in PBS	5	
		PRIME-XV FreezIS DMSO-Free	5	
		PBS	2	

Animals were observed daily for any abnormal signs, conditions, or health concerns. Any animals exhibiting severe clinical signs or found moribund were euthanized. Animals were assessed for survival after 7 days.

Table 3. PRIME-XV FreezIS DMSO-Free did not affect survival of guinea pig or mice hosts post-intravenous injection when compared to the PBS control.

Phase	Test Material	Number of Hosts Inoculated	Number of Hosts to Survive 24 Hours	Number of Hosts to Survive Observation Period	% Survival
Guinea pigs	AlloRX stem cells in DMSO-containing cryomedia	3	1	1	33
	AlloRX stem cells in PRIME-XV FreezIS DMSO-Free	3	3	3	100
	AlloRX stem cells in PBS	3	3	3	100
	PRIME-XV FreezIS DMSO-Free	3	3	3	100
	PBS	2	2	2	100
Mice	AlloRX stem cells in DMSO-containing cryomedia	5	4	4	80
	AlloRX stem cells in PRIME-XV FreezIS DMSO-Free	5	4	4	80
	AlloRX stem cells in PBS	5	5	5	100
	PRIME-XV FreezIS DMSO-Free	5	5	5	100
	PBS	2	2	2	100

The post-intravenous injection survival rate for the inoculated hosts of the PRIME-XV FreezIS DMSO-Free alone or of the AlloRX stem cells in PRIME-XV FreezIS DMSO-Free was $\geq 80\%$ and no abnormal clinical observations occurred, meeting the acceptance criteria.

PRIME-XV FreezIS DMSO-Free solution did not show toxic effects after administration through different entry routes.

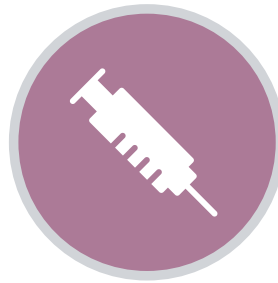
PRIME-XV FreezIS

Enable Full Cell Potency Potential for Effective Therapies



Maintain Marker Expression

Maintain cell surface marker expression of MSCs and T cells post-thaw



High Post-thaw Viability

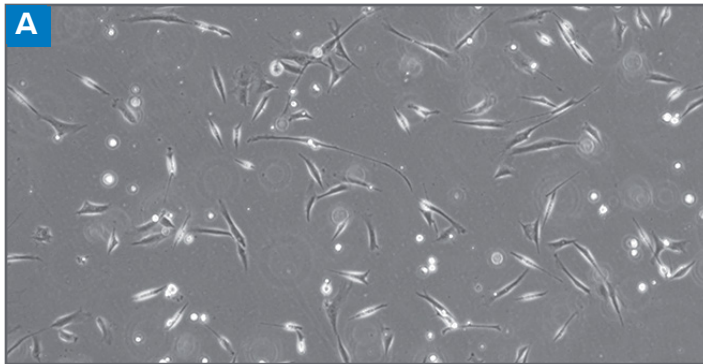
Utilize high post-thaw viability and growth to produce advanced therapies with a complete, ready-to-use medium



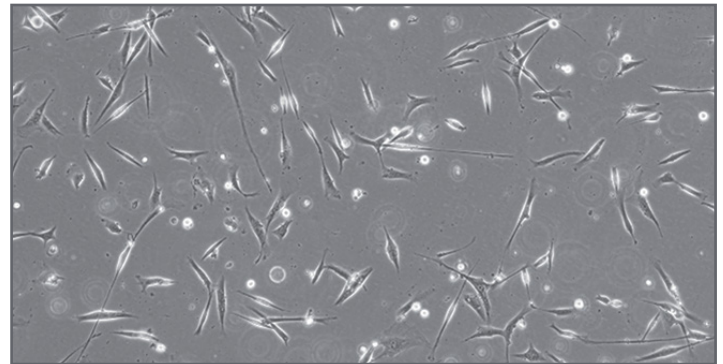
Maximum Protection

Enable cell preservation for short-term storage at -80°C^* and long-term storage in liquid nitrogen to -196°C

Maintains High Post-Thaw Viability of MSCs



PRIME-XV FreezIS



Commercially-available

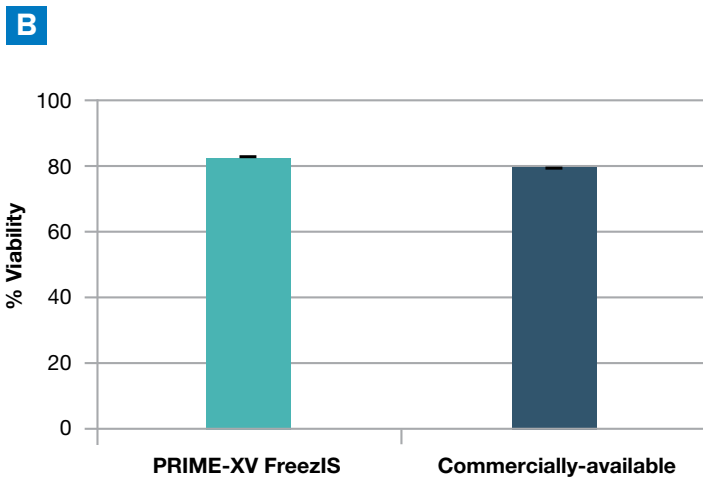


Figure 5. PRIME-XV FreezIS supports high post-thaw viability of MSCs. Human adipose-derived mesenchymal stem cells (MSCs) had high plating efficiency (A) and viability (B) 24 hours post-thaw after cryopreservation in PRIME-XV FreezIS compared to a commercially-available cryopreservation solution. Images were taken at 10X magnification.

*Human MSC and PBMC (T cell) data available for short-term storage. Human HSC data is not available.

Maintains PBMC Viability and Cell Recovery

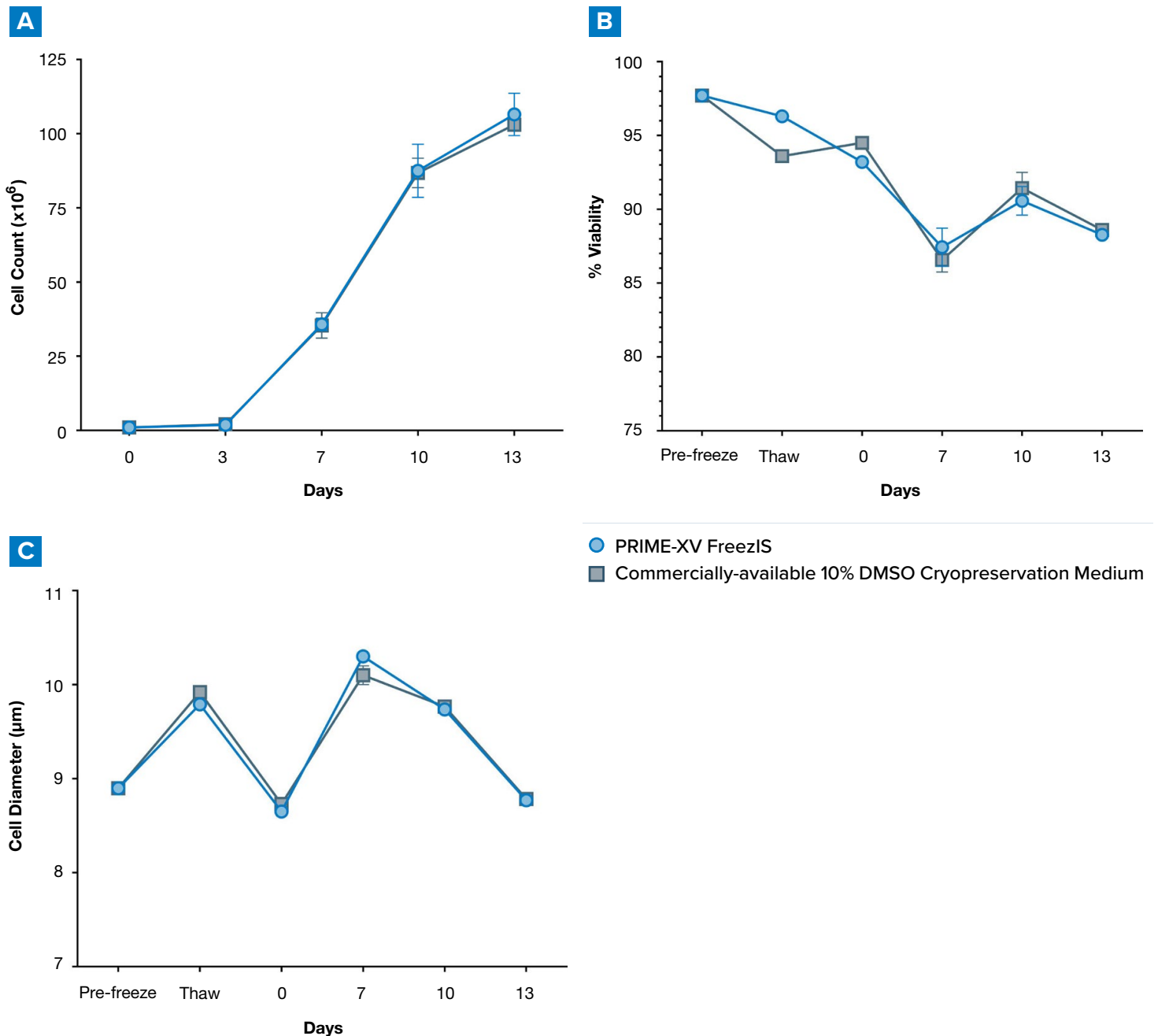


Figure 6. PRIME-XV FreeziS supports cryopreservation and recovery of PBMCs. (A) Fresh human peripheral blood mononuclear cells thawed and cultured for 13 days yielded 100-fold expansion. **(B)** PBMCs thawed from PRIME-XV FreeziS showed a slightly higher viability at thaw and maintained a viability above 85% over the 13 days in culture. **(C)** Cell diameter increases post-thaw as the cells recover from the cryopreservation, returning to baseline 24 hours later. Cell diameter is highest at the peak of the exponential growth phase around Day 7 and returns to baseline again at the end of expansion.



PRIME-XV FreezIS Cryopreservation Solutions offer reliable support and uphold quality standards

- FDA, Federal, and State registered – GMP manufacture
- EN ISO 13485:2016 certified
- MDSAP certified
- Extensive QC testing including functionality, sterility (USP <71>), endotoxin (USP <85>), and mycoplasma (USP <63>)
- Drug Master Files (DMFs) filed with the FDA – available upon request

Ordering Information

Product Description	Catalog #	Size*	Additional Information
PRIME-XV FreezIS	91139	10 mL 100 mL	Protein-free, chemically defined, animal component-free cryopreservation medium. Contains DMSO.
PRIME-XV FreezIS DMSO-Free	91140	10 mL 100 mL	Protein-free, chemically defined, animal component-free cryopreservation medium. Does not contain DMSO.
PRIME-XV FreezIS (Excipient)	91139EX	10 mL 100 mL	Protein-free, chemically defined, animal component-free cryopreservation medium. Contains DMSO.
PRIME-XV FreezIS DMSO-Free (Excipient)	91140EX	10 mL 100 mL	Protein-free, chemically defined, animal component-free cryopreservation medium. Does not contain DMSO.

Related Products

Product Description	Catalog #	Size*	Additional Information
PRIME-XV T Cell CDM	91154	1 L	Chemically defined, animal component-free formula. Does not contain antibiotics or phenol red.
PRIME-XV T Cell Expansion XSFM	91141	1 L	Xeno-free, serum-free T cell medium. Contains Gentamicin.
PRIME-XV MSC Expansion XSFM	91149	1 L 250 mL	
PRIME-XV MSC XSFM Dual Component Kit with Phenol Red	91149DC	10 mL supplement	Xeno-free, serum-free medium for MSC expansion.
PRIME-XV MSC XSFM Dual Component Kit without Phenol Red	91214DC	5 L basal	
Shenandoah CTGrade GMP rh IL-2 _{C126S}	500-01	50 µg 100 µg 1 mg	
Shenandoah CTGrade GMP rh IL-7	500-07	50 µg 100 µg 1 mg	Manufactured following GMP in a facility that does not use or process beta-lactam containing materials, no histidine tags, and 0.2 micron filtered. No animal- or human-derived materials were used during manufacturing or as ingredients.
Shenandoah CTGrade GMP rh IL-15	500-08	50 µg 100 µg 1 mg	
Shenandoah CTGrade GMP rh IL-21	500-09	50 µg 100 µg 1 mg	

*Custom sizes and services available.



Close the distance from research
to bringing therapies to life.

See how PRIME-XV FreezIS Cryopreservation Solutions meet manufacturing needs no matter how they evolve. Visit our website or contact getinfo@fujifilm.com for more information.

FUJIFILM
Value from Innovation

www.irvinesci.com

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