29th Annual Gabor Racz Advanced Interventional Pain Conference and Workshop

Budapest, Hungary August 24-26, 2026

Evidence of Intradiscal Stem Cells: Autologous vs. Allogenic Cells

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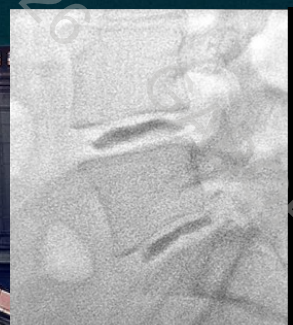
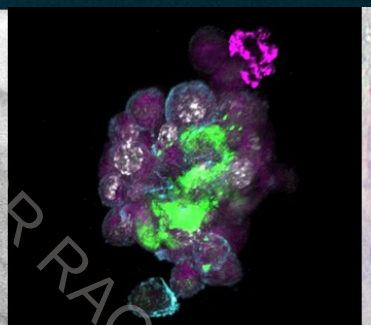
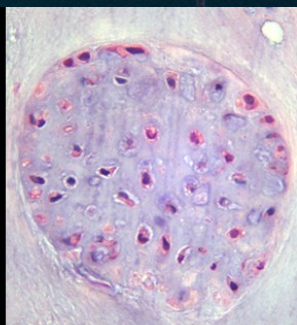
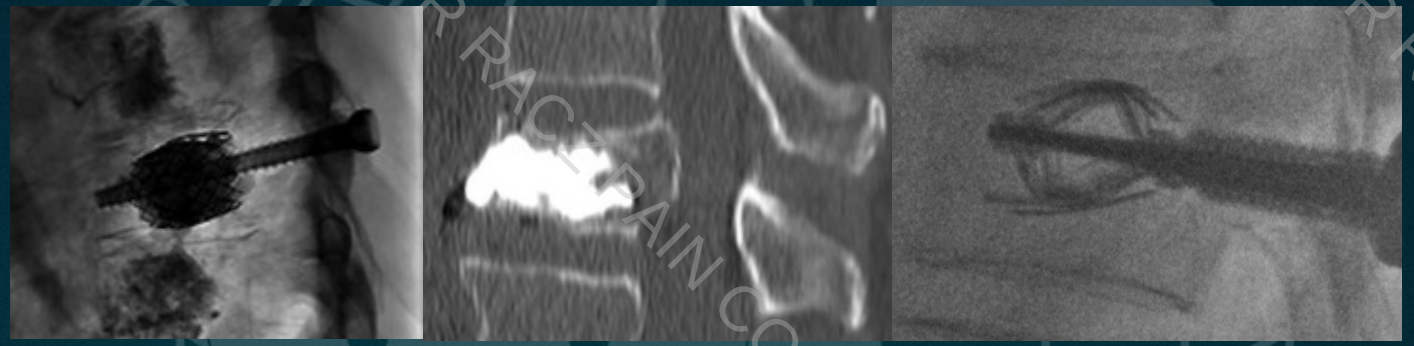




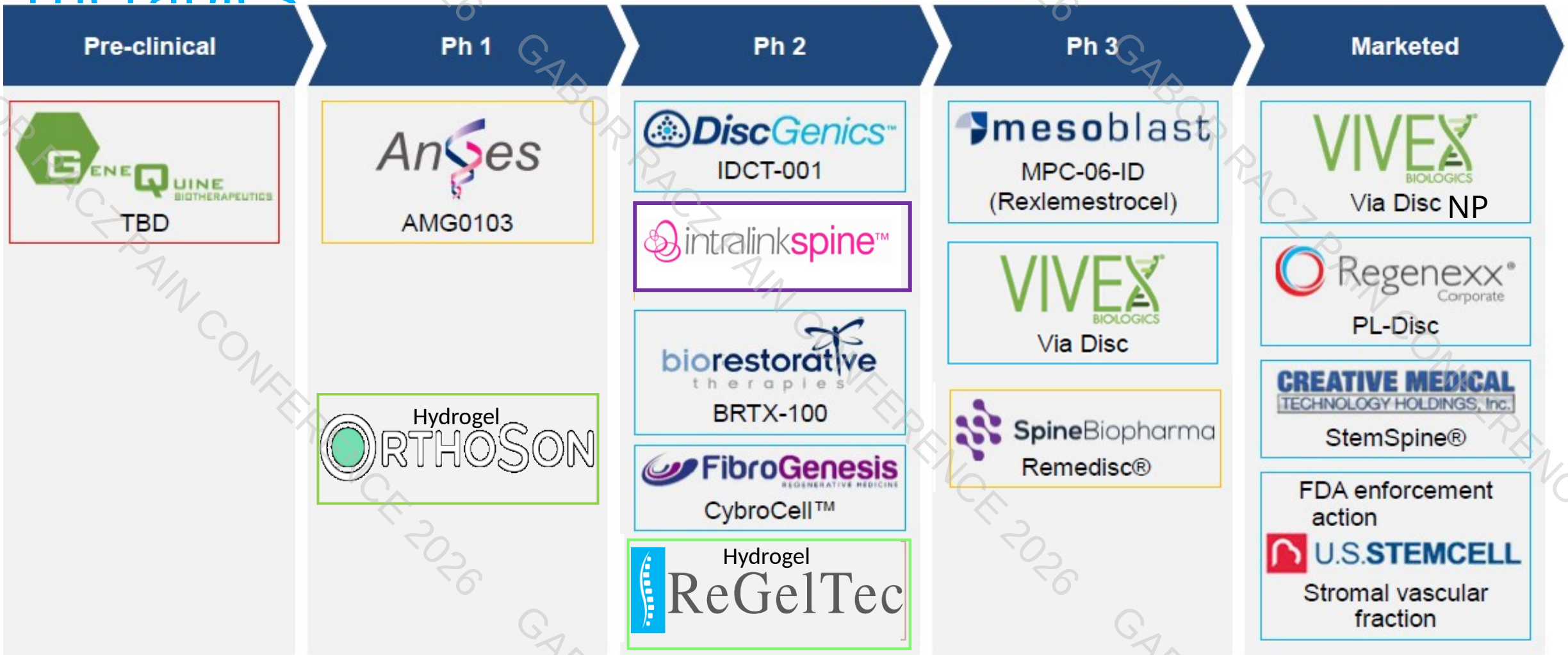


Conflict of Interest



Type of affiliation/financial interest	Name of commercial company
Consultant/Receipt of grants/research supports:	ReGelTec, Orthoson, Vivex, Discgenics, Mesoblast, Discure, Tissue Tech, Smart Soft, Spine Biopharma
Receipt of honoraria or consultation fees:	ReGelTec, Vivex, Mesoblast, Discure
Participation in a company sponsored speaker's bureau:	ReGelTec
Research Funding	ReGelTec, Orthoson, Vivex, Discgenics, Mesoblast, Discure, Tissue Tech, Spine Biopharma, Kolon TissueGene

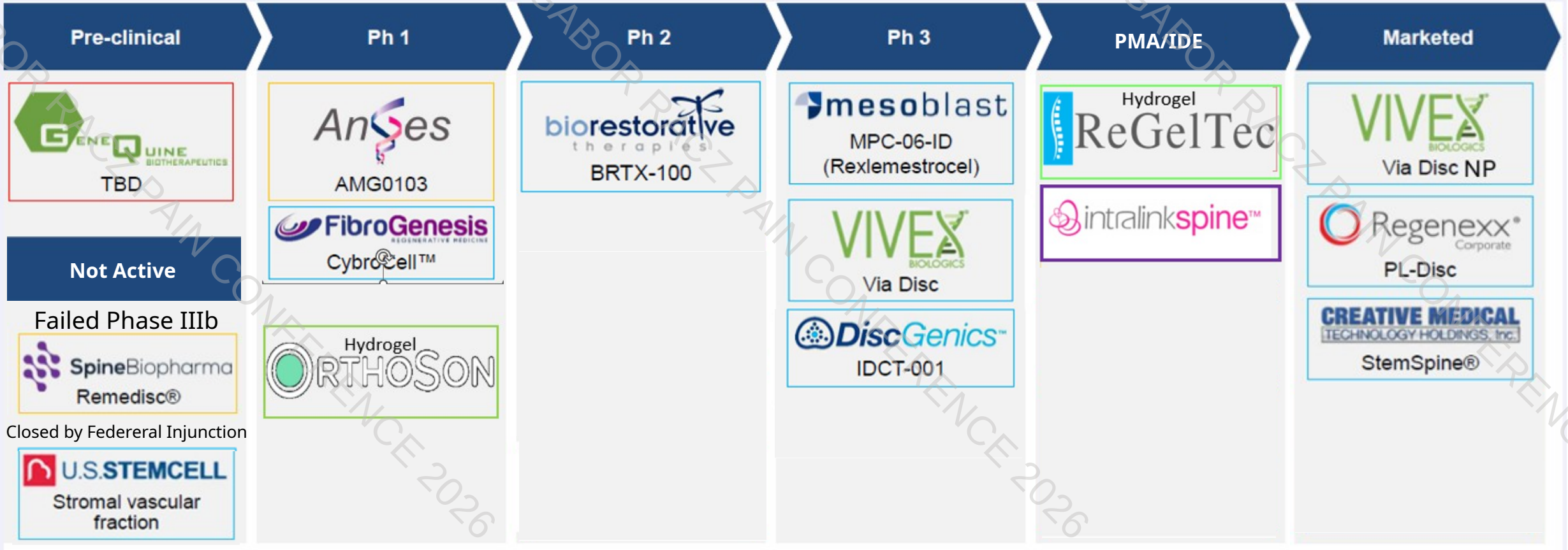
Treatment Landscape for Intradiscal Therapies



Cells, Gells, Nanotethers, Peptides, Oligonucleotide Decoy & GeneTherapy

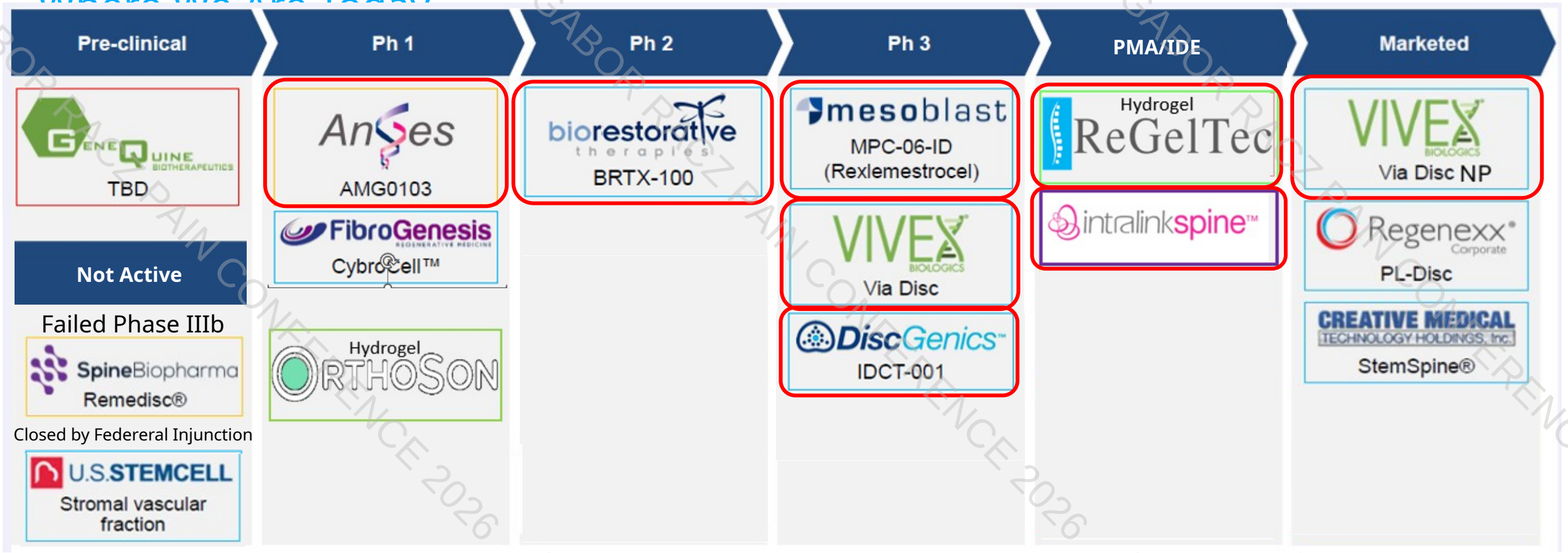
Treatment Landscape for Intradiscal Therapies

Where We Are Today



Treatment Landscape for Intradiscal Therapies

Where We Are Today



Over Past 20 Yrs, 15 Therapies Developed, 7 Remain Active (for FDA Approval): DiscGenics, Mesoblast, BioRestorative, ReGelTec, AnGes,

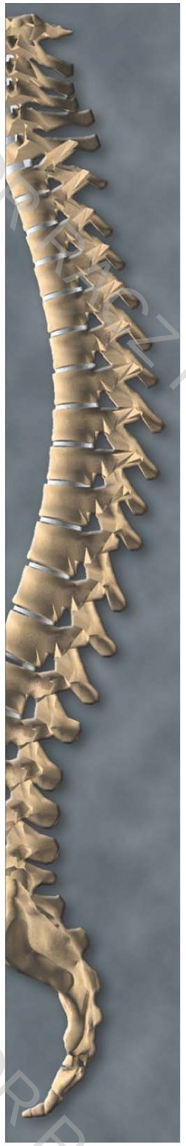
RCTs of Biologics for Discogenic LBP

Sponsor	Product	Phase	Intervention	Control	Primary Endpoint	Secondary Endpoints	Key Results
BioRestorative Therapies n=68 (goal n=99)	BRTX-100 FDA Fast Track Designation	Phase II	40M hypoxia-cultured autologous BM-MSCs	Needle sham 2:1	≥30% ↓ VAS ≥30% ↑ ODI @52 weeks	VAS, ODI, RMDQ, SF-12, FRI	Blinded Data: 90% VAS >50% ↓ @52w 70% ODI >50% ↑ @52w
Mesoblast n=100	Rexlemestrocel-L + HA	Phase II	Low dose (6M) and high dose (18M) MPCs + HA	Intradiscal HA or saline 3:3:2:2	• Safety (AEs)	Pfirmann grade (MRI), VAS. QoL, ODI, SF-36, WPAI	6M MPC group ↓ VAS @24m compared to baseline (-43.93 vs -23.55) 6M MPC ODI change ↑ @24m compared to baseline (-23.70% vs -15.47%)
Mesoblast n=404	Rexlemestrocel-L + HA	Phase III (Part A)	6M MPCs + 1% HA and 6M MPCs	Intradiscal saline 1:1:1	• ≥50% ↓ VAS • 15 pt ↓ ODI @12/24 months	Pain/Function responders, opioid use	• CLBPLTM w/ MPC+HA had significantly improved pain @36m (VAS, ODI) • ↓ in pain through 24 months with enhanced results in CLBPLTM subjects (VAS, ODI) • 40% ↓ opioid use @24m
Mesoblast (goal n=300)	Rexlemestrocel-L + HA	Phase III (Part B)	6M MPCs + 1% HA	Intramuscular Saline 1:1	• VAS @12 months	30% VAS ↓, EQ-5D, ODI, Opioid cessation	Ongoing
DiscGenics n=60	IDCT (DGX-A01)	Phase I/II	Low (3M/mL) & High (9M/mL) IDCT	Intradiscal saline or Vehicle (Placebo) 2:2:1:1	• ≥30% ↓ VAS @52 weeks	• ODI • EQ-5D • MRI • Mobility	• 62.8% ↓ VAS • ↑ Disc volume @52w in high dose group (mean change = 249.01 mm^3) • Continued to increase @104w (mean change = 402.12 mm^3)
VIVEX n=28	VIA Disc NP (VIA-2021-001)	Pilot Study	Nucleus Pulposus Allograft	N/A	• MCID (≥30% ↓ VAS) @24m	• NRS • ODI • MRI • EQ-5D	• NRS ↓ 7.1 → 3.6 • 64% achieved/exceeded MCID back pain severity • ~55% participants reported back pain severity score of ≤3 @24m • ODI ↓ 53%
VIVEX	VIA Disc NP		Needle sham				

Autologous

Allogeneic

Intradiscal Cellular Treatment for CLBP



Spine

- 4 Studies Allogeneic Cells – 1 Study Human Umbilical Cord Cells – 1 Study Expanded Allogeneic Calls

Cell-Based Therapies for lumbar discogenic low back pain - a Systematic Review and Single Arm Meta-Analysis

Tao Wu1†, MD; Hai-xin Song2†, MD; Yan Dong3, MD; Jian-hua Li4*, MD

1 Department of Rehabilitation Medicine, Sir Run Run Shaw Hospital, College of Medicine, Zhejiang University
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3 Department of Rehabilitation Medicine, Hangzhou Hospital of Zhejiang CAPF
4 Department of Rehabilitation Medicine, Sir Run Run Shaw Hospital, College of Medicine, Zhejiang University

RESULTS

Search ID's 1393 articles, of which 6 studies were eligible for this review. Studies were from 2006 to 2015 & 74 pts were included.

SAFETY

No SAE's reported in the studies.

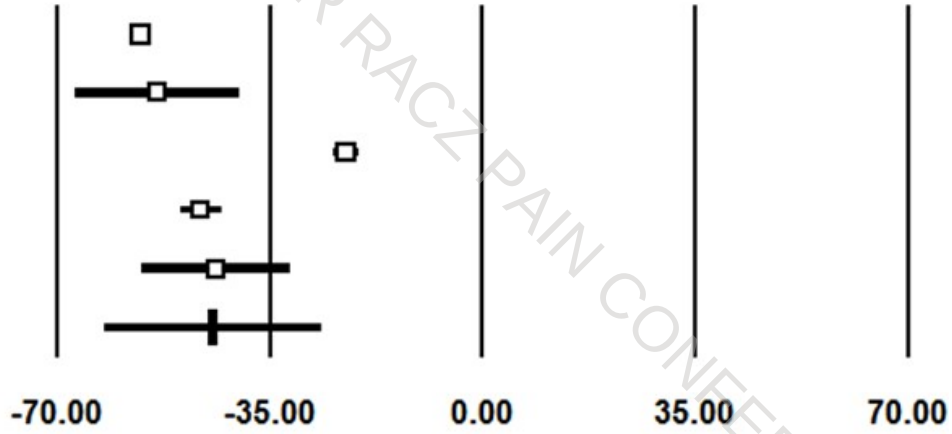
No tumor formation observed during fellow up period.

VAS Response after Treatment

Study name	Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Kenneth Pettine 2015	-56.125	0.800	0.639	-57.692	-54.558	-70.188	0.000
Xiaodong Pang 2014	-53.333	6.770	45.833	-66.602	-40.064	-7.878	0.000
Domagoj Coric 2013	-22.333	1.030	1.061	-24.352	-20.314	-21.681	0.000
Lluis Orozco 2011	-46.200	1.659	2.752	-49.451	-42.949	-27.851	0.000
Hans Joerg Meisel 2006	-43.703	6.137	37.664	-55.731	-31.674	-7.121	0.000
	-44.158	9.000	81.008	-61.799	-26.518	-4.906	0.000

Statistics for each study

Difference in means and 95% CI



Heterogeneity Q-value	df(Q)	P-value	I-squared	Tau squared	Tau
675.9	4	0.000	99.4	388.4	19.7

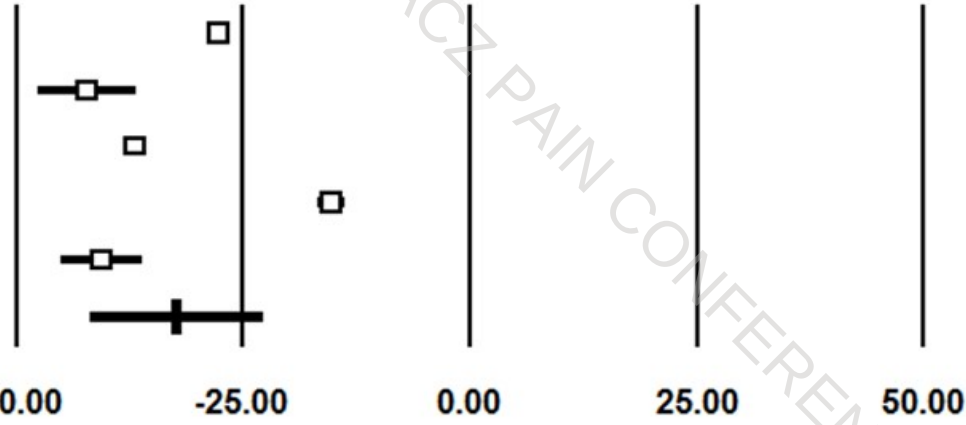
Decreased pain score (NRS & VAS, 0-100) after treatment: The pooled mean difference in pain score from baseline to follow-up points was 44.2 points decreased (95%CI: -61.8 to −26.5, p<0.001, I^2=99.4%)

ODI Decrease after Treatment

Study name	Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Domagoj Coric 2013	-27.649	0.555	0.308	-28.737	-26.562	-49.849	0.000
Hans Joerg Meisel 2006	-42.083	2.665	7.104	-47.307	-36.859	-15.789	0.000
Kenneth Pettine 2015	-36.768	0.369	0.136	-37.491	-36.044	-99.606	0.000
Lluis Orozco 2011	-15.158	0.663	0.440	-16.457	-13.858	-22.861	0.000
Xiaodong Pang 2014	-40.444	2.205	4.861	-44.766	-36.123	-18.345	0.000
	-32.249	4.770	22.751	-41.597	-22.900	-6.761	0.000

Statistics for each study

Difference in means and 95% CI



Heterogeneity					
Q-value	df(Q)	P-value	I-squared	Tau squared	Tau
887.1	4	0.000	99.5	111.2	10.5

Decreased Oswestry Disability Index (ODI, 0-100) after treatment: The pooled mean difference in ODI from baseline to follow-up points was 32.2 points decreased (95%CI: -41.6 to −22.9, p<0.001, I^2=99.5%).

Intradiscal Autologous vs Allogeneic Cellular Treatment for CLBP

- Autologous Cells – 23 Studies
  - Mean VAS Reduction – 45
  - Mean ODI Improvement – 32 (65% overall fxn improvement)
- Allogeneic Cell – 7 Studies
  - Mean VAS Reduction – 43
  - Mean ODI Improvement – 32

North American Spine Society Journal (NASSJ)
journal homepage: www.elsevier.com/locate/xnsj

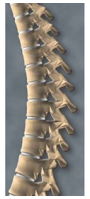
Advances in Spinal Regenerative Therapies

Comprehensive narrative review on the analysis of outcomes from cell transplantation clinical trials for discogenic low back pain

Jordy Schol, Daisuke Sakai*
Tokai University School of Medicine, Department of Orthopedic Surgery, 143 Shimokasuya, Isehara, Kanagawa 259-1193, Japan

VAS – 44 pts decreased

ODI – 31.6 pts decreased



Cell-Based Therapies for lumbar discogenic low back pain - a Systematic Review and Single Arm Meta-Analysis

Tao Wu1†, MD; Hai-xin Song2†, MD; Yan Dong3, MD; Jian-hua Li4*, MD

in score (NRS & VAS, 0-100) after treatme
points was 44.2 points decreased (95%CI: -
Oswestry Disability Index (ODI, 0-100)
points was 32.2 points decreased (95%(

$$\text{Mean percentage reduction} = \frac{\sum(\text{percentage reduction}_i \times n_i)}{\text{total } n}$$

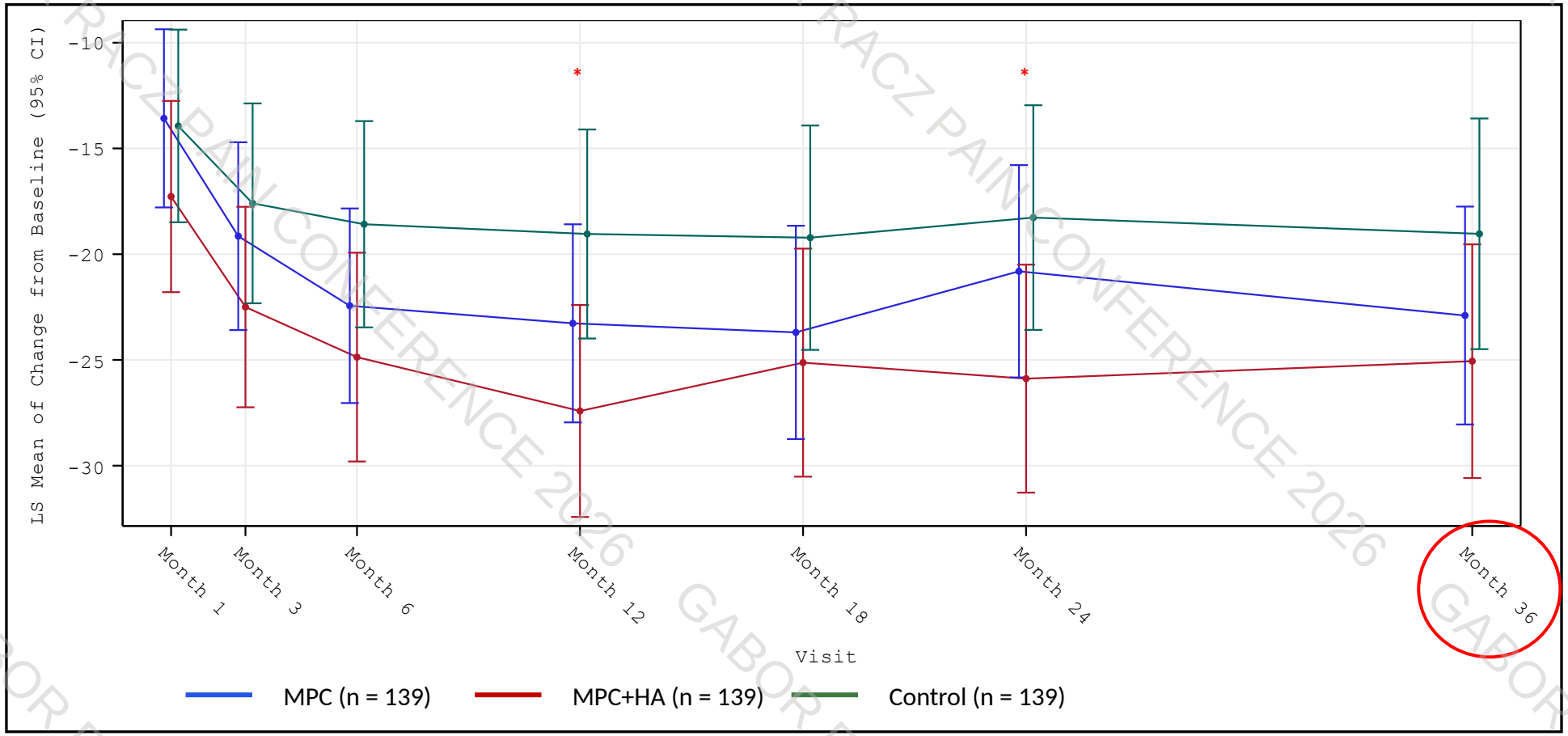
General overview of included clinical studies and human case reports examining the effect of cell transplantation for low back pain alleviation or disc degeneration repair.

Author	Year	Ref	FU (y)	Site	Mode	Product	Cell density	Volume and carrier	n	Control(s)	n	Efficacy	Safety	Type
Yoshikawa	2010	[36]	2	ID	Autologous	BM-MSC	*Unclear*	0.54mL collagen sponge	2	-	-	✔	✔	Mesenchymal stromal cells
Orozco	2011	[37]	1	ID	Autologous	BM-MSC	10×10^6/mL	0.5-1.5mL saline	10	-	-	✔	✔	
Centeno	2017	[38,39]	6	ID*	Autologous	BM-MSC	23×10^6/disc	1-3mL 10-20% PL/PBS	33	-	-	✔	✔	
Noriega	2021	[40–42]	3.5	ID	Allogenic	BM-MSC	12.5×10^6/mL	2mL saline	*Unclear*	Muscle anesthetic	*Unclear*	✔	✔	
Papadimitriou	2021	[43,44]	2	ID	Autologous	BM-MSC	1×10^6/mL	1mL 20% serum/F12	10	-	-	✔	✔	
Amirdelfan	2021	[45,46]	3	ID	Allogenic	MPC	High: 18×10^6/disc Low: 6×10^6/disc	2mL HA	60	HA (Vehicle) Saline (Placebo)	20 20	✔	✔	
Jung	2013	[47]	<0.5	IV	Autologous	AD-MSC	*Unspecified*	*Unspecified*	3	-	-	✘	✔	
Piccirilli	2017	[48]	1	ID	Autologous	AD-MSC	*Unspecified*	1mL solution	2	-	-	✘	✔	
Kumar	2017	[49]	1	ID	Autologous	AD-MSC	High: 20×10^6/disc Low: 10×10^6/disc	2mL HA	5 5	-	-	✔	✔	
Bates	2022	[50]	1	ID	Autologous	AD-MSC	10×10^6/disc	1mL saline	9	-	-	✔	✔	
Zhang	2022	[51]	2	ID	Autologous	AD-MSC	High: 20×10^6/disc Mid: 10×10^6/disc Low: 5×10^6/disc	2mL HA	25 25 25	Saline (Placebo)	25	✘	✘	
Pang	2014	[52]	2	ID	Allogenic	UC-MSC	10×10^6/mL	1mL solution	2	-	-	✔	✔	
Meisel	2006	[53–55]	2	ID	Autologous	IVD-C	*Unspecified*	*Unspecified*	12	Discectomy-only	16	✔	✘	Chondrogenic cells
Mochida	2015	[56]	3	ID	Autologous	NPC	$\sim1.5\times10^6$	0.7 mL saline	9	-	-	✔	✔	
Tschugg	2017	[57,58]	<0.5	ID	Autologous	IVD-C	*Unclear*	PEG + serum + media	12	Discectomy + HA (Vehicle)	12	✘	✔	
Schwan	2017	[59]	*n.a.*	ID	Autologous	IVD-C	*Unspecified*	Saline OR 'polymerizing-scaffold'	10	Discectomy-only	10	✘	✔	
Beall	2020	[60]	1	ID	Allogenic	NPC	*Unclear*	1.75mL NP tissue	16	Saline (Placebo) Conservative care	4 4	✔	✔	
Hunter	2022	[61,62]	1	ID	Allogenic	NPC	*Unclear*	1.75mL NP tissue	140	Saline (Placebo) Conservative care	39 39	✔	✔	
Foley	2022	[63]	1.5	ID	Allogenic	NPC	High: 9×10^6/disc Low: 3×10^6/disc	1mL HA	20 20	Saline (Placebo) HA (Vehicle)	10 10	✔	✔	
Xuan	2022	[64]	6	ID	Autologous	IVD-C	$4\text{-}7\times10^6$/disc	1-3mL saline	18	Discectomy-only	22	✔	✔	
Coric	2013	[65]	1	ID	Allogenic	AC	10×10^6/mL	1-2mL fibrin	15	-	-	✔	✔	
Comella	2017	[66]	1	ID	Autologous	SVF	$30\text{-}60\times10^6$/1-3 disc	1mL PRP	15	-	-	✔	✔	Mixture of cells
Pettine	2017	[67–69]	3	ID	Autologous	BMC	130×10^6/mL	2-3mL solution	26	-	-	✔	✔	
Wolff	2020	[70]	1	ID	Autologous	BMC	*Unspecified*	3mL solution	33	-	-	✔	✔	
Ramos	2020	[71]	1	ID	Autologous	BMC	*Unspecified*	Unspecified mL PRP	1	-	-	✘	✔	
El-Kadiry	2021	[72]	1	ID	Autologous	BMC	*Unspecified*	1-6mL solution	13	-	-	✔	✔	
Jerome	2021	[73]	<0.5	ID	Autologous	BMC	*Unspecified*	*Unspecified*	3	-	-	✘	✔	
Xu	2021	[74]	2	ID	Autologous	BMA	Unspecified	~1.25mL gelatin sponges	15	Discectomy-only Discectomy + AF suture	15 15	✔	✔	
Subach	2011	[75]	1	ID	Autologous	BMA + AT + Plasma	Unspecified	3mL solution	1	-	-	✘	✔	
Haufe	2005	[76]	1	ID	Autologous	HSC	Unspecified	Unspecified	10	-	-	✔	✘	

Schol J, Sakai D. Comprehensive narrative review on the analysis of outcomes from cell transplantation clinical trials for discogenic low back pain. N Am Spine Soc J. 2022 Dec 22;13:100195

Allogeneic MSC's – Rexlemestrocel-L

LS Mean VAS for LBP in Entire Pt Population



* = p < 0.05 MPC+HA vs. Placebo

MPC + HA: VAS improvement 60.4 to 31.4: 29 **points**

48% @ 12 Mos*

MPC + HA: VAS improvement 60.4 to 33: 27.4 **points**

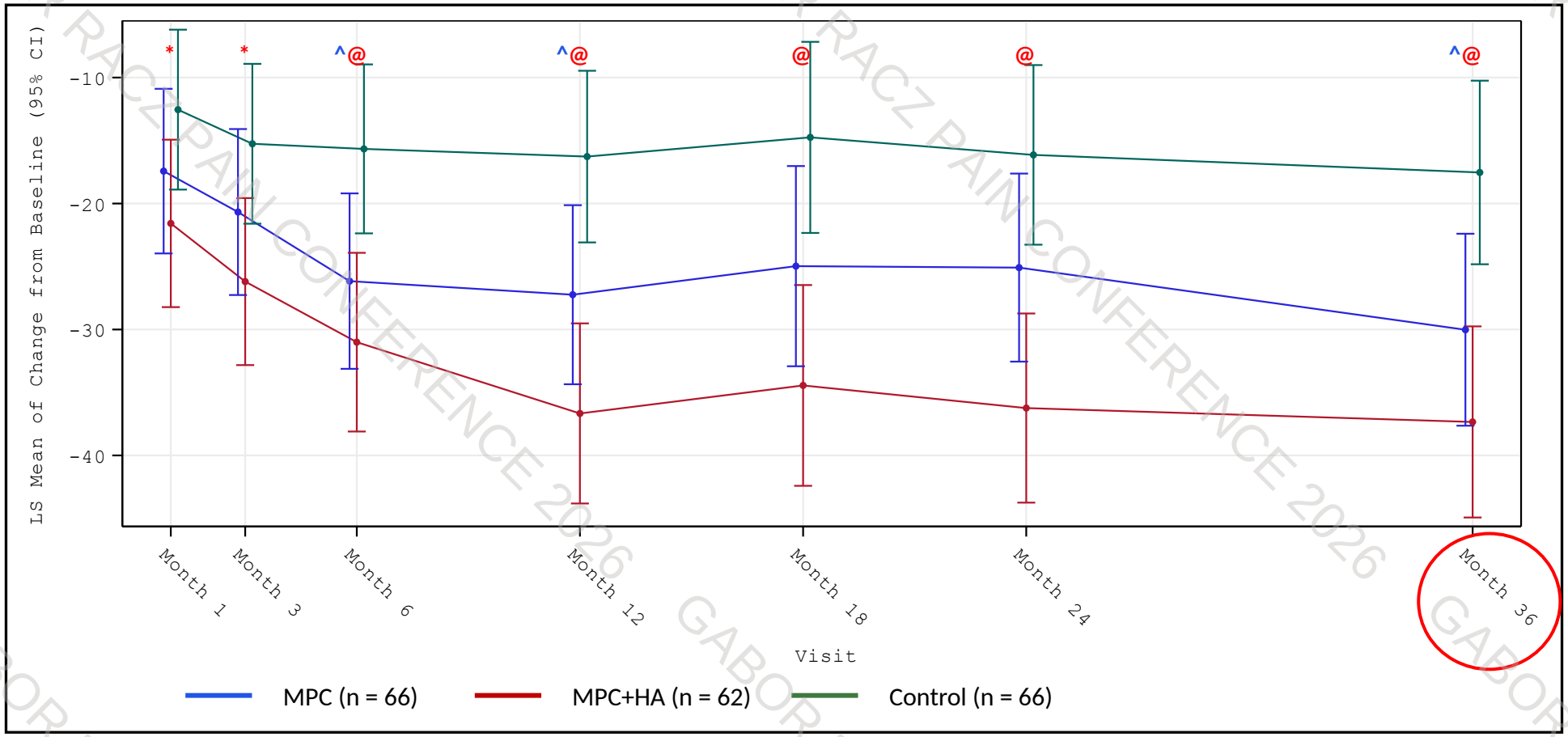
45.4% @ 24 Mos*

*stat sig

Improvements consistent out to 3 yrs

Allogeneic MSC's – Rexlemestrocel-L

LS Mean VAS for LBP in Pts with CLBP of Shorter Duration than the Study Median of 68 Mos



MPC + HA: VAS improvement: 36.7 **points**

61.9% @ 12 Mos

MPC + HA: VAS improvement: 36.2 **points**

61% @ 24 Mos

MPC + HA: VAS improvement: 37.3 **points**

62.9% @ 36 Mos

@ ^ stat sig

Improvements consistent out to 3 yrs

* = p < 0.05 MPC+HA vs. Control # = p < 0.01 MPC+HA vs. Control @ = p < 0.005 MPC+HA vs. Control ^ = p < 0.05 MPC vs. Control

FINAL PRODUCT PREPARATION

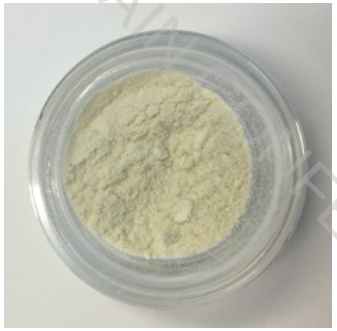
Cell Solution

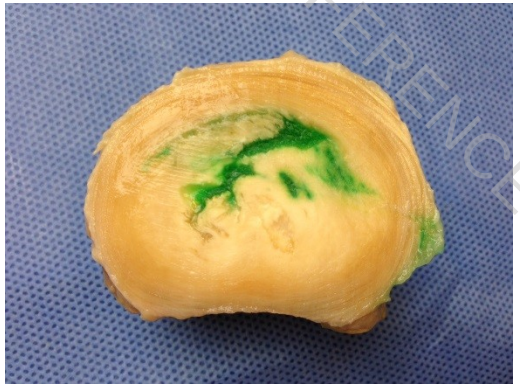
+

Nucleus Pulposus Matrix

=

Hydrated Allograft

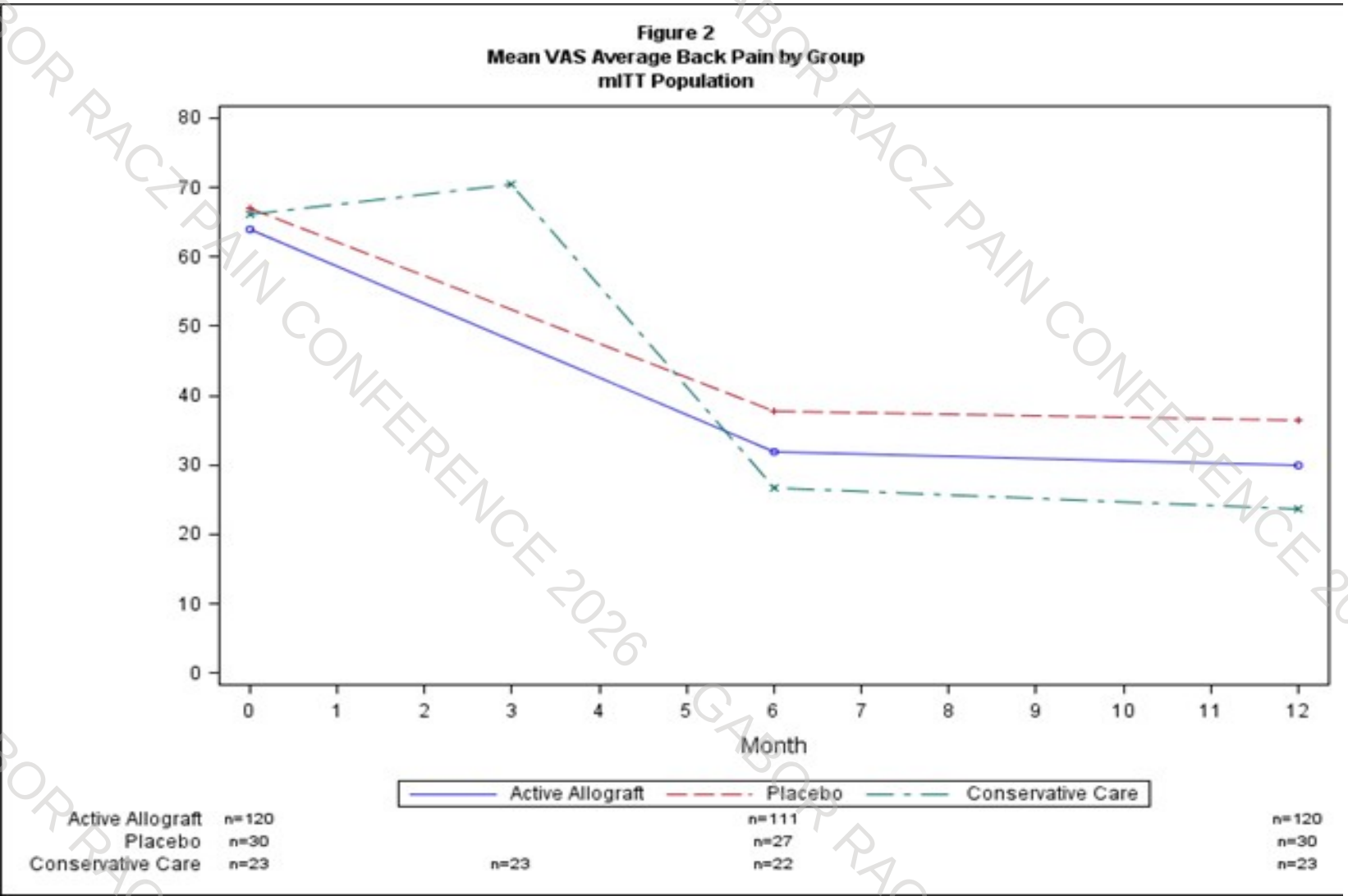




- Cells are suspended in DMSO-Free Cryoprotectant
- Reconstitute with Normal Saline
- Add to 0.75 cc NP Matrix
- Inject with 20 g spine needle

Allogeneic MSC's & Micronized Disc Material

12-Month, 173-subject Pain Evaluation (VAS)



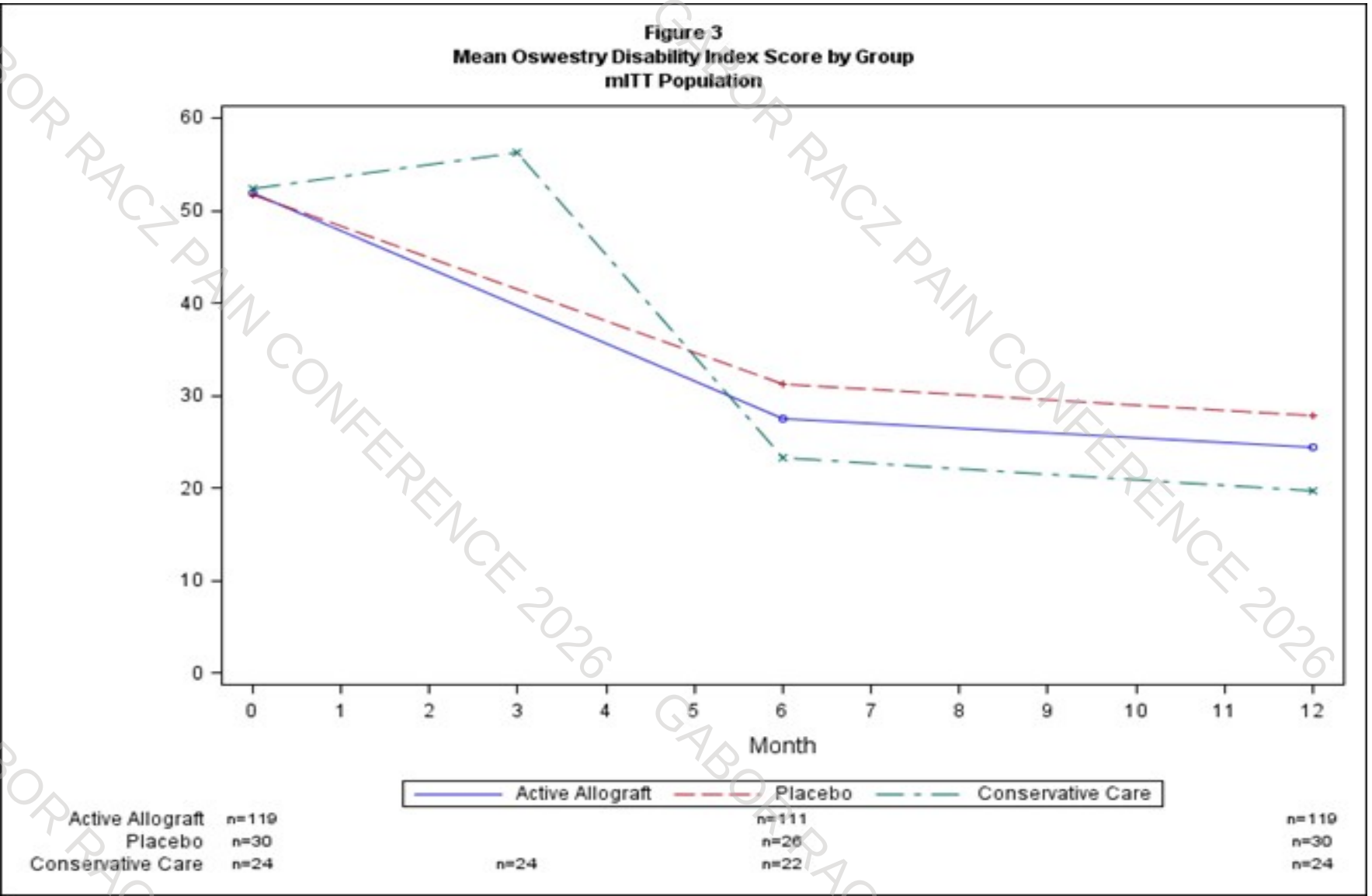
Active allograft: VAS improvement 63.9 to 29.9:
34 points
53%

Placebo (saline) 12-month VAS Improvement 66.9 to 36.43:
29.6 points
45%

Conservative 1 are crossover to VIA Disc VAS improvement 70.39 to 23.8:
46.6 points
66%

Allogeneic MSC's & Micronized Disc Material

12-Month, 173 subject Oswestry Disability (ODI)



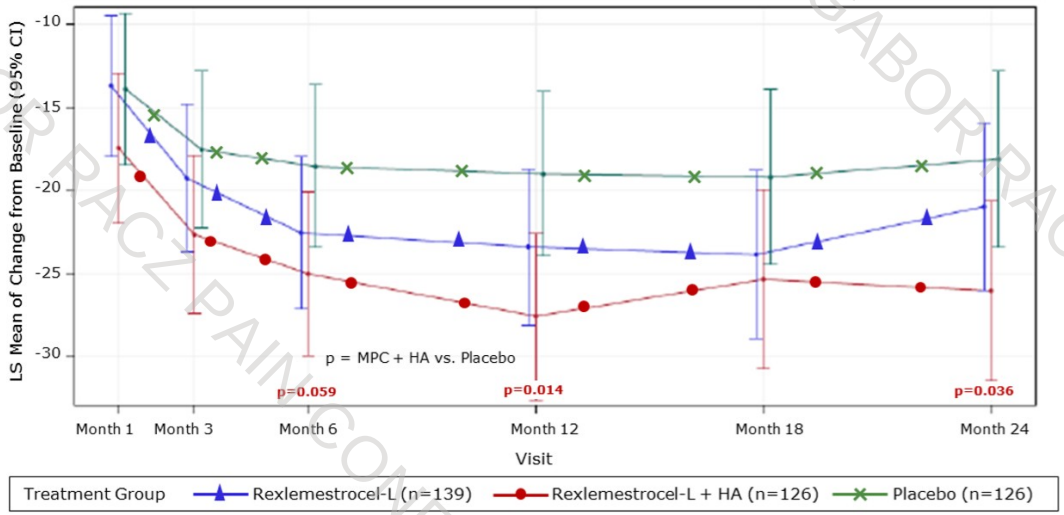
Active allograft ODI improvement
51.9 to 24.5:
27.4 points
53%

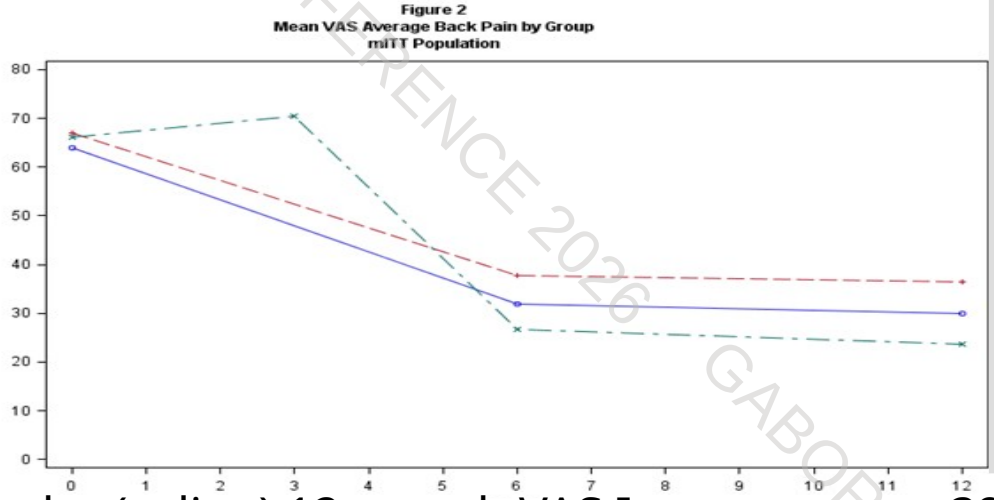
Placebo (saline) 12-month ODI Improvement
51.8 to 27.8:
21 points
42%

Conservative care cross over to VIA Disc 56.2 to 19.8
36.4 points
65%

VAS of LBP: Mesoblast (Rexlemestrocel L) vs Vivex's ViaDisc

Figure 1: LS Mean VAS Low Back Pain Change from Baseline VAS of 60.4 – Entire Study (n=391)





Placebo (saline) 12-month VAS Improvement: **29.6 points (45%)**

Rexlemestrocel-L

MPC + HA: VAS improvemt 60.4 to 31.4: 29 **points**
<u>48</u>% (All Pts)

improvement: 36.7 **points**
<u>61.9</u>% (LBP < 68 mos)

MPC + HA: **<u>ODI</u>** improvement
17.7 points – Phase II
32.7%

VIAdisc

Active allograft: **<u>VAS</u>** improvement 63.9 to 29.9:
34 points
53.2%

Conservative care crossover **<u>VAS</u>** improvement:
46.6 points
66.1%

Active allograft **<u>ODI</u>** improvement:
27.4 points
53%

Crossover to VIADisc **<u>ODI</u>** Imprvmnt
36.4 points
65%

VAS of LBP: NP Progenitor Cells vs MSCs + Allograft

Disc Progenitor Cells

High Dose (9 MM)

VAS

1 Yr (**62.79%**, p=0.0005)

&

2 Yrs (60.32%, p 0.0034)

ODI

1 Yr (**25.7**, p=0.004)

2 Yrs (29.6, p <0.0001),

EQ-5D

1 Yr (**0.197**, p=0.003)

2 Yrs (0.2174, p <0.0001)

MSCs + Allograft

VIAdisc: **VAS** improvement:

1 Yr 53.2 to 66.1%

2 Yr 43.8%

3 Yr 54% (includes some retreated pts)

VIAdisc **ODI** improvement:

1 Yr 27.1 to 36.1 point

2 Yr 23 points

3 Yr 26.5 (includes some retreated pts)

Rebonuputemcel

Figure 2. Mean Change from Baseline in VAS by Visit (Completed Cases)

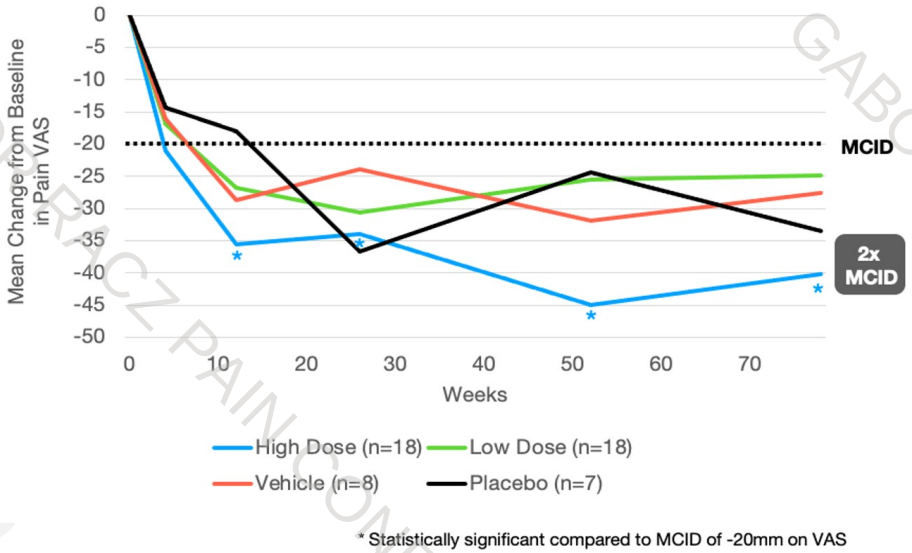
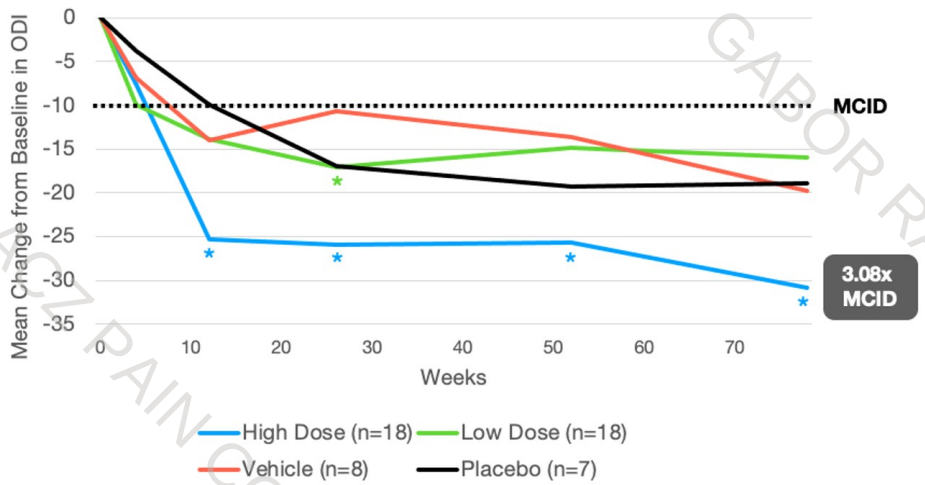
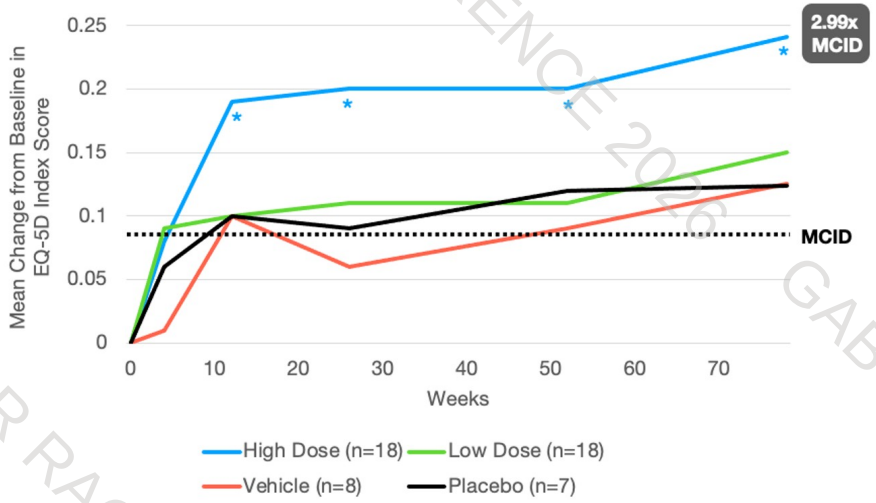


Figure 3. Mean Change from Baseline in ODI by Visit (Completed Cases)



- Low-dose cells w/ carrier (3,000,000 cells; N=20)
- High-dose cells w/ carrier (9,000,000 cells; N=20)
- Carrier alone (sodium hyaluronate; N=10)
- Placebo (normal saline; N=10)

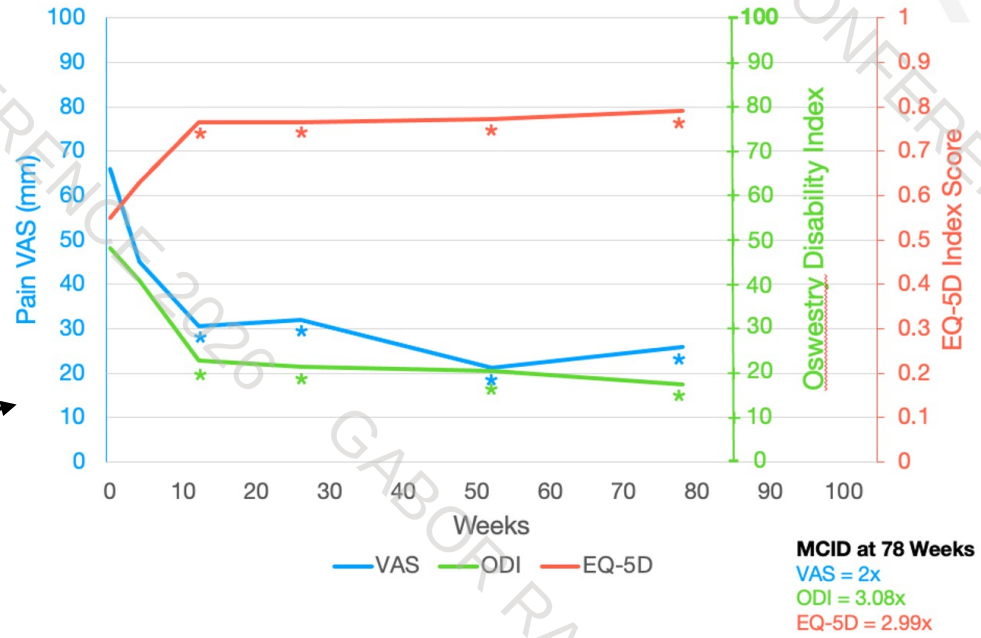
Figure 4. Mean Change from Baseline in EQ-5D Index Score by Visit (Complete Cases)



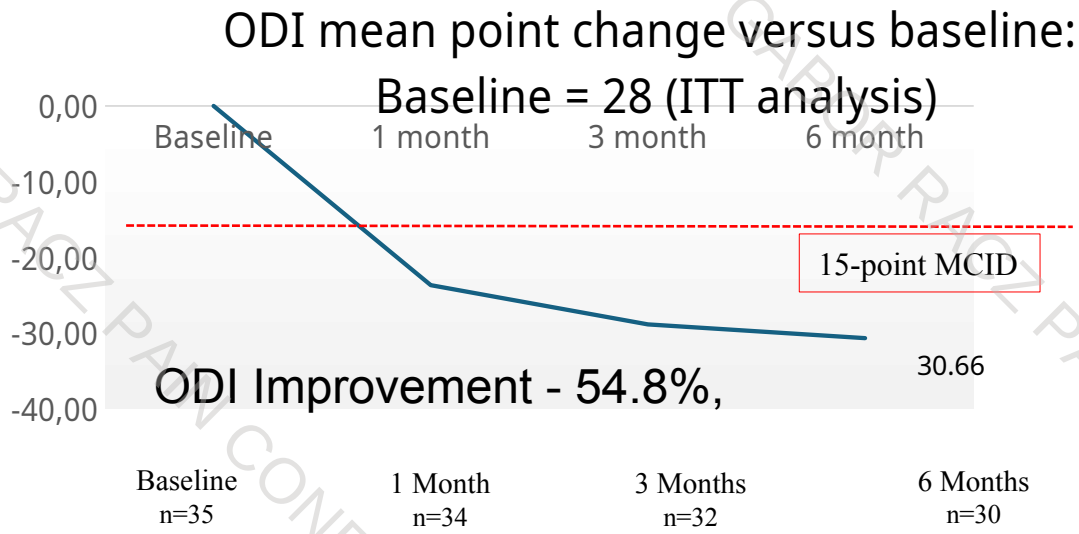
Dose Response Separation

* = Stat Sig

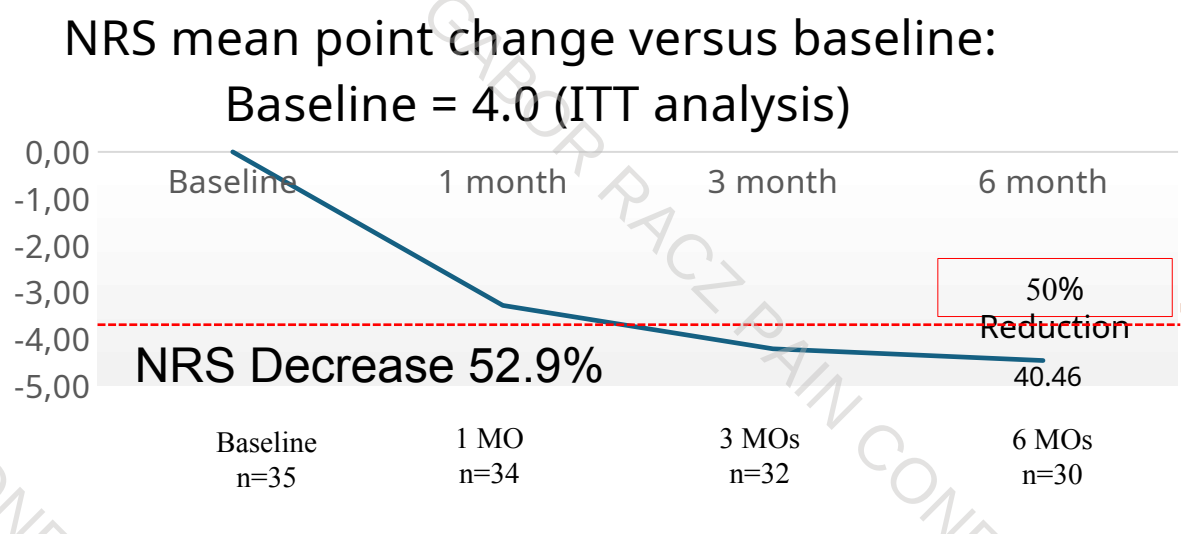
Combined Statistics



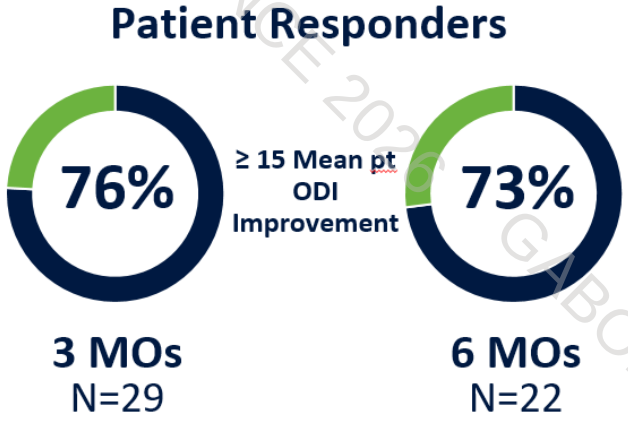
Allograft NP + Saline – Approved HCTP 361 Product

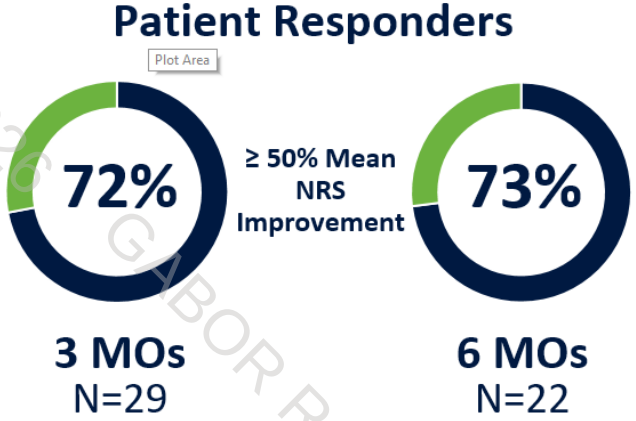


	Baseline n=35	1 Month n=34	3 Months n=32	6 Months n=30
Percent ODI Improvement		46%	56%	60%

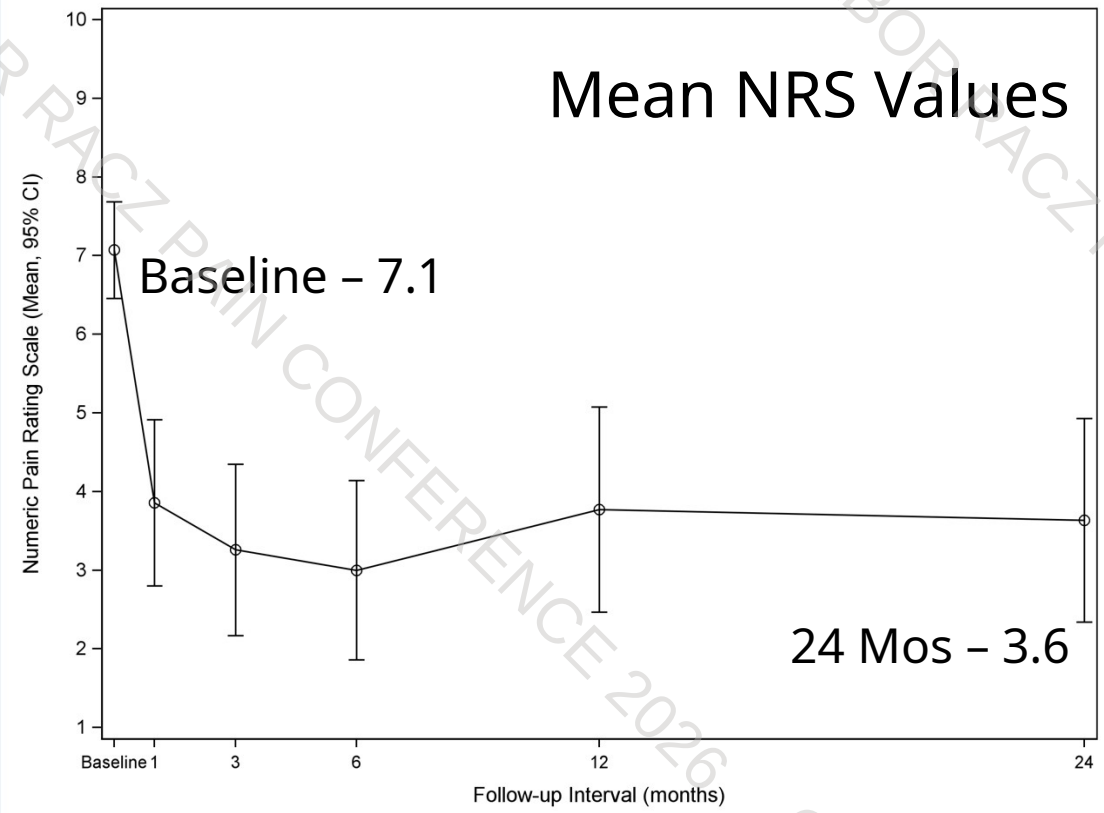


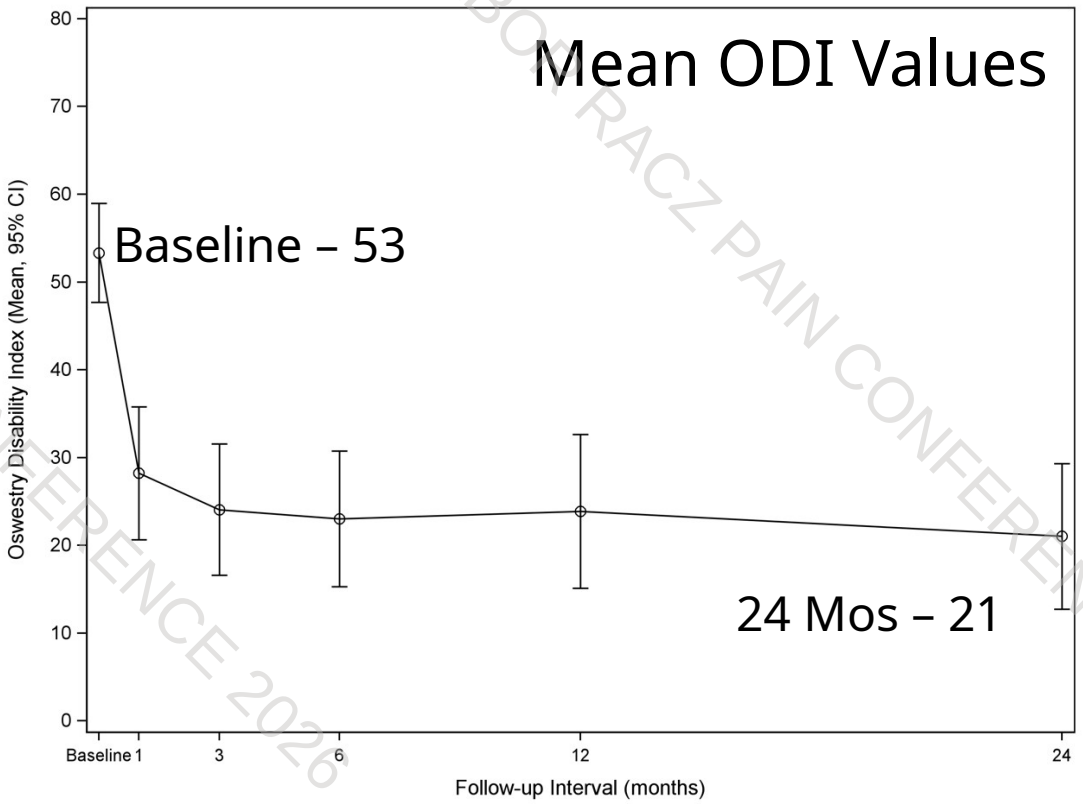
	Baseline n=35	1 MO n=34	3 MOs n=32	6 MOs n=30
Percent NRS Improvement		44%	56%	60%





Allograft NP + Saline – Follow-up to 2 Yrs





24-month NRS Improvement:
3.5 points (49.3%)

24-month ODI Improvement: **32 points 60.4%)**

ASCEND Trial - Design & Overview

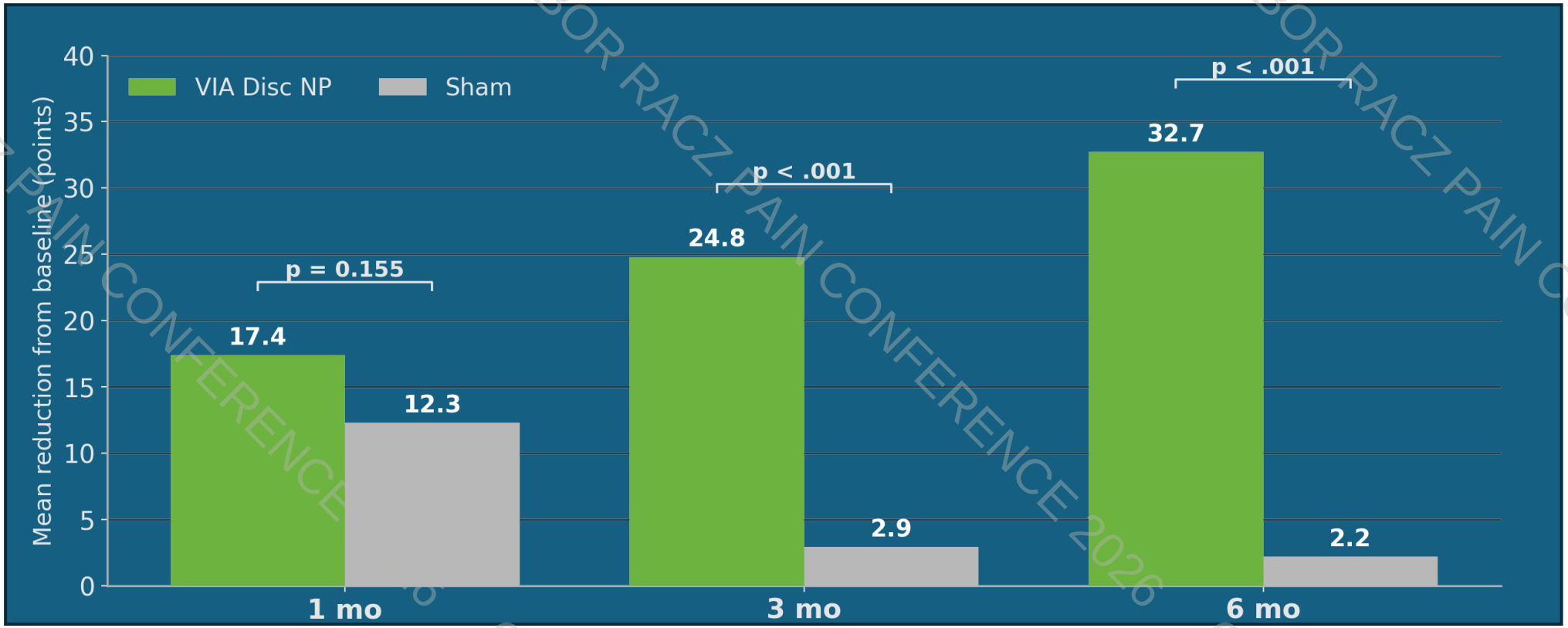
121	5	1:1	98%	1–2
Participants Enrolled	Clinical Sites in Australia	Allograft vs. Sham Randomization	Follow-Up at 6 Months	Lumbar Disc Level(s)

ALLOGRAFT GROUP (N=60)	SHAM GROUP (N=61)
100 MG NP Allograft reconstituted with saline	Identical setup, sedation, and procedural duration
20G cannula with fluoroscopic guidance under conscious sedation	20G cannula inserted through skin/muscle but did not penetrate the disc
Allograft delivered into target disc(s)	No saline or allograft delivered

Crossover Eligibility: Participants randomized to the sham group were offered the option to cross over to the allograft group at 3 months post-procedure (if less than 30% reduction in back pain severity).

VAS Back: Change From Baseline (points)

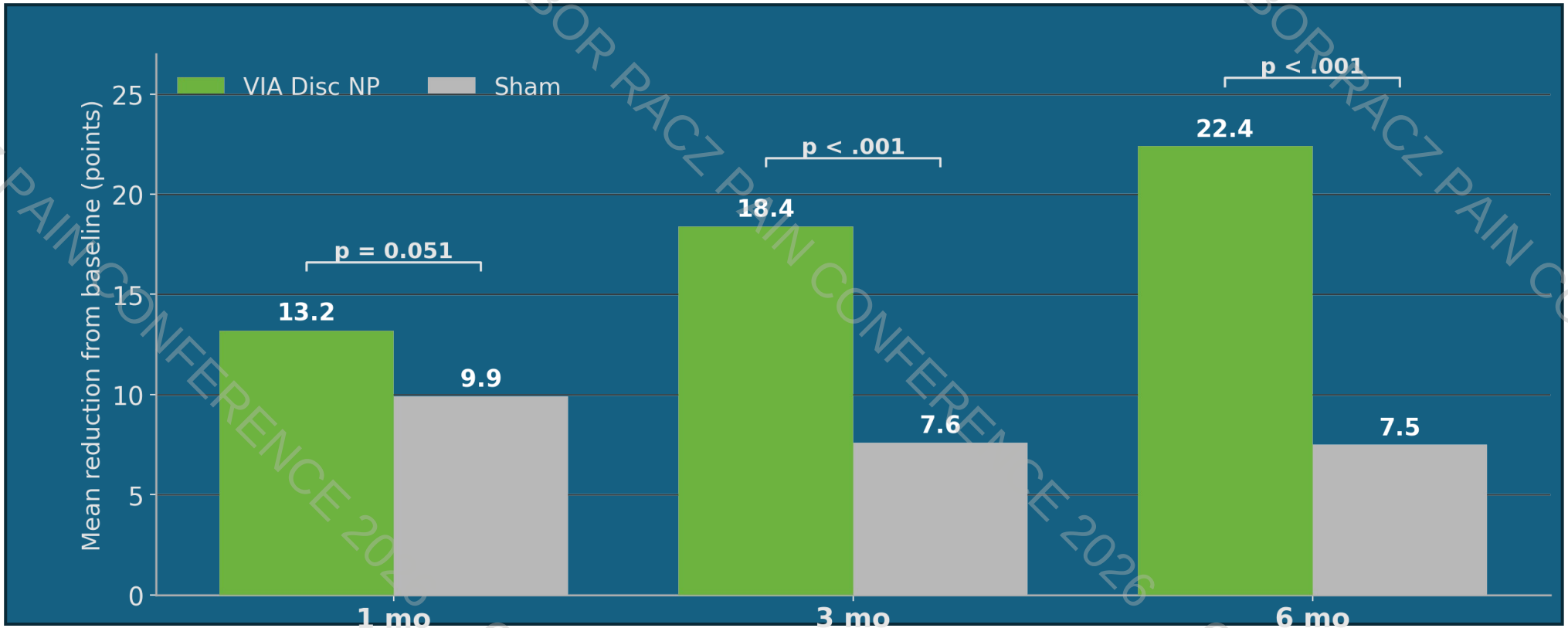
By 3 months NP Allograft separates sharply from sham and the gap widens to 30.5 points by 6 months



Full Analysis Set, LOCF. *Two-sided Wilcoxon rank-sum test (nominal p, not adjusted for multiplicity). Bars show absolute mean reduction from baseline — higher = greater improvement.

ODI: Change From Baseline (points)

Function improves in parallel with pain: NP Allograft separates from sham by 14.9 points at 6 months



Full Analysis Set, LOCF. ODI = Oswestry Disability Index (0–100). *Two-sided Wilcoxon rank-sum test (nominal p). Bars show absolute mean reduction from baseline.

Saline + Micronized Disc Allograft

(HCTP 361 Product)

Trial	Size	Location	Comparator	Goal
VAST (HCTP 351)	218 Subjects	U.S.	saline / NSM	feasibility and early efficacy
ASCEND (HCTP 361)	110	Australia	sham procedure	confirm efficacy signal
RESTORE (HCTP 361)	~400	U.S.	sham procedure	large Level-1 evidence

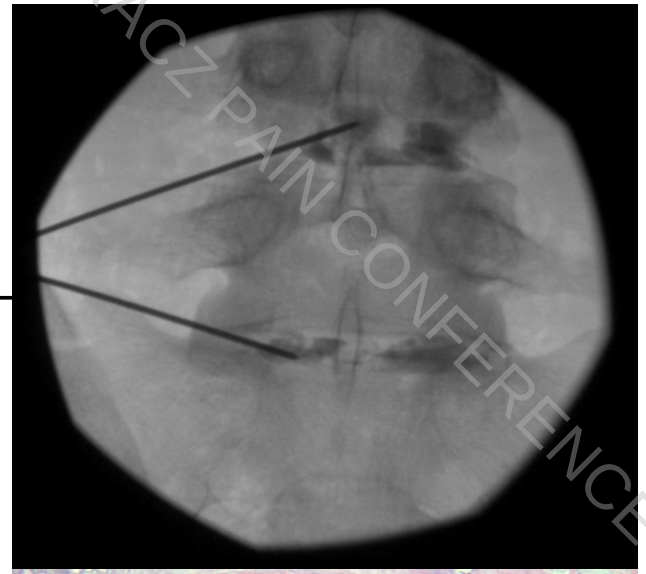
- VAST & ASCEND Completed
- Data from RESTORE not yet available (~2/3 enrolled)
- Category 1 CPT Approval application anticipated Q4 of 2026

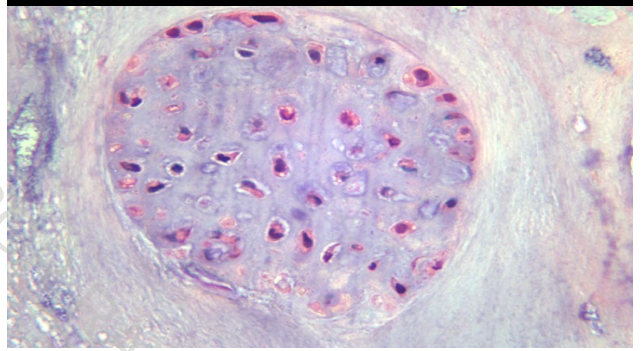
Intradiscal Cellular Therapy Trials - Summary

- **Three large RCTs (VAST, CASCADE & ASCEND) show significant improvement in pain & function that is sustained clinical improvements up to 3 years c/w previous reported data**

- First Phase II Trial showing sig dose response curve difference & **sig pain, fxn & QOL improvements** after injection **of NP cell line** out to 2 yrs

- Micronized NP is available product showing similar results to ViaDisc in single arm cohort trial



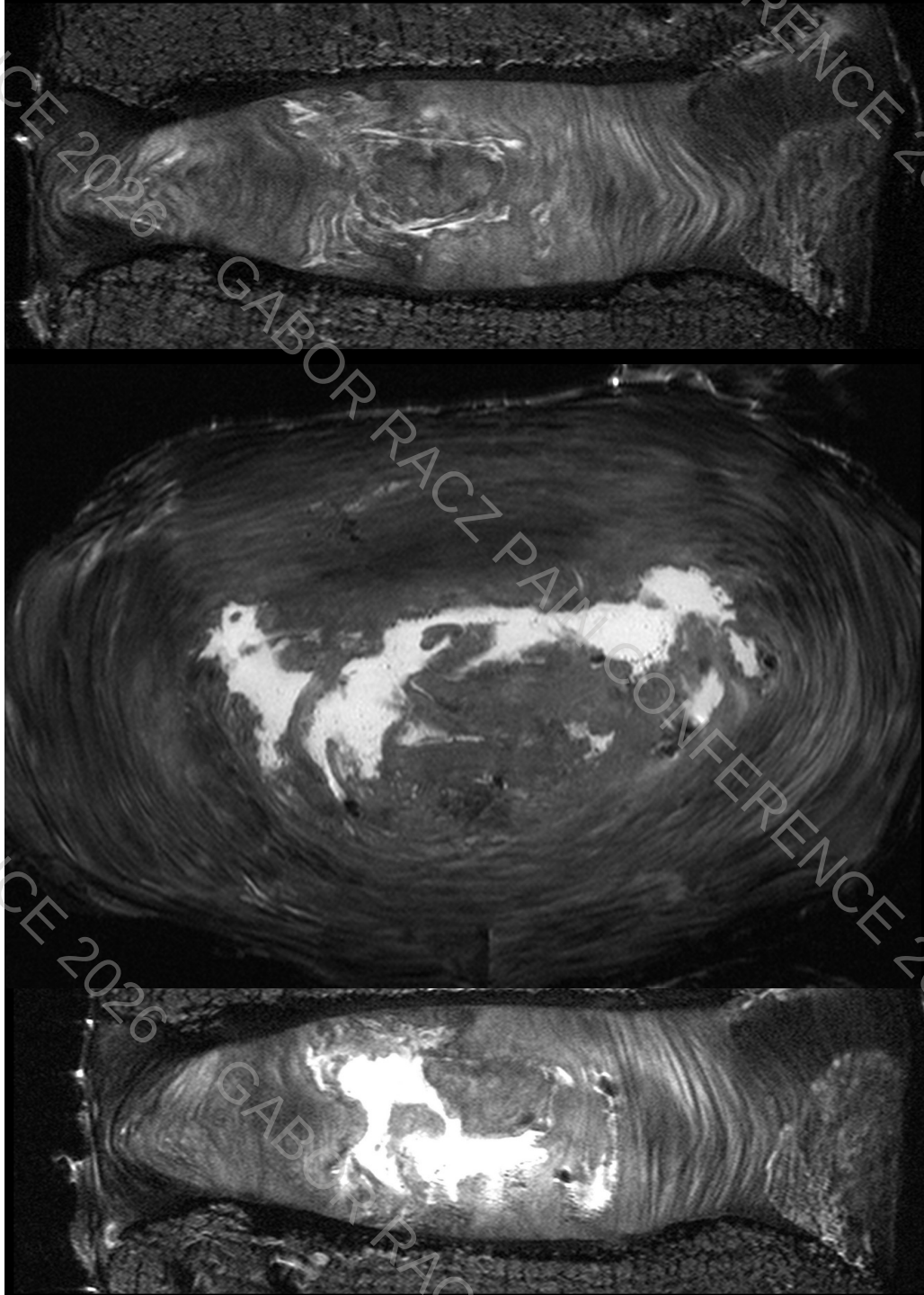


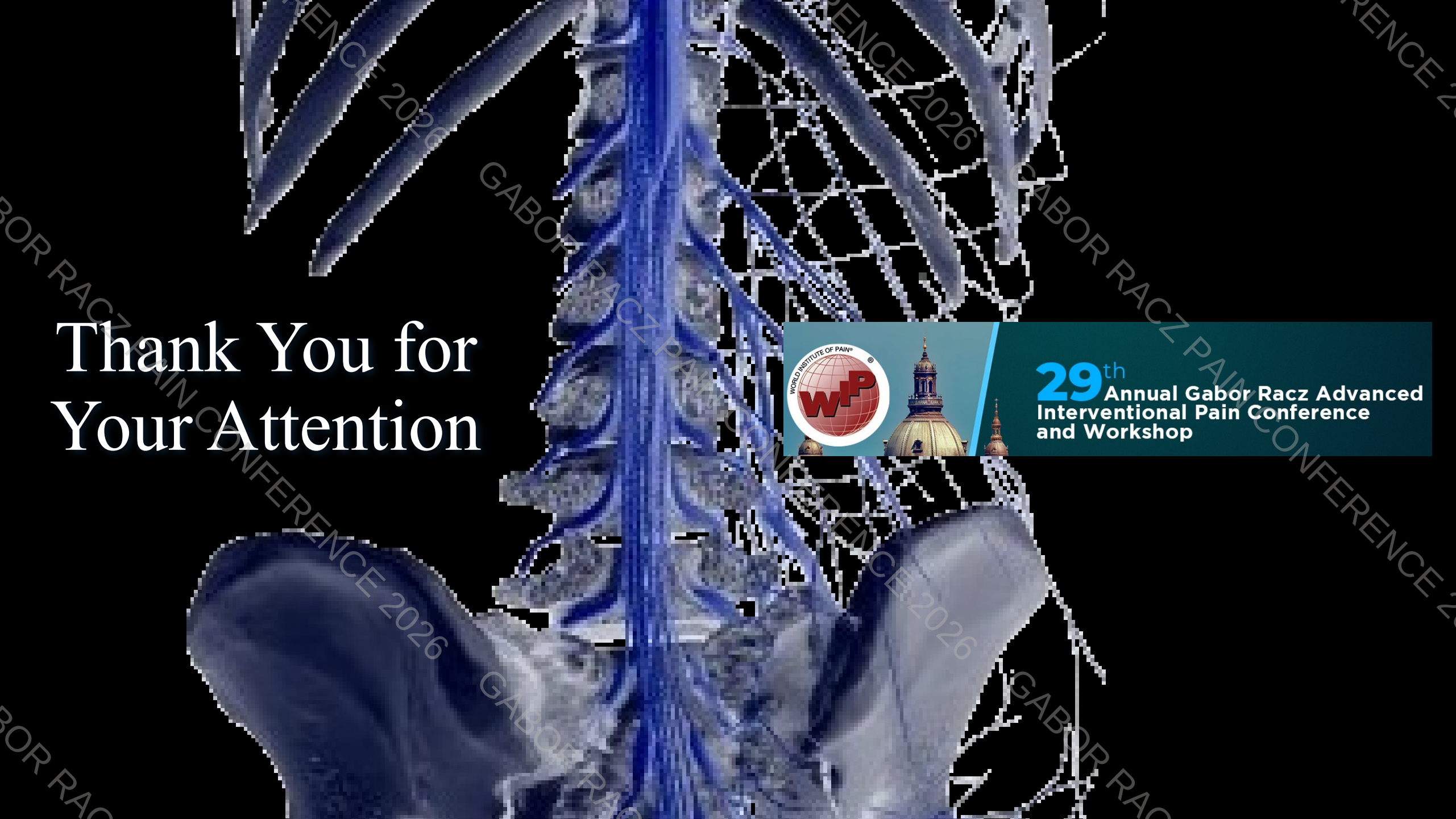
Conclusion

- Micronized NP Use & Results are Growing Rapidly w/ Cat I Approval Possibly in 2027
- Rexlemestrocel-L Phase III Completed May 2026 w/ Likely FDA Approval Q2 of 2028
- Trial Complete for BioRestorative

Bottom Line:

- The Time for Intradiscal Treatment Options has Arrived and the Future Remains Bright

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