NATURE CELL

September 16, 2025

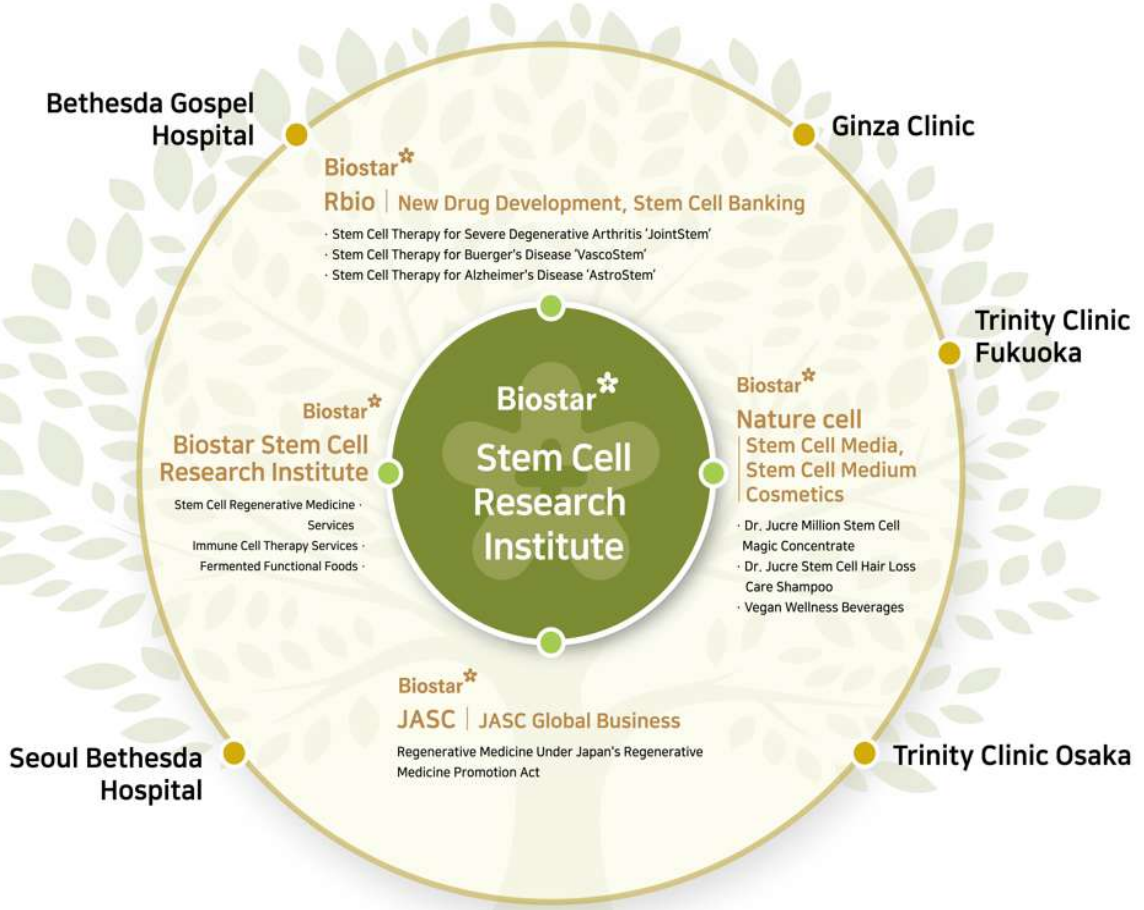
미국에서 생명의 빛을 밝히겠습니다!

Contents

Biostar
Nature Cell

개요 및 핵심기술

개요


Bethesda Gospel Hospital
Ginza Clinic
Trinity Clinic Fukuoka
Trinity Clinic Osaka
Seoul Bethesda Hospital
Biostar
Rbio | New Drug Development, Stem Cell Banking
· Stem Cell Therapy for Severe Degenerative Arthritis 'JointStem'
· Stem Cell Therapy for Buerger's Disease 'VascoStem'
· Stem Cell Therapy for Alzheimer's Disease 'AstroStem'
Biostar
Stem Cell Research Institute
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Stem Cell Regenerative Medicine · Services
Immune Cell Therapy Services ·
Fermented Functional Foods ·
Biostar
Nature cell
Stem Cell Media, Stem Cell Medium Cosmetics
· Dr. Jucre Million Stem Cell Magic Concentrate
· Dr. Jucre Stem Cell Hair Loss Care Shampoo
· Vegan Wellness Beverages
Biostar
JASC | JASC Global Business
Regenerative Medicine Under Japan's Regenerative Medicine Promotion Act
Biostar

핵심 기술 : 엔젤 스템셀 기술

“Angelic” Side of Mesenchymal Stem Cells (Benefit)

Multilineage differentiation potential

Immunomodulation

Trophic support

Homing ability

Anti-aging

Tissue regeneration

“Demonic” Side of Mesenchymal Stem Cells (Risk)

Pro-tumorigenic

Immune response

Short survival

Not spectacular improvements

Unspecified optimal methods of cell administration

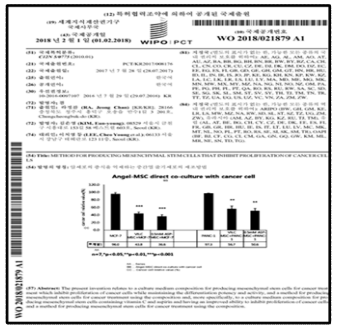
Problem Solved

(Adapted from Lukomska et al., 2019)

PATENTED

Biostar’s Patented Stem Cell Culture Technology

to eliminate demonic sides and
improve angelic characteristics as Angel MSC



핵심 기술 : 엔젤 스템셀 기술

1. Stem Cell Reverse-aging Techonolgy

- Successful development of a medium composition for making aged stem cells into young stem cells
- Developed a technology that can make stem cells collected from elderly people have traits similar to young stem cells

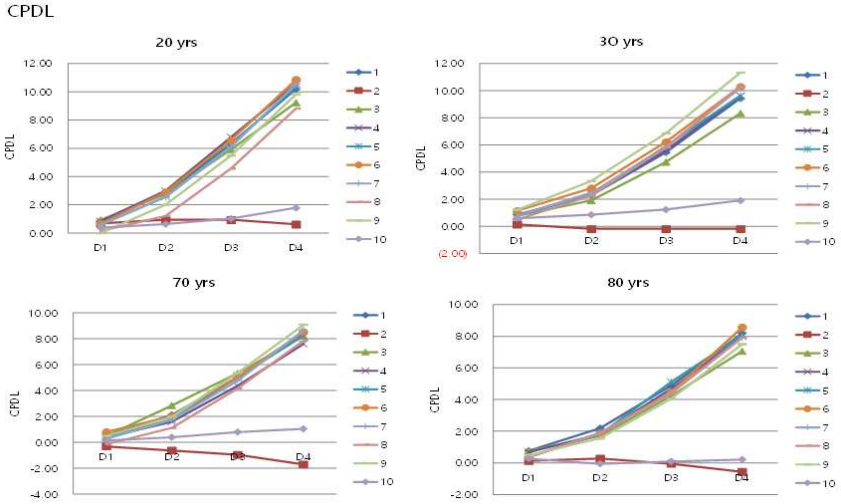


Figure . Cell population do level (CPDL) by age in young people (20s and 30s) and old people (70s and 80s) cultured ubling in 10 types of media.
#1 media: Biostar media, #2~10: Media lacking one of supplements in Biostar media.

Telomerase activity assay

Age \ Media	1	2	3	9	10
20	2.254	0.158	0.410	2.591	0.112
30	3.016	0.099	0.805	3.329	0.102
70	1.672	0.121	0.124	1.520	0.084
80	2.342	0.099	0.105	1.120	0.070

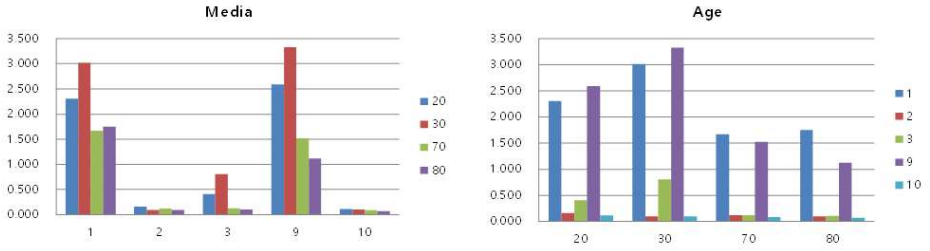


Figure . Telomerase activity of adipose stem cells cultured in five types of media by age and media.
#1 media: Biostar media, #2~10: Media lacking one of supplements in Biostar media.

핵심 기술 : 엔젤 스템셀 기술

2. Stem Cell Size Optimization Technology

- Techniques that prevent stem cells from being shredded or fused before being administered intravenously
- Successfully developed a stem cell composition for intravenous administration with a diameter of 10 to 20 ㎛ suitable for administration

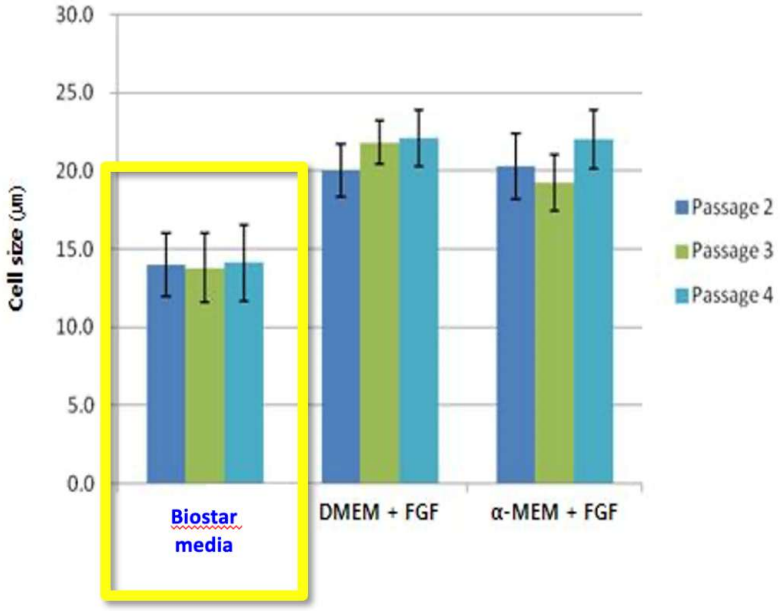


Figure . The size of stem cells cultured in media made with *Biostar technology* maintained at a stable small size when administered intravenously.

핵심 기술 : 엔젤 스템셀 기술

3. Anti-tumor Effect Stem Cell Technology

- Successfully devised the technology and resolved the issue of culturing cells that do not exhibit pro-tumorigenic traits ensuring their safety
- Furthermore, co-culture with Angel MSC significantly inhibited cell proliferation and viability of representative cancer cell lines

Human Breast & Pancreatic Cancer Cells

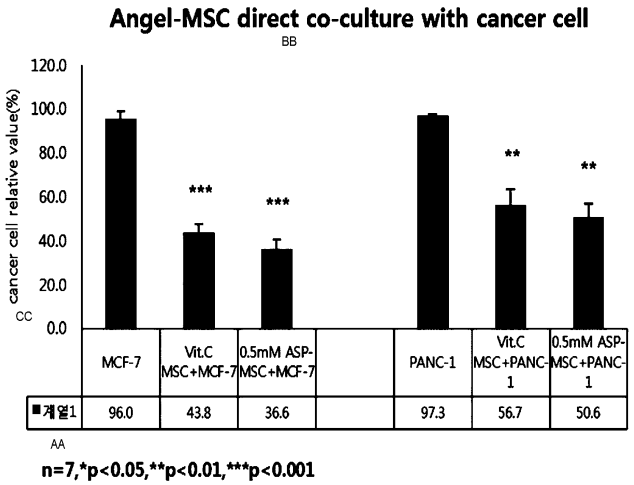


Figure . Vit.C-MSCs cultured in aspirin-containing medium and breast cancer MCF-7 or pancreatic cancer PANC-1 cancer cells were directly co-cultured in the cancer cell culture medium, and the effect of inhibiting cancer cell proliferation was confirmed.

Human Ovarian Cancer Cells

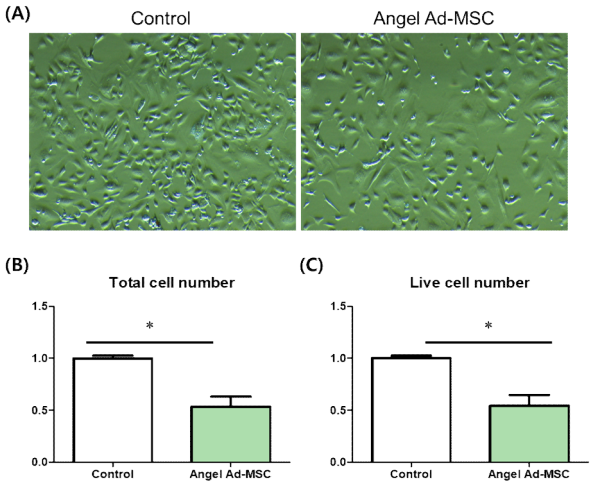


Figure . (A) Representative images of human ovarian cancer cell line after co-culture with Angel Ad-MSC. (B) Total cell number (normalized). (C) Live cell number (normalized). Data are expressed as the mean ± standard error of the mean (SEM). Significant differences ($p < 0.05$) are indicated by an asterisk.

핵심 기술 : 엔젤 스템셀 기술

4. Stability Improving formulation technology

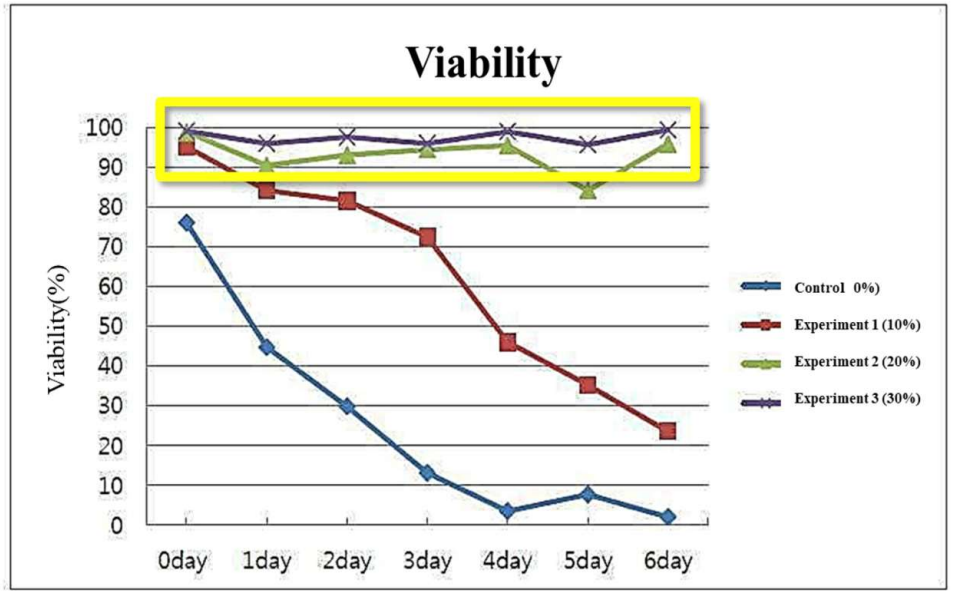


Figure . Experimental group 3 (stem cells containing 30% serum) maintained a survival rate of over 98% for up to 144 hours

핵심 기술 : 엔젤 스템셀 기술

5. Ready-to-use (RTU) Freezing Formulation Technology

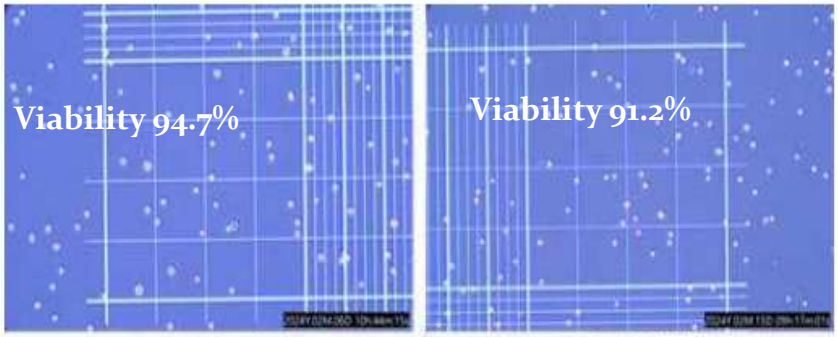


Figure . Stem cell viability is maintained after cryopreservation in the cryo-formulation, with fresh Ad-MSCs showing a viability of 94.7% and thawed cryopreserved Ad-MSCs retaining a viability of 91.2%.

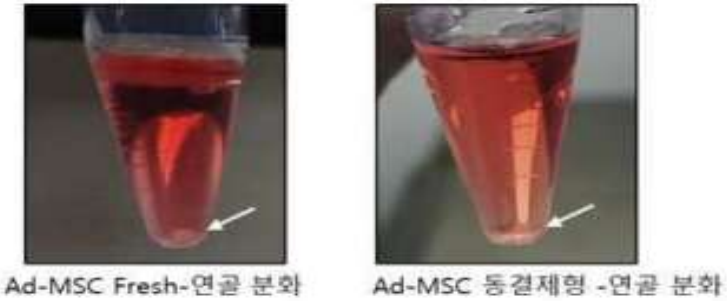


Figure . Chondrogenic differentiation of stem cells was successfully induced after cryopreservation in the cryo-formulation. Following thawing, Ad-MSCs exhibited clear chondrogenic differentiation, and adipogenic and osteogenic differentiation were also confirmed (data not shown).

6. Stem Cell Banking Technology for Semi-Permanent Use

The world's largest bank for adipose tissue-derived mesenchymal stem cells

- Since 2006: Stem cells stored from 19,346 people
- Regenerative treatments: Experienced by 32,867 individuals
- Enhanced safety: Simultaneous storage in Korea (Rbio) & Japan (JASC, Japan Angel Stem Cell)
- Efficiency: 5 vials of P0 cells can provide up to 250 treatments

Rbio, Korea

JASC, Japan

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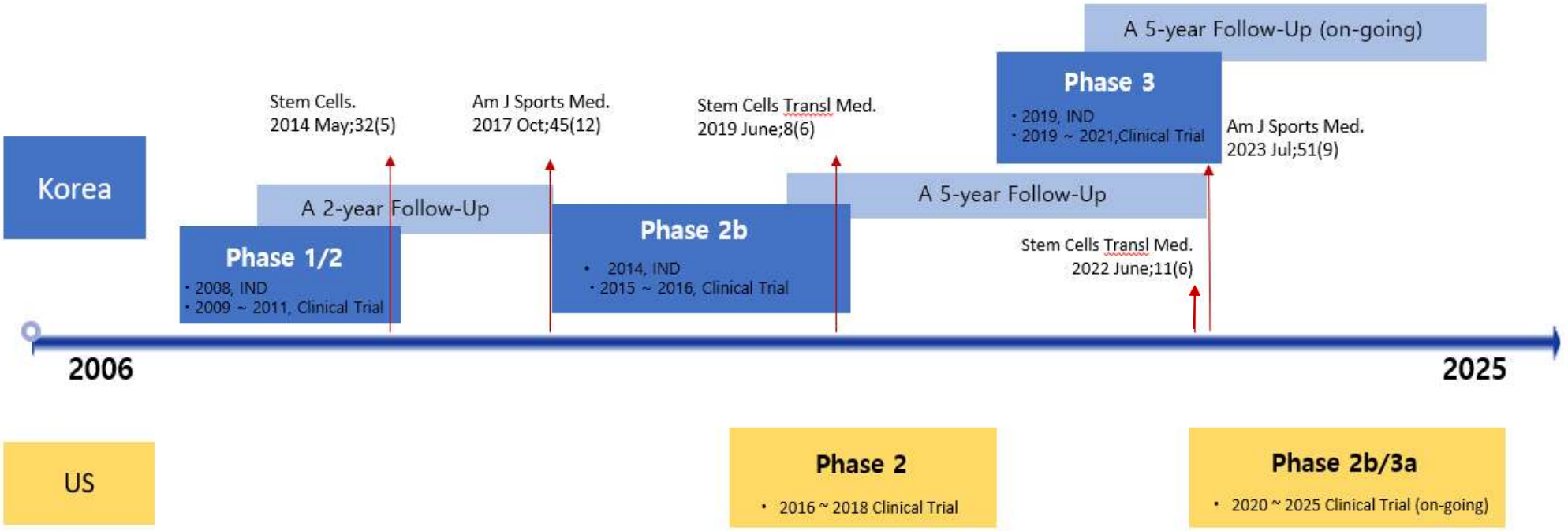
당면 과제와 해결 전략

조인트스템 개발 진행 경과

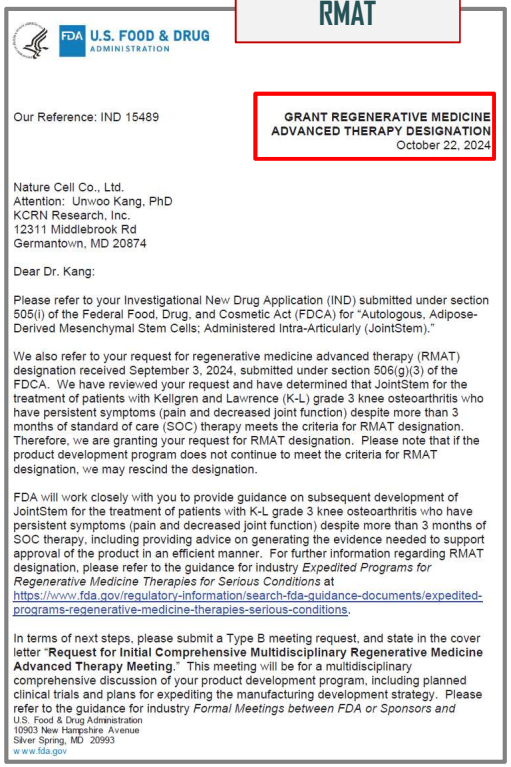
Demonstrating safety and efficacy through about 20 years' global development



FDA 신속 프로그램 3대 인증

FDA's Grant on Expedited Development Programs

RMAT



U.S. FOOD & DRUG ADMINISTRATION

Our Reference: IND 15489

GRANT REGENERATIVE MEDICINE ADVANCED THERAPY DESIGNATION
October 22, 2024

Nature Cell Co., Ltd.
Attention: Unwoo Kang, PhD
KCRN Research, Inc.
12311 Middlebrook Rd
Germantown, MD 20874

Dear Dr. Kang:

Please refer to your Investigational New Drug Application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act (FDCA) for "Autologous, Adipose-Derived Mesenchymal Stem Cells; Administered Intra-Articularly (JointStem)."

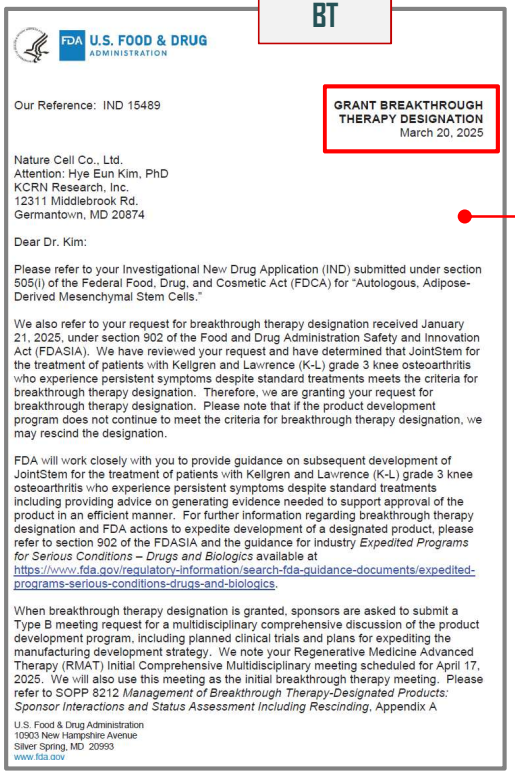
We also refer to your request for regenerative medicine advanced therapy (RMAT) designation received September 3, 2024, submitted under section 506(g)(3) of the FDCA. We have reviewed your request and have determined that JointStem for the treatment of patients with Kellgren and Lawrence (K-L) grade 3 knee osteoarthritis who have persistent symptoms (pain and decreased joint function) despite more than 3 months of standard of care (SOC) therapy meets the criteria for RMAT designation. Therefore, we are granting your request for RMAT designation. Please note that if the product development program does not continue to meet the criteria for RMAT designation, we may rescind the designation.

FDA will work closely with you to provide guidance on subsequent development of JointStem for the treatment of patients with K-L grade 3 knee osteoarthritis who have persistent symptoms (pain and decreased joint function) despite more than 3 months of SOC therapy, including providing advice on generating the evidence needed to support approval of the product in an efficient manner. For further information regarding RMAT designation, please refer to the guidance for industry *Expedited Programs for Regenerative Medicine Therapies for Serious Conditions* at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/expedited-programs-regenerative-medicine-therapies-serious-conditions.

In terms of next steps, please submit a Type B meeting request, and state in the cover letter "**Request for Initial Comprehensive Multidisciplinary Regenerative Medicine Advanced Therapy Meeting.**" This meeting will be for a multidisciplinary comprehensive discussion of your product development program, including planned clinical trials and plans for expediting the manufacturing development strategy. Please refer to the guidance for industry *Formal Meetings between FDA or Sponsors and*

U.S. Food & Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993
www.fda.gov

BT



U.S. FOOD & DRUG ADMINISTRATION

Our Reference: IND 15489

GRANT BREAKTHROUGH THERAPY DESIGNATION
March 20, 2025

Nature Cell Co., Ltd.
Attention: Hye Eun Kim, PhD
KCRN Research, Inc.
12311 Middlebrook Rd.
Germantown, MD 20874

Dear Dr. Kim:

Please refer to your Investigational New Drug Application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act (FDCA) for "Autologous, Adipose-Derived Mesenchymal Stem Cells."

We also refer to your request for breakthrough therapy designation received January 21, 2025, under section 902 of the Food and Drug Administration Safety and Innovation Act (FDASIA). We have reviewed your request and have determined that JointStem for the treatment of patients with Kellgren and Lawrence (K-L) grade 3 knee osteoarthritis who experience persistent symptoms despite standard treatments meets the criteria for breakthrough therapy designation. Therefore, we are granting your request for breakthrough therapy designation. Please note that if the product development program does not continue to meet the criteria for breakthrough therapy designation, we may rescind the designation.

FDA will work closely with you to provide guidance on subsequent development of JointStem for the treatment of patients with Kellgren and Lawrence (K-L) grade 3 knee osteoarthritis who experience persistent symptoms despite standard treatments including providing advice on generating evidence needed to support approval of the product in an efficient manner. For further information regarding breakthrough therapy designation and FDA actions to expedite development of a designated product, please refer to section 902 of the FDASIA and the guidance for industry *Expedited Programs for Serious Conditions – Drugs and Biologics* available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/expedited-programs-serious-conditions-drugs-and-biologics.

When breakthrough therapy designation is granted, sponsors are asked to submit a Type B meeting request for a multidisciplinary comprehensive discussion of the product development program, including planned clinical trials and plans for expediting the manufacturing development strategy. We note your Regenerative Medicine Advanced Therapy (RMAT) Initial Comprehensive Multidisciplinary meeting scheduled for April 17, 2025. We will also use this meeting as the initial breakthrough therapy meeting. Please refer to SOPP 8212 *Management of Breakthrough Therapy-Designated Products: Sponsor Interactions and Status Assessment Including Rescinding*, Appendix A

U.S. Food & Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993
www.fda.gov

EAP

We remind you that under section 561A(f)(2) of the FDA, you are required to make your **expanded access policy for JointStem** publicly available within 15 days of the signature date of this letter. For further information regarding how to make your expanded access policy publicly available, you may visit our expanded access webpage on FDA.
gov at https://www.fda.gov/news-events/expanded-access/expanded-accessinformation-industry.

조인트스템 한국 허가 신청 반려 상황 발생 !

[HIT 포커스] 조인트스템, 2년간 정답 없는 '숨은그림' 찾았다

(2025.09.02. 히트뉴스 기사)

Rembrandt Harmenszoon van Rijn
Nederlands, Born 1606

갈릴래아 호수의 폭풍 1633

조인트스템 !

미국시장 진출을 가속화하겠습니다!

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미국시장 진출의 가속화

- FDA 신약 허가 가속화
- FDA 가속 승인 검토 진행
- 미 플로리다 주에서 줄기세포 재생의료 상용화 추진

미 플로리다 주에서 줄기세포 재생의료 상용화 추진

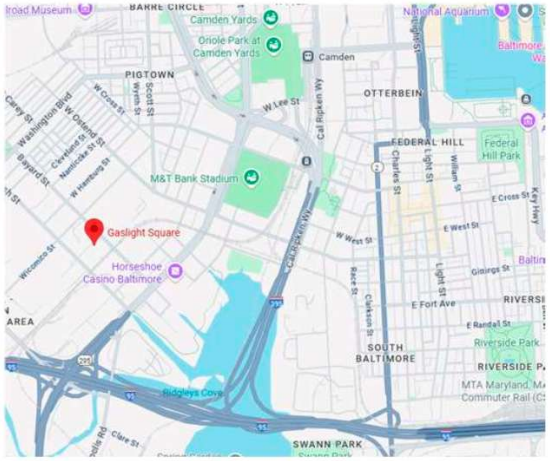
법안명 : **SB 1768**

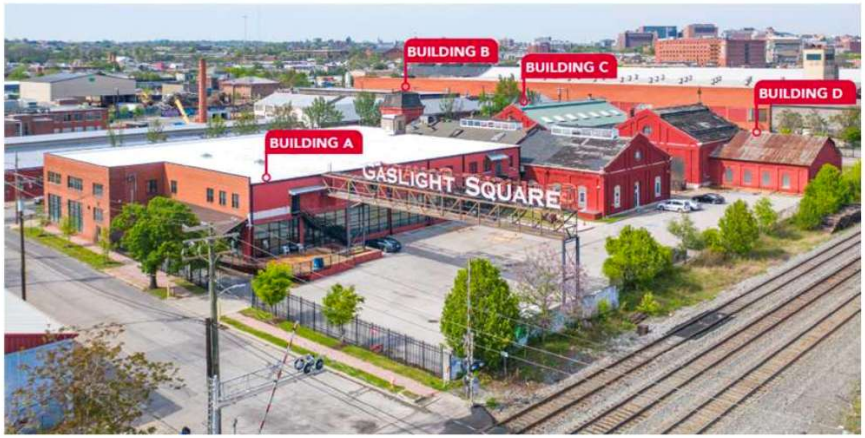
- **발효일** : 2025년 7월 1일
- **법안개요** : 면허가 있는 의사(MD 또는 DO)가 FDA(미국식품의약국)의 승인을 받지 않은 줄기세포 치료를 특정 조건 하에 시행할 수 있도록 허용하는 법률
- **법안 내용 :**
  - 허용 치료 범위 : 정형외과적 질환, 통증 관리, 상처 치료 목적에 한정
  - 제조 기준
    - 줄기세포는 FDA 등록 시설에서 제조되어야 함
    - 국립골수기증자프로그램(National Marrow Donor Program), 세계골수기증자협회(World Marrow Donor Association), 혈액 및 생물요법 발전을 위한 협회(Association for the Advancement of Blood and Biotherapies), 미국조직 은행협회(American Association of Tissue Banks) 등의 인증 필수
    - 시설은 치료 전 의사에게 해동 후 생존율 분석 보고서 제공이 필수

미국 바이오스타 스템셀 캠퍼스 구축

❖ Plan for BIOSTAR Stemcell Campus

- Stemcell Therapy research and development
- GMP facility; Annual supply plan of 1 million JointStem doses
  - ✓ Gaslight Square : working on LOI targeting a settlement in this year





~104K SF mixed-use in 4 buildings (Lot; 2.56 Acres)

루푸스(만성통증) 적응증 IND 신청

朝鮮日報

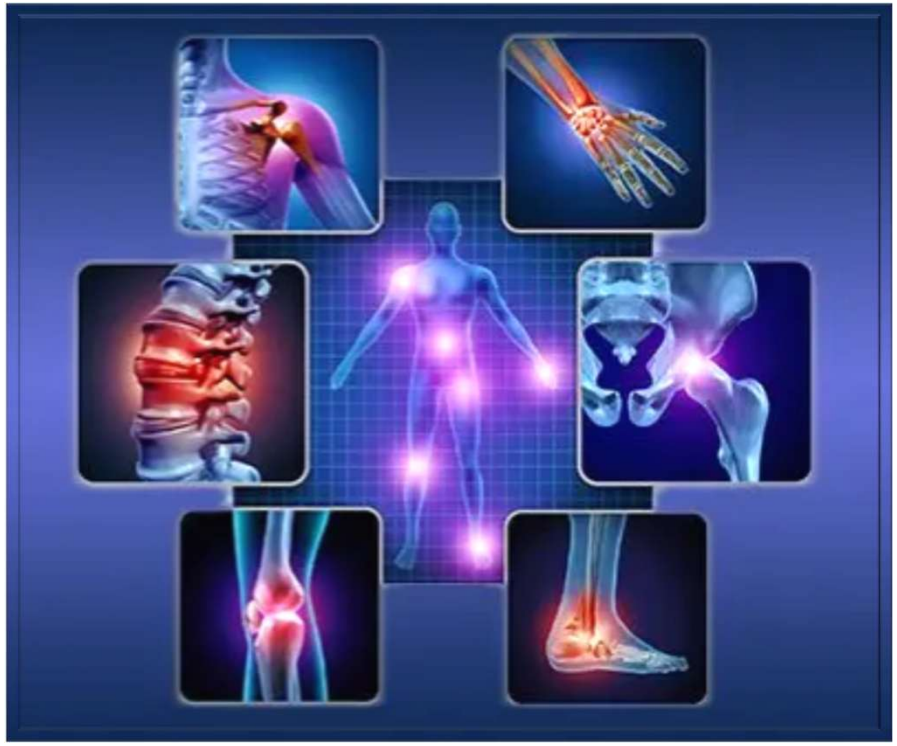
조선경제 오피니언 정치 사회 국제 건강 재테크 스포츠 문화·연예 조선몰 콘텐츠판

사회 >

[사람과 이야기] "저를 신뢰한 분들께 죄송… 700가지 통증에 시달려…"

'행복전도사' 최윤희씨, 남편과 동반 자살
2년 전부터 면역질환… 남편이 극진하게 돌봐
10일전쯤부터 주변 정리… 경비원들에게 밤 선물도

700가지 통증에 시달린 끝에 자살을 택했다는 최씨는 2년 전부터 '홍반성 루푸스(lupus)'라는 만성 질환을 앓아 왔던 것으로 밝혀졌다. 홍반성 루푸스는 면역 세포가 오히려 자기 몸을 공격하는 자가면역성 질환이다. 피부 발진, 관절염, 뇌염, 폐렴 등 증상이 다양한 데다 완치가 어려운 것으로 알려져 있다.



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한국 시장에서의 조인트스템 계획

JointStem demonstrated Favorable Benefit-Risk Assessment

Unmet Medical Needs	● K-L grade 3의 퇴행성 관절염 중증 단계 특히 SOC를 사용함에도 증상이 지속될 때 다른 선택할 약물이 부재함 ● 세포치료제로서 허가된 제품의 경우 '국한된 연골결손 부위의 치료 목적 ' 으로 환자의 증상 개선과 직접적 관련이 없으며, 전신마취가 필요한 수술적 방법임 ● '신의료기술(보건복지부)' 로 승인 받은 관절강 내 주사제 가 최근 환자들에게 선택지로 사용되고 있음		
		통계적 유의성	**임상적 유의성**
효능	**기능 및 통증 지표 (WOMAC total, VAS)**	1차 지표 우수성 입증: 6 개월 ・WOMAC total, p=0.002 ・VAS, p<0.0001 2차 지표 우수성 입증: 6개월 ・WOMAC-subscales, KOOS,IKDC,SF-36	장기지속: 3년 이상 ・Baseline 대비, WOMAC total, p<0.0001, ・Baseline 대비, VAS, p<0.0001 ・현재 허가된 보존적 요법; <6개월
	2차 유효성 평가변수	우수성 입증: 6 개월 : 모든 2차 평가변수들, p<0.05	장기지속: 3년 이상 ・Baseline 대비, WOMAC-subscales, p<0.0001 ・SF-36 9개 항목, p<0.05
	생체지표 (Biomarker, MRI)	우수성 입증: 6개월 : 연골결손면적, p<0.0001	장기지속: 3년 이상 : 현재 허가된 보존적 요법 <6개월
	Clinical Outcome (인공관절치환술)	Not relevant	장기지속: 3년 이상 • 현재 허가된 보존적 요법 자료 전무
	보존적 요법 (SOC)	구제약 총 용량과 사용횟수 감소 입증 • 총용량, p=0.0008, 횟수, p=0.0338	효과 간접적 입증
안전성	**약물이상반응, 부작용**	우려 없음 입증	
	보존적 요법 (SOC)	구제약 총 용량과 사용횟수 감소 입증 • 총용량, p=0.0008, 횟수, p=0.0338	비마약성 진통제 사용 시 예상되는 간독성, 소화기부작용 감소와 마약성 진통제 남오용 감소
	RWD		2015년부터 2023년까지 일본에서 조인트스템과 동일한 제형을 투여 받은 총 3,533건 중 3,510건(99.3%)이 이상반응 없었음
Regulatory Reference	• 위와 같은 자료로 FDA로 부터 재생혁신적 신약 (RMAT,10/22/2024) 과 혁신적 신약 (BT, 03/20/2025) 지정 승인을 통해 임상적 유의성 인정받음 • 위와 같은 자료로 FDA로 부터 신약허가 사전에 동정적 사용 (EAP) 공인 받음 (06/09/2025)		

WOMAC : Western Ontario and McMaster Universities Arthritis Index, VAS : Visual analog scale, KOOS : Knee injury & osteoarthritis outcome score, IKDC: International knee documentation committee, SF-36 : 36-Item short form health survey questionnaires, SOC : Standard of Care, PRO : Patient-Reported Outcome, RWD : Real-World Data, RMAT : Regenerative Medicine Advanced Therapy, BT : Breakthrough Therapy

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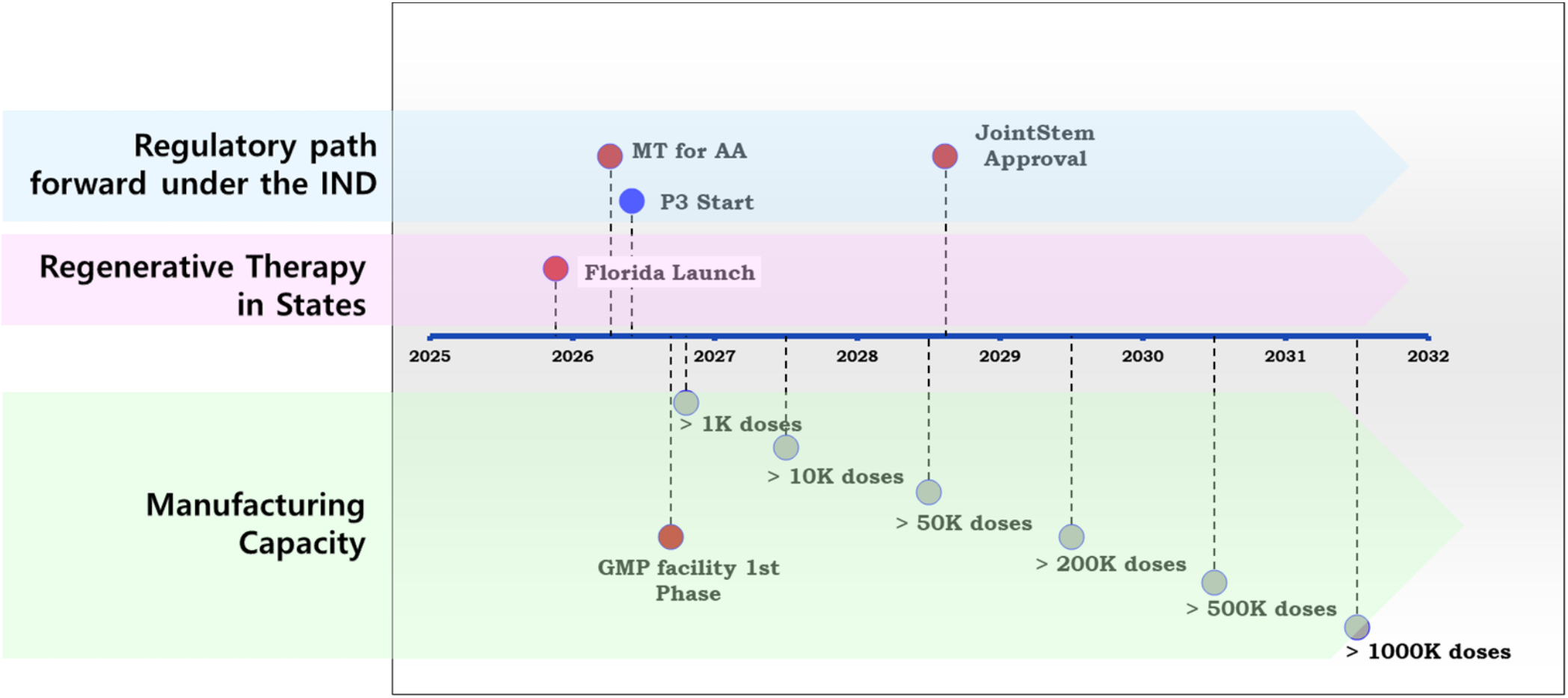
미국에서의 실용화를 통한 세계 표준 완성

미국 실용화의 향후 로드맵



네이처셀의 경영이념: 敬天愛人

생명의 빛을 밝혀가는 길에
당신의 동행이 큰 힘이 됩니다