TreeFrog therapeutics

Making cell therapies

safer & more efficient | more available & affordable

for **millions** of patients

BOSTON, NOUS VOILÀ

ANY QUESTIONS ? CONTACT ELIZA SCHLEIFSTEIN
jpatreefrog@jpa.com or call 917-763-8106

www.treefrog.fr

$75 million

Series B & New CEO

On September 13th, TreeFrog Therapeutics announced the closing of a $75 million (€64 million) Series B financing led by Bpifrance Large Venture, with the participation of Leonard Green & Partners, Bristol Myers & Squibb and Xange.

Read press release

Former Board Member Frédéric Desdouits, was appointed Chief Executive Officer, with the mission of advancing a comprehensive pipeline of allogeneic cell therapies to the clinic and drive the international development of TreeFrog in the USA and Japan.

Watch video

Frédéric Desdouits, PhD
New CEO
TreeFrog Therapeutics

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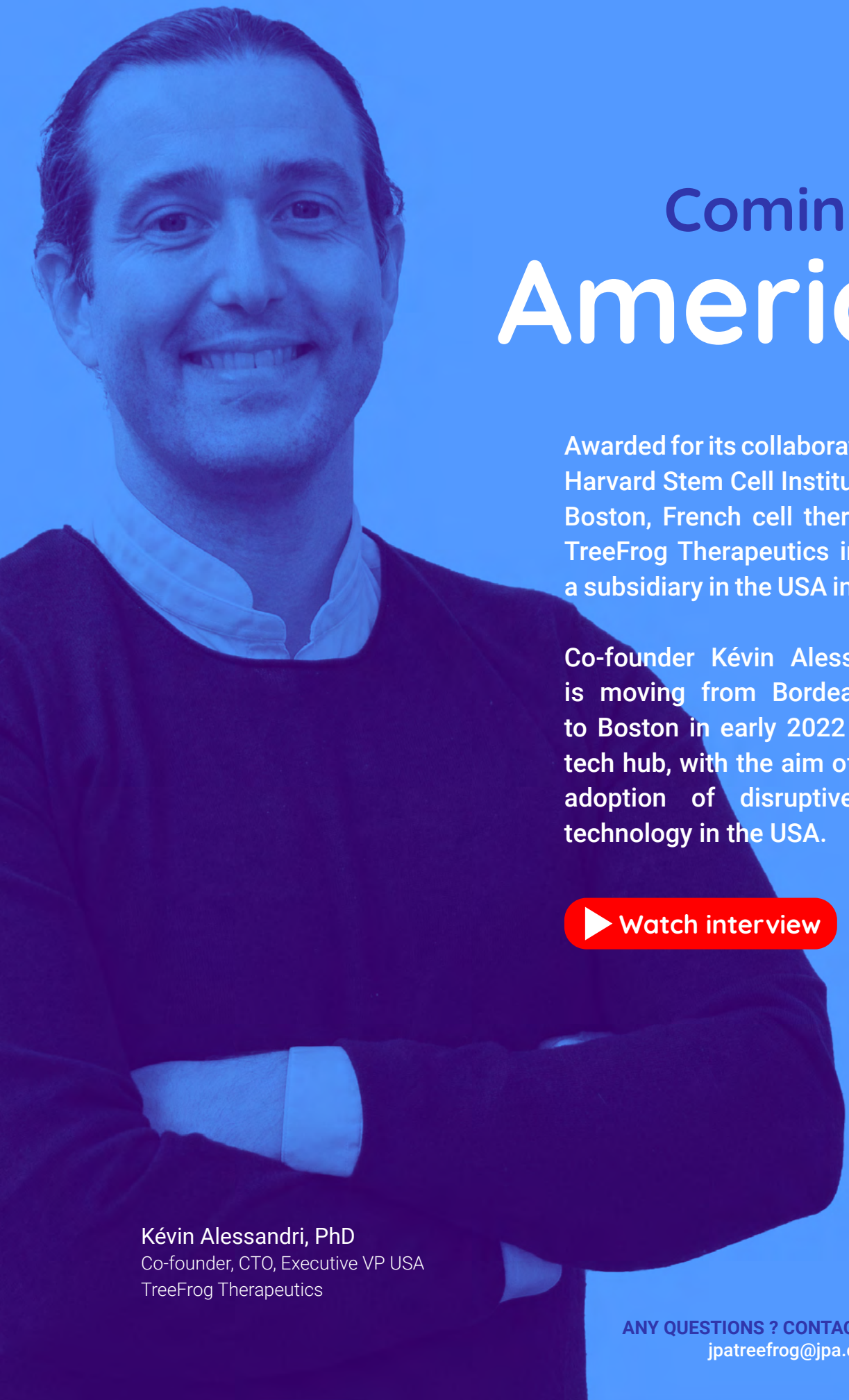

Coming to America

Awarded for its collaboration with the Harvard Stem Cell Institute (HSCI) in Boston, French cell therapy biotech TreeFrog Therapeutics incorporated a subsidiary in the USA in June 2021.

Co-founder Kévin Alessandri, PhD, is moving from Bordeaux, France, to Boston in early 2022 to set up a tech hub, with the aim of driving the adoption of disruptive C-Stem™ technology in the USA.

Watch interview

Kévin Alessandri, PhD
Co-founder, CTO, Executive VP USA
TreeFrog Therapeutics

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About
TreeFrog Therapeutics

VISION
Cell therapy for all

Incorporated in Bordeaux in 2018, TreeFrog Therapeutics is a French-based biotech startup aimed at **making cell therapies safer, more efficient, more accessible and more affordable for millions of patients.**

TECHNOLOGY
C-Stem™

Protected by 8 patents, biomimetic C-Stem™ technology introduces:

1. **A highly scalable manufacturing process** allowing for the mass-production of cell therapies based on induced pluripotent stem cells (iPSC), while drastically reducing costs.
2. **A new quality standard** for iPSC-derived cell therapy products
3. **A 3D transplantation format** enhancing therapeutic outcomes

CELL THERAPY PIPELINE
Going for mass market

TreeFrog is advancing a pipeline of cell therapies targeting high-burden and currently incurable chronic and degenerative diseases, including **blood and immune disorders, Parkinson's disease, and heart failure.**

2014
meeting in Geneva

The TreeFrog story
TreeFrog Therapeutics was co-founded by Kévin Alessandri, PhD, an expert in 3D-printed microfluidics, and Maxime Feyeux, a stem cell biologist who was one of first PhD students worldwide to work on pluripotent stem cells.

$82M
raised since 2018

A $75M Series B just announced
Awarded with top innovation grants at French & European level (i-LAB, i-Nov, EIC accelerator), TreeFrog also attracted over $82M in private investments over the past 3 years.

50+
froggies in Bordeaux

Expanding in the US & Japan
Bringing together physicists, cell biologists and bioproduction engineers endearingly self-dubbed *the froggies*, the TreeFrog team will grow 3-fold over the next 3 years, with a dedicated **team in Boston.**

3
ongoing contracts

Two contracts with Fortune 500 companies and one in-licensing deal with the French Blood Agency (EFS)
Focused on bringing the benefits of C-Stem™ as fast as possible to patients, TreeFrog is **partnering with market leaders in EU, USA and Japan** to co-develop cell therapies with mass-market potential.

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World's first: from 50 million to

pluripotent stem cells in a week

Tackling critical bottlenecks limiting the mass-production of stem cell-derived therapies, TreeFrog Therapeutics announced in April 2021 an unprecedented 276-fold expansion of human induced pluripotent stem cells (hiPSC) in a 10L bioreactor within 6.59 days. **This single batch of 15 billion cells is enough raw material for 10,000 doses for Parkinson's disease.**

Read press release

In June 2021, TreeFrog presented data from two 10L bioreactors demonstrating outstanding reproducibility and best-in-class cell quality.

Read press release

Large-scale expansion of human pluripotent stem cells in 10L bioreactors using C-Stem™ technology.

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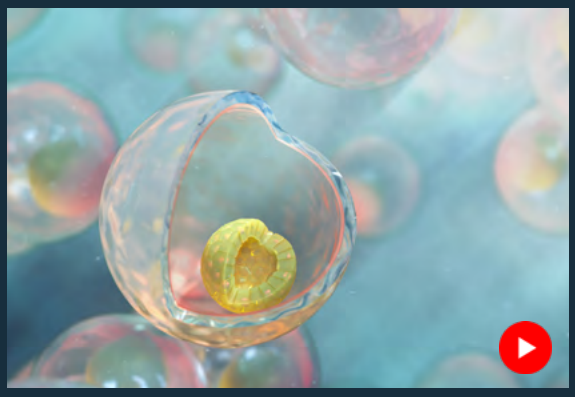
C-Stem™
the difference

AUTOMATED CELL ENCAPSULATION
Over 1,000 capsules per second

BIOMIMETIC 3D STEM CELL CULTURE
In vivo-like cell growth in capsules



LARGE-SCALE BATCHES IN BIOREACTORS
Billions of cells, 10x less manpower

> **Manufacturing large-scale batches of stem cells —the raw material of cell therapies— with low costs and consistent quality currently constitutes a critical bottleneck for the whole industry.**
>
> *Maxime Feyeux, PhD*
> *Co-founder & chief scientific officer, TreeFrog*

Leapfrogging current manufacturing technologies for stem cell-based therapies

C-Stem™ versus 2D culture

Manufacturing 15 billion stem cells:
- 600 Petri dishes with 2D culture
- 1 single 10L bioreactor with C-Stem™

Cell culture in Petri dishes enabled the launch of the first clinical trials with hiPSC-derived therapeutic cells. However, maintaining hundreds of plates over several weeks is labor intensive, expensive, and inevitably causes batch variability. With C-Stem™, automated bioreactor culture doubles the amplification factor obtained in 2D to produce commercial-size batches of several billion cells with 10 times less manpower.

C-Stem™ versus Aggregates in bioreactors

10,000 times better stem cell amplification with C-Stem™

Current bioreactor-based technologies for stem cell culture struggle to reach the 5L scale. Within 6 months, TreeFrog moved to the 10L scale, and recently released a benchmark demonstrating a 151 millionfold stem cell amplification factor over 28 days versus 13 thousandfold amplification with standard bioreactor culture.

Safer cells, at scale, while reducing costs

Benchmark data presented at the 2021 Annual Meeting of the American Society for Cell & Gene Therapy demonstrates that C-Stem™ matches current technologies in terms of stem cell viability and pluripotency.

Furthermore, preliminary results suggest that **C-Stem™ is the only technology capable of maintaining genomic integrity through large-scale hiPSC expansion.**

Stem cell quality obtained with C-Stem™ will be further assessed by the awarded QC-Stem consortium, uniting world-class experts from the **Harvard Stem Cell Institute in Boston, USA**, the FBRI in Kobe, Japan, and the Imagine Institute in Paris, France.

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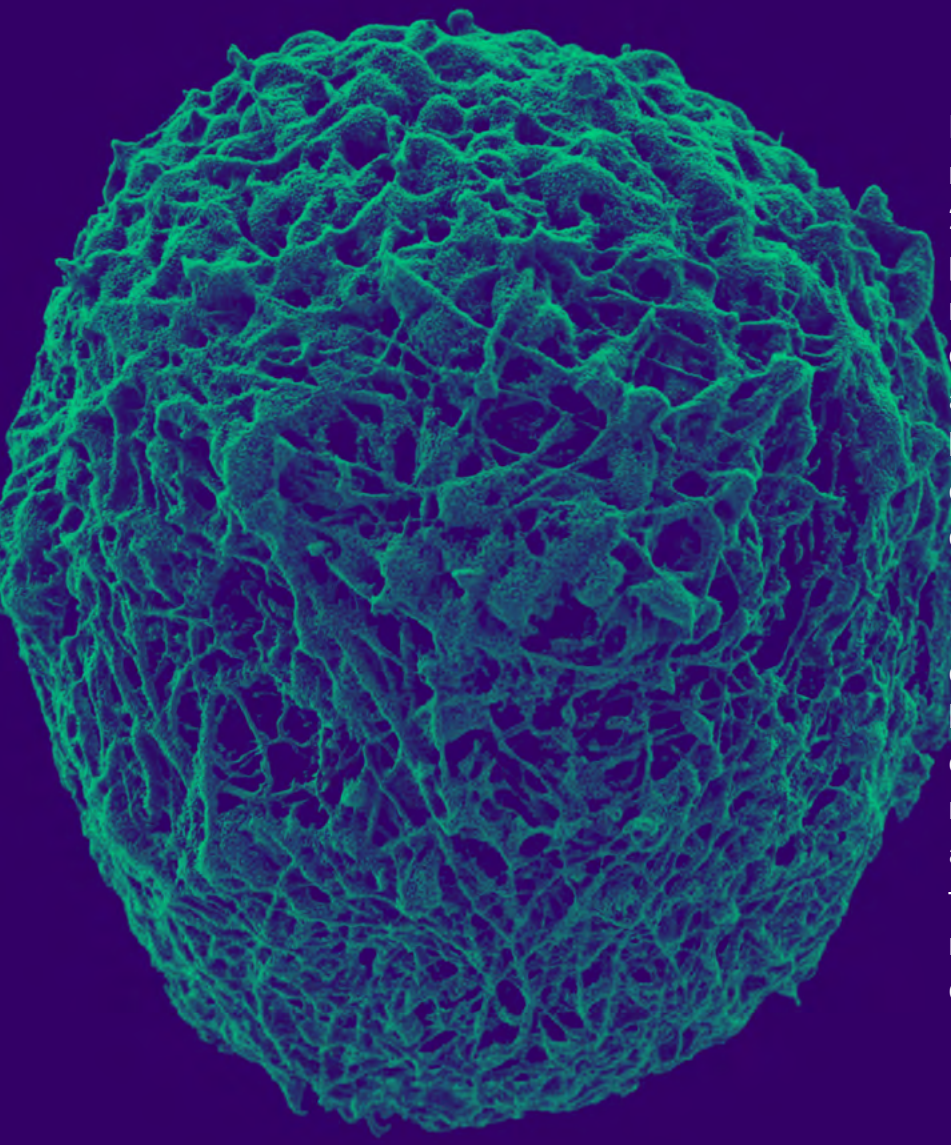
3D brain microtissues
to cure Parkinson's disease



Because harvesting mature neurons is close to impossible in 2D cell culture, current cell therapy programs for Parkinson's disease rely on the transplantation of stem cell-derived progenitors, which are left to differentiate in the host brain, in the hope of replacing the dopaminergic neurons lost in the course of the disease.

In 2018, TreeFrog co-founders demonstrated that with C-Stem™, human pluripotent stem cells could be differentiated into 3D microtissues of mature neurons and performed the world's first transplantation into a non-clinical model of Parkinson's disease, demonstrating best-in-class results.

3D neural microtissue containing dopaminergic neurons, differentiated in capsule from hiPSCs with the C-Stem™ technology.

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About
Parkinson's disease

1 million patients
in the US in 2020,
doubling by 2040

$52 billion
direct and indirect costs
in the U.S. every year

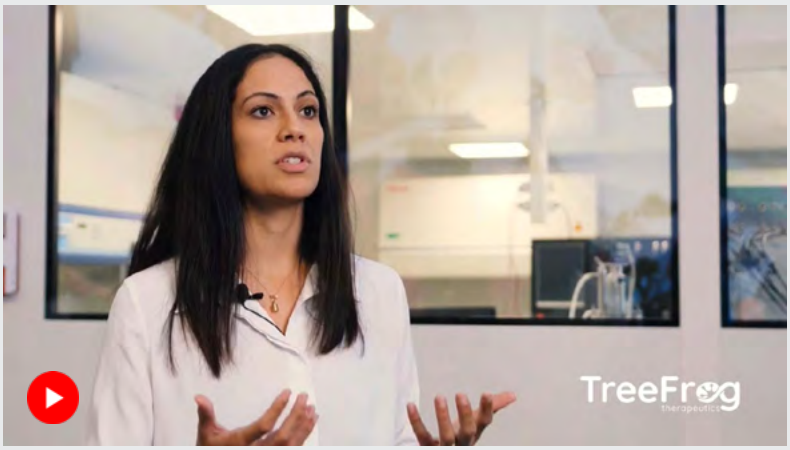
Only symptomatic treatments, NO CURE

Patients currently have 2 options to alleviate motor symptoms:

- **Levodopa**, an oral small molecule drug replacing dopamine
- **Deep brain stimulation**, requiring the insertion of electrodes in the brain

No available treatment slows disease progression and remedies the loss of dopaminergic neurons.

Parkinson's Foundation. Statistics.



Advancing a robust & efficient approach for Parkinson's disease cell therapy

Currently interacting with EU & US regulators and patient associations, TreeFrog aims to move its **cell therapy program to the clinic in 2024**, bringing distinctive benefits to patients.

Twice faster recovery

TreeFrog demonstrated **full motor function recovery in 8 weeks vs. 16 weeks** with progenitors in three separate in vivo studies. The mechanical resistance of the 3D microtissue facilitated surgery and allowed better integration, with **8 times more engrafted dopaminergic neurons.**
See data presented at ISSCR 2021

A safer and more reproducible product

Left to "mature" in the brain of the host, progenitors provide little control over the dose and pose risks of undesired cell proliferation. Starting with genomically safe pluripotent stem cells, TreeFrog generates standardized transplants of **mature differentiated neurons, preventing dose and proliferation issues.**

A readily available and affordable cell therapy

Taking advantage of the C-Stem™ technology, TreeFrog's capacities already allow for the production of 10,000 doses per batch, while dropping production costs by 10-fold.

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Partnering with U.S. players to unleash the mass-market potential of cell therapies

Out of 1,000 cell and gene therapy players worldwide, over 500 are based in North America. In the field of stem cell-derived cell therapies, the world's most funded biotechs are all based in the U.S., including Sana Biotech (2021: $587M IPO), Century Tx (2021: $160 Series C), BlueRock Tx (2019: $240M Acq. by Bayer) and Fate Tx (2020: $201M PO).

TreeFrog's hub in Boston will aim to deploy the C-Stem™ technology in the U.S. through an open innovation strategy, blending co-development, in-licensing and out-licensing deals with local industrial, clinical and academic leaders.

Encapsulated cardiac cells differentiated from hiPSCs (beating).

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Cell therapy
today

FINANCING

$19.9 billion
raised in 2020

The cell & gene therapy industry witnessed a 50% increase in investments in 2020, according to the Alliance for Regenerative Medicine.

FDA-APPROVED PRODUCTS

The case of CAR-T cell therapies

Current autologous CAR-T cell therapies consist in engineering the patient's own immune cells to kill the tumor:

High efficacy
Allowing full remission from liquid cancer (>80% response rate)

Manufacturing issues
7-9% of enrolled patients not receiving treatment, 30% receiving out-of-specification product

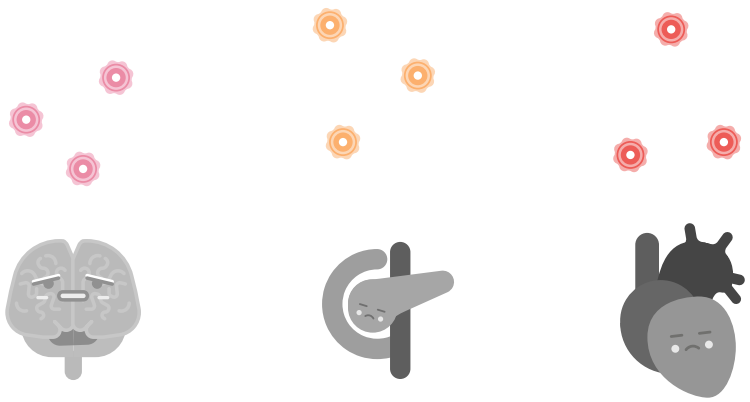
High costs
Average $373,000 per dose and additional $350,000 care costs

High lead times
54 days median turnaround time

Low patient access
Only a few thousand patients treated per year

BioPharmaDive on manufacturing

Prime Therapeutics' cost study



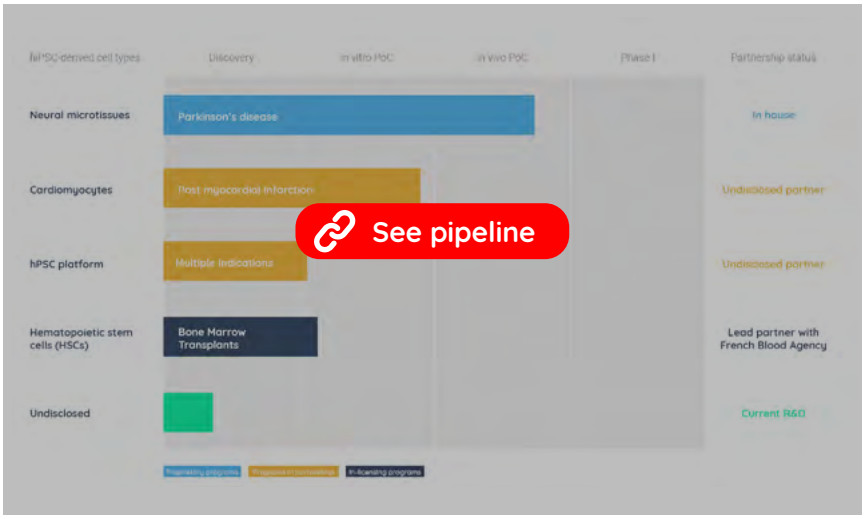
C-Stem™ platform
mass-producing off-the-self, readily available, cell therapies for millions of patients

Introducing all at once a scalable manufacturing process, a new quality standard and a new transplantation format, C-Stem™ is currently being used to develop novel stem cell-based cell therapies for high-burden diseases, such as blood and immune disorders, heart failure, liver failure, and neurodegenerative disorders.

Cell therapy pipeline
partnering from research to market

To move cell therapy programs as fast as possible to the clinic, TreeFrog developed several partnership modalities:

- **Proprietary programs** for out-licensing (Parkinson's)
- **In-licensing programs** for off-the-self bone marrow transplants licensed from the French Blood Agency
- **Co-development deals** for 2 contracts with undisclosed Fortune 500 pharmaceutical companies



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Cell therapy for all

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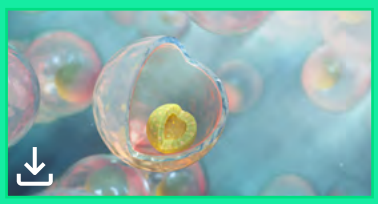
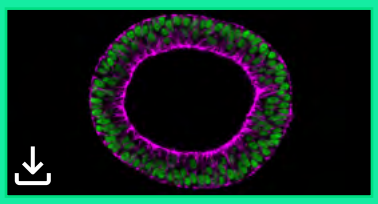
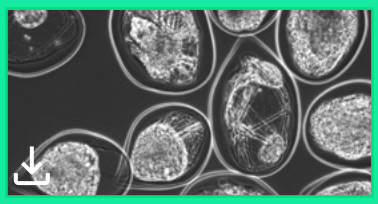
Downloads

Credits: TreeFrog Therapeutics



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