CELL GENE

STATE *of the* INDUSTRY BRIEFING

Regenerative Medicine: New Paradigms

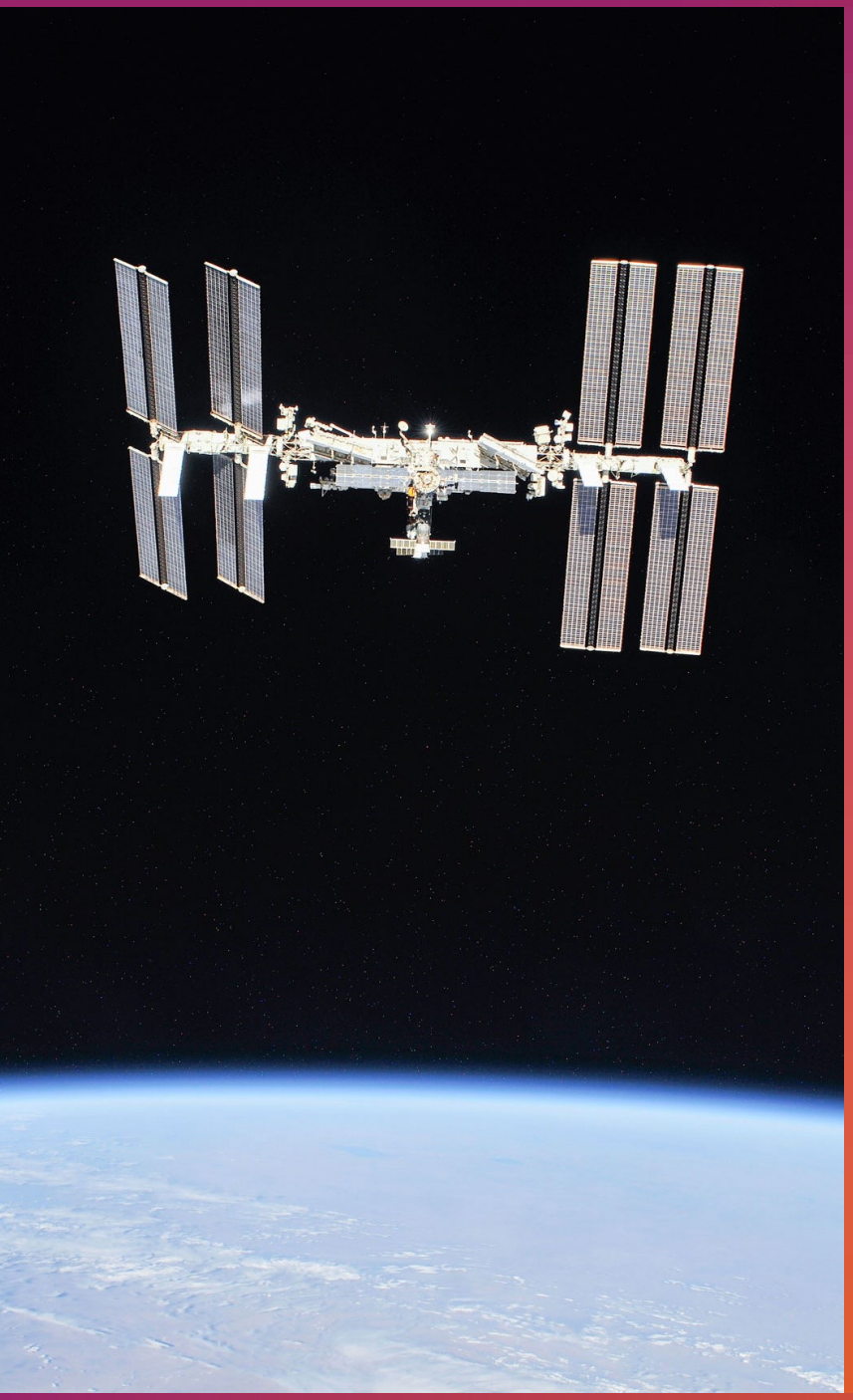
Emile Nuwaysir, Chair
Janet Lambert, CEO

January 10, 2022

Alliance *for* Regenerative Medicine

In 2021, we challenged the constraints, and the scientific dogma:

Constraint:	Challenged By:
"CAR-Ts are a last line of defense." ✗	CAR-T outperforms 2nd line SoC
"Immune rejection will limit allogeneic cell utility." ✗	Allo-edited CAR-T cells match auto cells
"*In vivo* gene editing is in the future, not now." ✗	Curative *in vivo* CRISPR editing in liver
"Genetic medicines change DNA sequence." ✗	The promise of altering the genome "memory"
"Damage that has already occurred can't be reversed." ✗	"Reversible" damage from AADC deficiency?
"Complex, polygenic diseases are out of reach." ✗	Cell therapy can restore lost function in diabetes



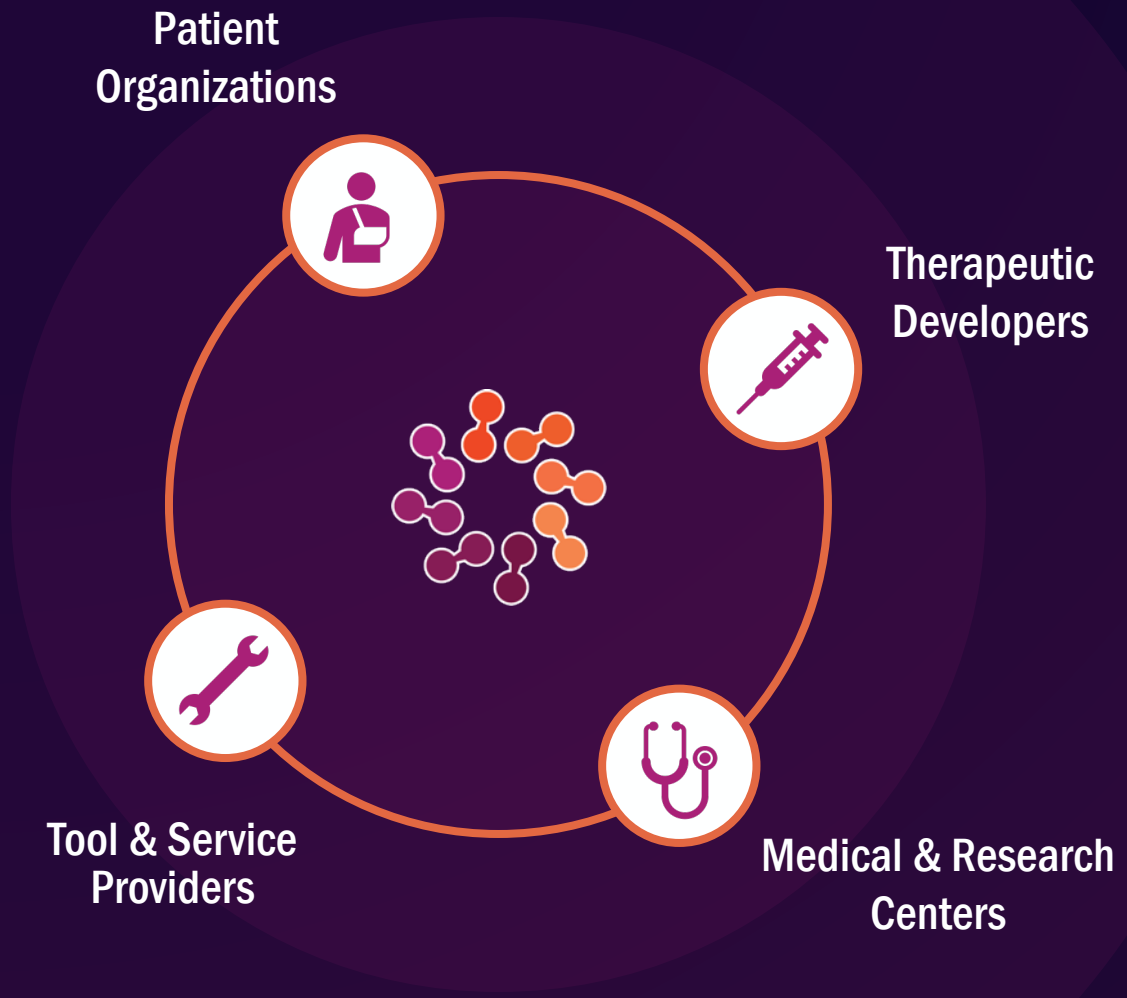
Pushing the Frontier

- Moving earlier in the patient journey, with durable cures
- Broadening accessibility
- Medicines that blur the line between prevention and cure

2021 Highlights & Looking Ahead to 2022

ARM is the Global Voice of the Sector

Representing 400+ members worldwide



Promote Clear Regulation

Enable Innovative Reimbursement

Address Manufacturing Barriers

Educate Stakeholders

The next era of regenerative medicine

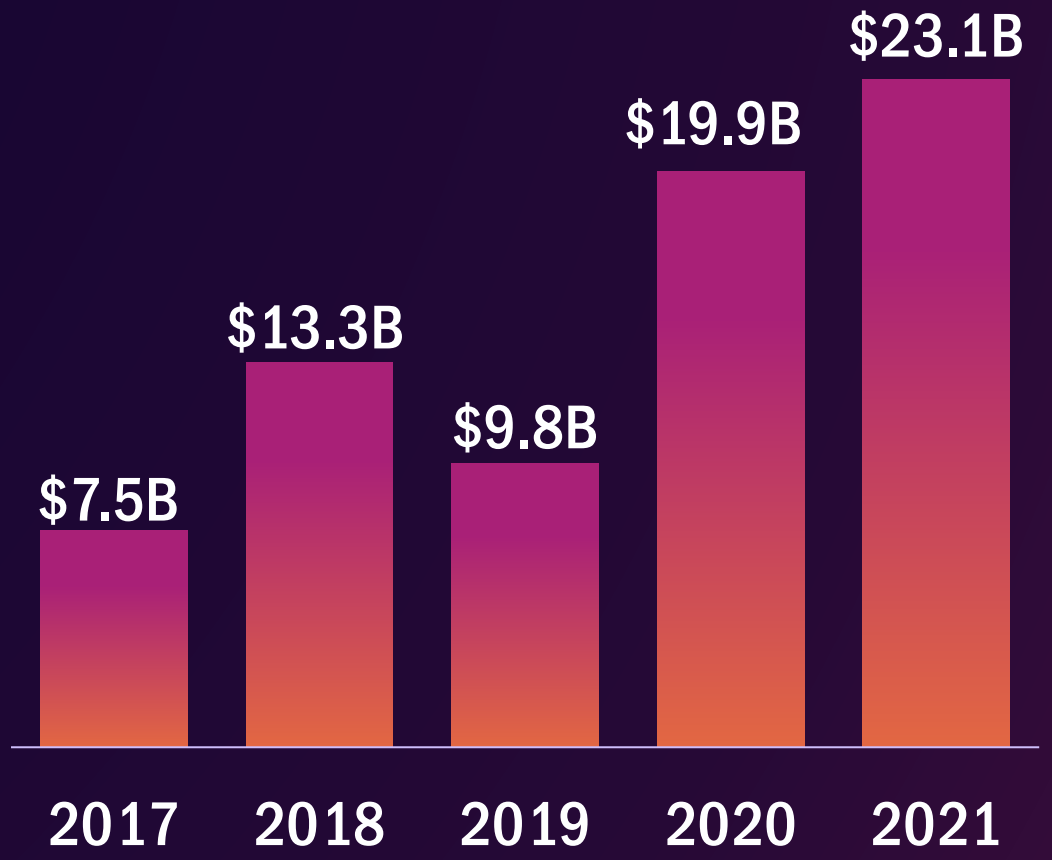
Investment Landscape

Long-term growth and short-term volatility

- Record breaking investment
- Gene editing rising in prominence
- Venture capital ascendant
- Down year for public equities

$23.1B raised in 2021

↑16% from 2020



$23.1B raised in 2021

↑16% from 2020

$10.6B RAISED IN GENE THERAPY
14% increase YoY

$10.1B RAISED IN CELL IO
26% increase YoY

$2.0B RAISED IN CELL THERAPY
15% decrease YoY

$341M RAISED IN TISSUE ENGINEERING
10% increase YoY

$23.1B raised in 2021

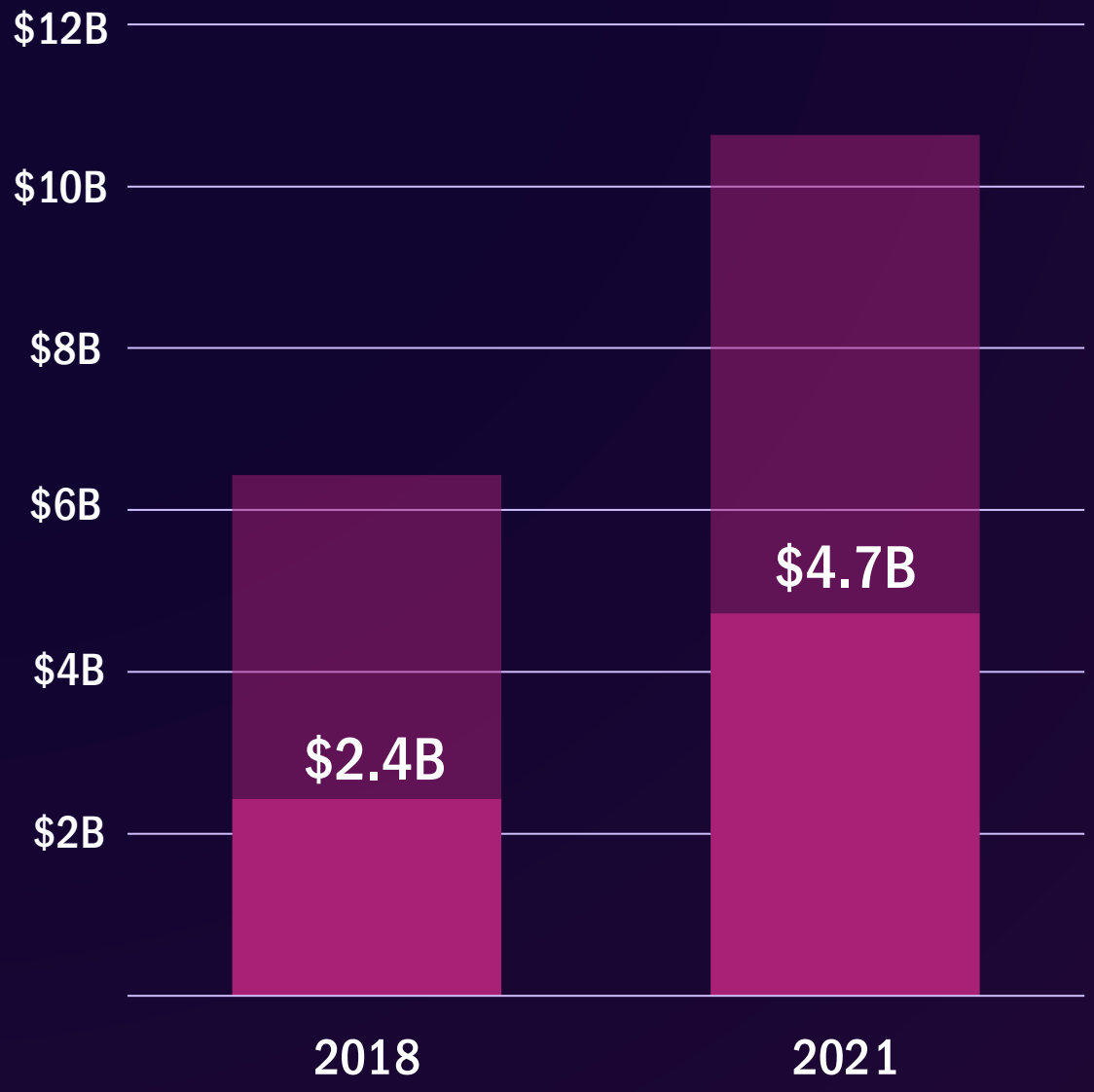
↑16% from 2020

$18.0B RAISED BY US DEVELOPERS
53% increase YoY

$3.3B RAISED BY EUROPEAN DEVELOPERS
8% decrease YoY

$2.2B RAISED BY APAC DEVELOPERS
4% decrease YoY

Gene Editing Gains Prominence

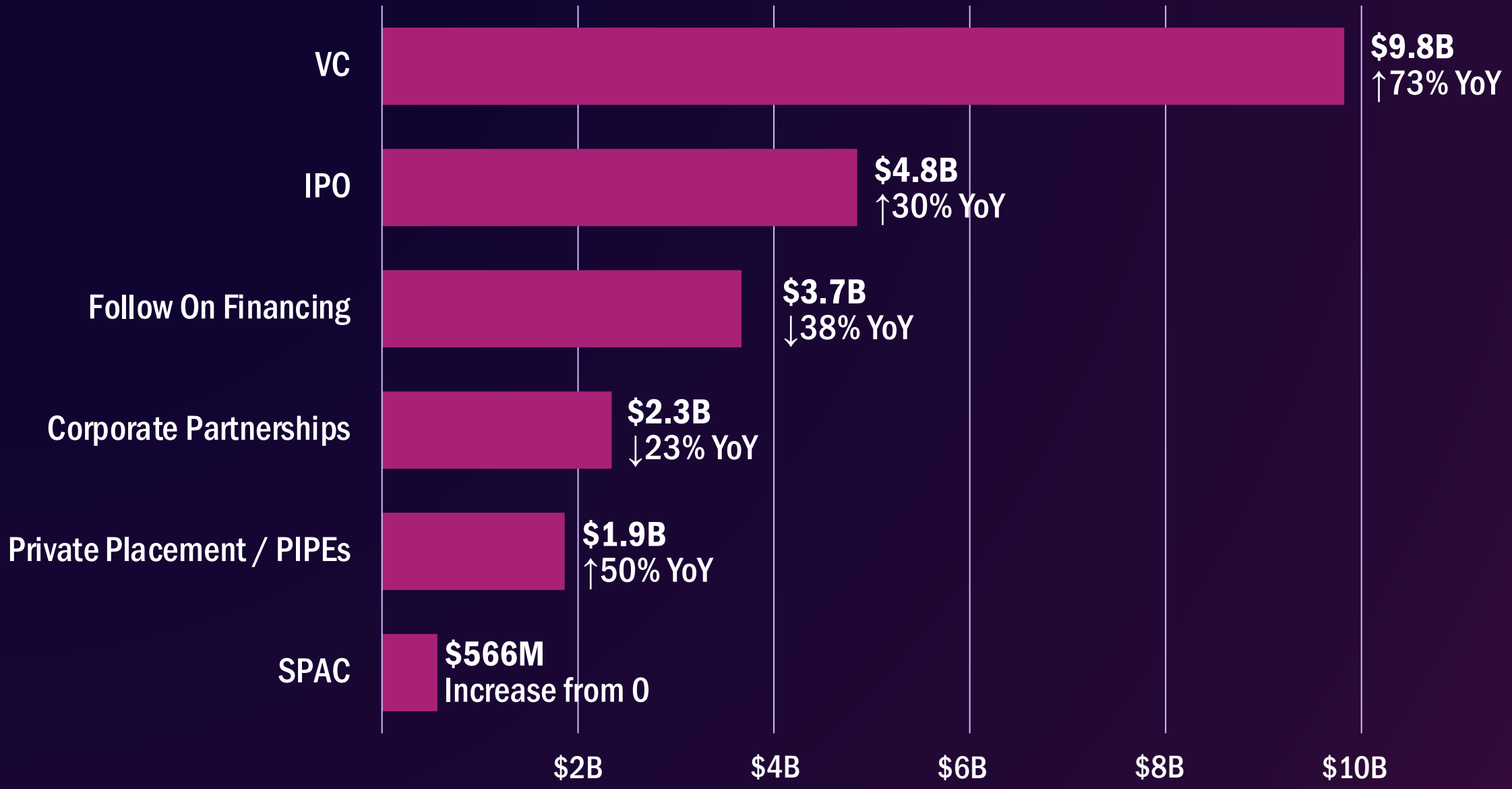


The proportion of gene therapy financings raised by companies active in gene editing increased from 38% to 45% over the past 3 years

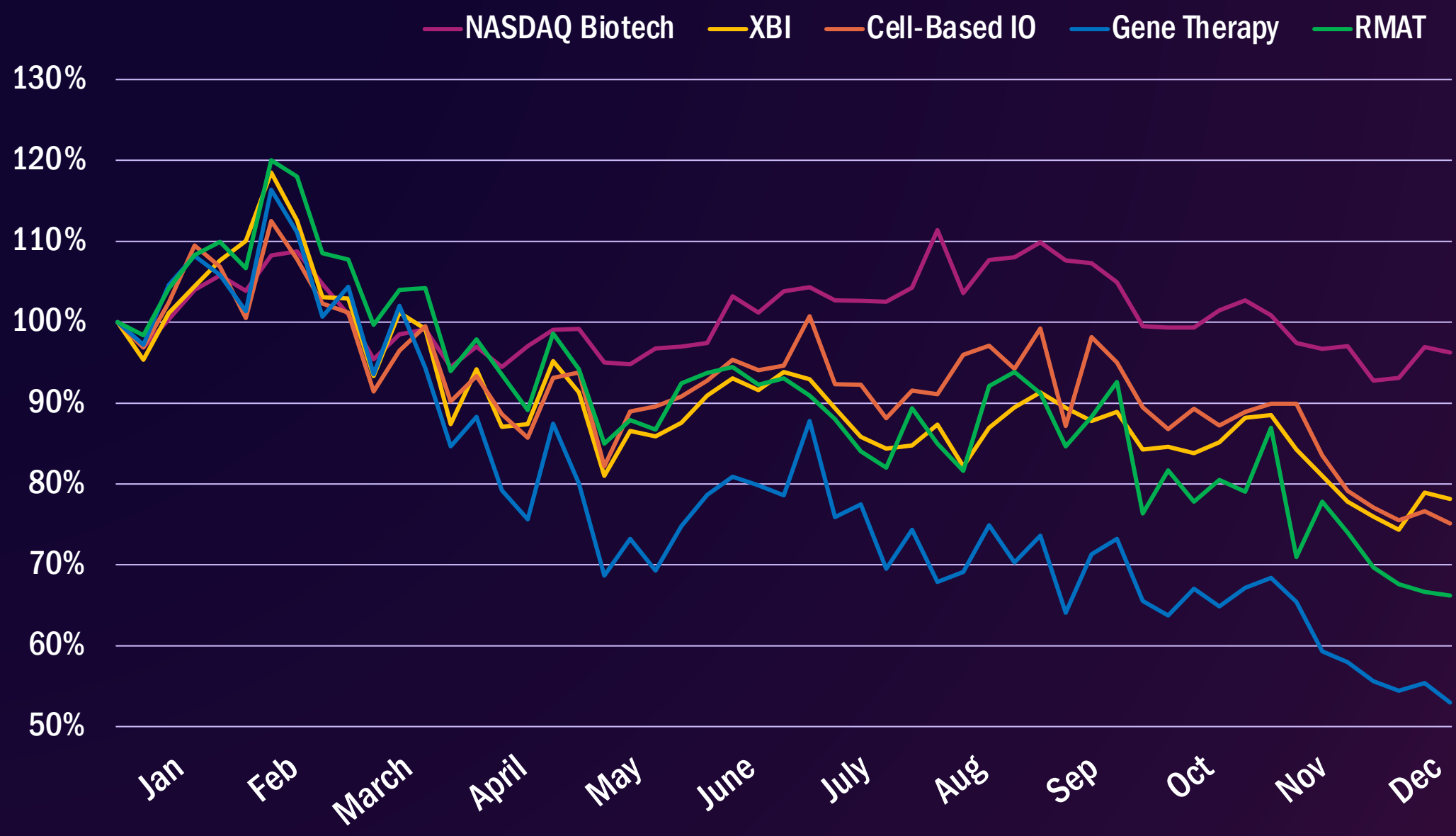
Total gene therapy financings

Raised by companies active in gene editing

Venture Capital Drives Record-Breaking Investment



Market Factors Depress Public Equity Performance



Commercial & Clinical Landscape

Approvals of New Products in 2021

Breyanzi* (US)
CAR-T Therapy
DLBCL
BMS

Abecma (US & EU)
CAR-T Therapy
Multiple myeloma
bluebird bio & BMS

Stratagraft* (US)
Tissue Therapy
Severe burns
Mallinckrodt

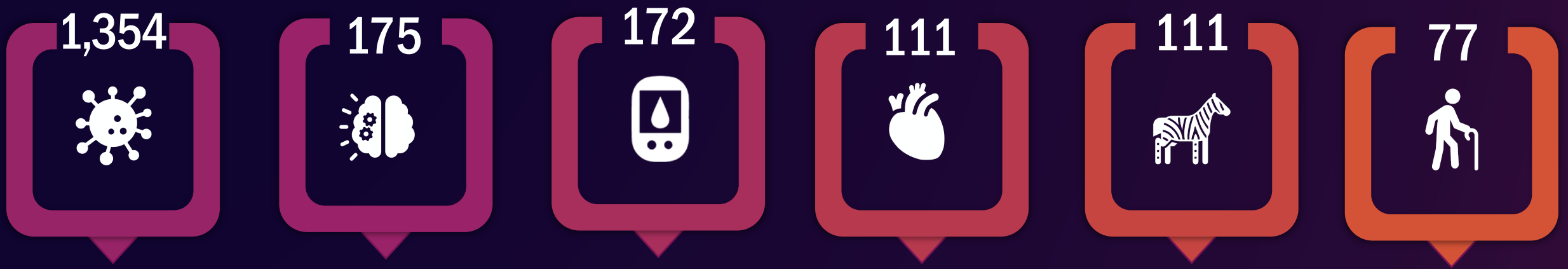
Skysona (EU)
Gene Therapy
Cerebral ALD
bluebird bio

Carteyva (China)
CAR-T Therapy
LBCL
JW Therapeutics

Rethymic* (US)
Tissue Therapy
Congenital Athymia
Enzyvant

* RMAT designated product

2,261 Ongoing Global Clinical Trials in Regenerative Medicine



CANCER

Including leukemias, lymphomas, breast cancer, brain cancer, lung cancer, prostate cancer, & others

NEUROLOGICAL

Including disorders such as Alzheimer's, Parkinson's, ALS, multiple sclerosis, cerebral palsy & others

DIABETES

Including Type 1 & Type 2, as well as related conditions such as diabetic kidney failure

CARDIOVASCULAR

Including damage caused by heart attack and vascular disease

RARE DISEASES

Including many fatal diseases that affect infants and children

STROKE

Including stroke recovery and paralysis due to stroke

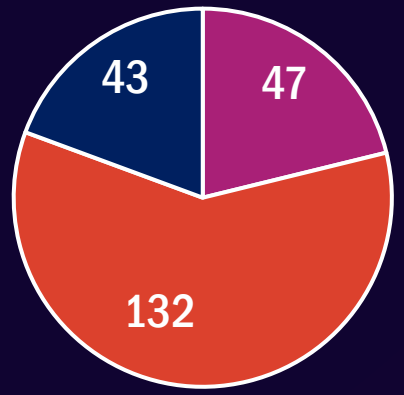
Data by GlobalData.

**Data as of Q3 2021*

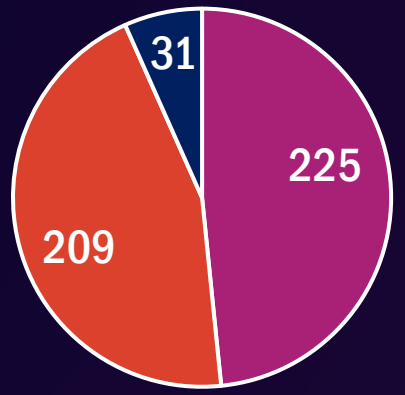
1,129 Industry-Sponsored Clinical Trials

Ph 1 Ph 2 Ph 3

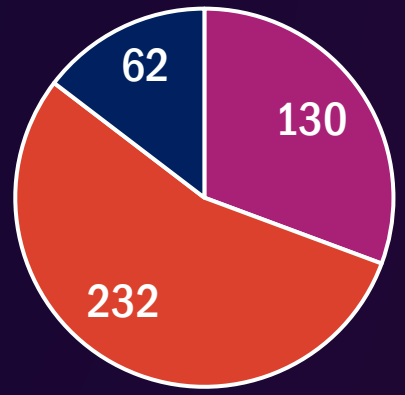
Gene Therapy: 222



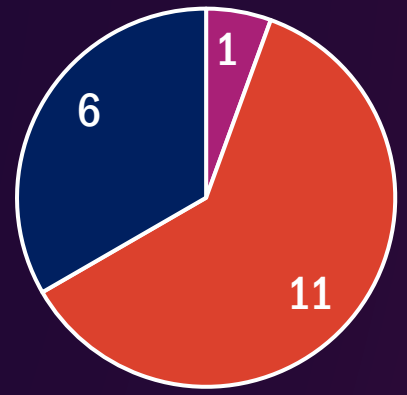
Cell-Based IO: 465



Cell Therapy: 424

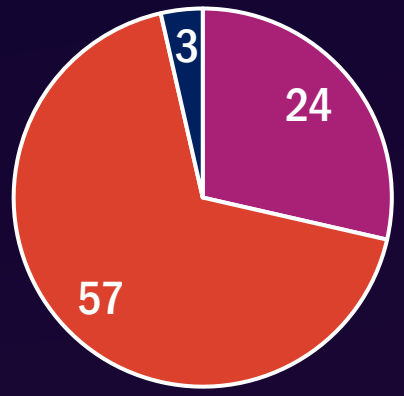


Tissue Engineering: 18

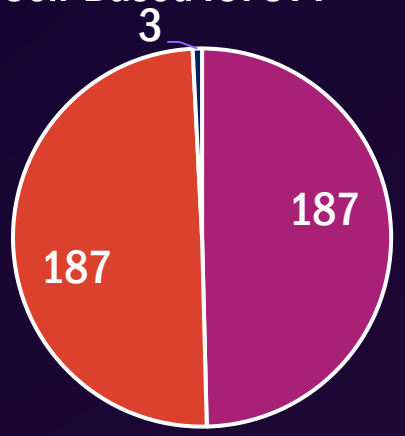


1,132 Academic & Government Sponsored Trials

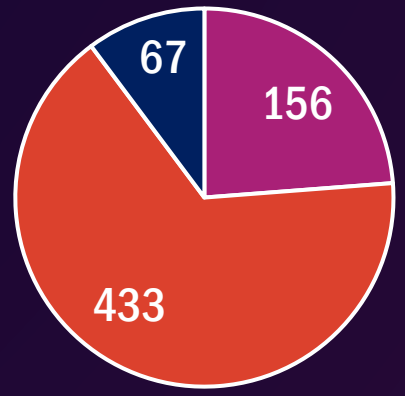
Gene Therapy: 84



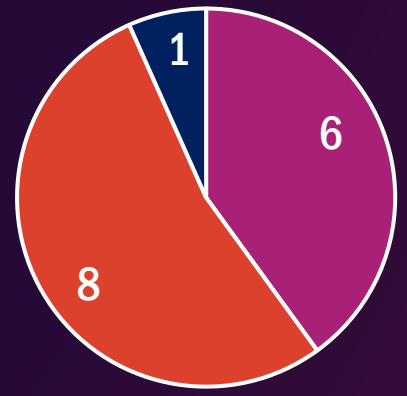
Cell-Based IO: 377



Cell Therapy: 656



Tissue Engineering: 15

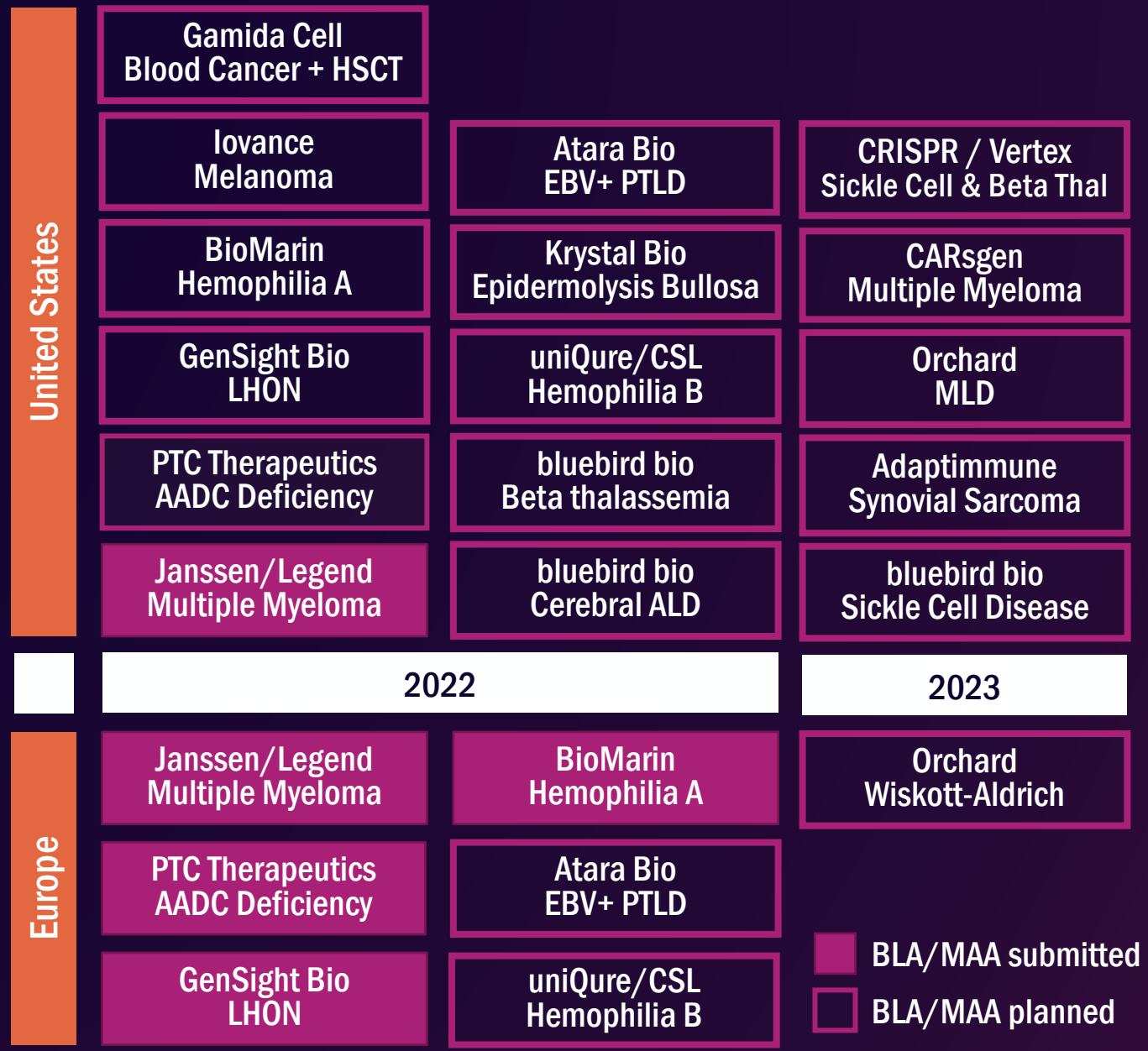


Data by GlobalData. *Data as of Q3 2021

Looking Ahead: 2022+

- 2022 is a big year for rare disease approvals…
- … amid an evolving shift in focus to more prevalent diseases in coming years

Upcoming Cell & Gene Therapy Regulatory Decisions



Additional 2022 Milestones

Late-stage data readouts
- Pfizer, BioMarin, Solid Bio

Early data in prevalent disorders
- Vertex

Gene editing continues march to the clinic
- ViaCyte/CRISPR, Beam, Verve begin trials
- Data from Caribou, Intellia, & others

Beyond 2022

Evolution from rare monogenetic diseases and cancers to more prevalent

10-20 approvals a year by 2025?

Examples of Ph 3 Industry Trial Indications:

- Bladder Cancer
- Breast Cancer
- Cartilage Defects
- Cirrhosis
- Congestive Heart Failure
- Critical Limb Ischemia
- Diabetic Foot Ulcers
- Diabetic Neuropathy
- Esophageal Cancer
- Glioblastoma
- Head & Neck Cancer
- Leukemia & Lymphoma
- Lung Cancer
- Macular Degeneration
- Myocardial Infarction
- Osteoarthritis
- Ovarian Cancer
- Prostate Cancer
- Refractory Angina

Key Sector Challenges

Dosing & Delivery

CMC

Policy & Reimbursement

Jayla Turner

Jayla was born in 2007 and diagnosed with complete DiGeorge syndrome

Without treatment, life expectancy is 2-3 years

She received the therapy now known as Rethymic in 2008

Jayla is now 14 years old in the 9th grade

She enjoys gymnastics, cheering, & volleyball and is an honor roll student

Visit us at www.alliancerm.org!

Slides & a recording of this presentation will be made available at bit.ly/2022-SOTI

Stay up-to-date with ARM's newsletter, *The Sector Vector:* bit.ly/ARM-SV

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2022: A Banner Year for Rare Genetic Disease Therapies?