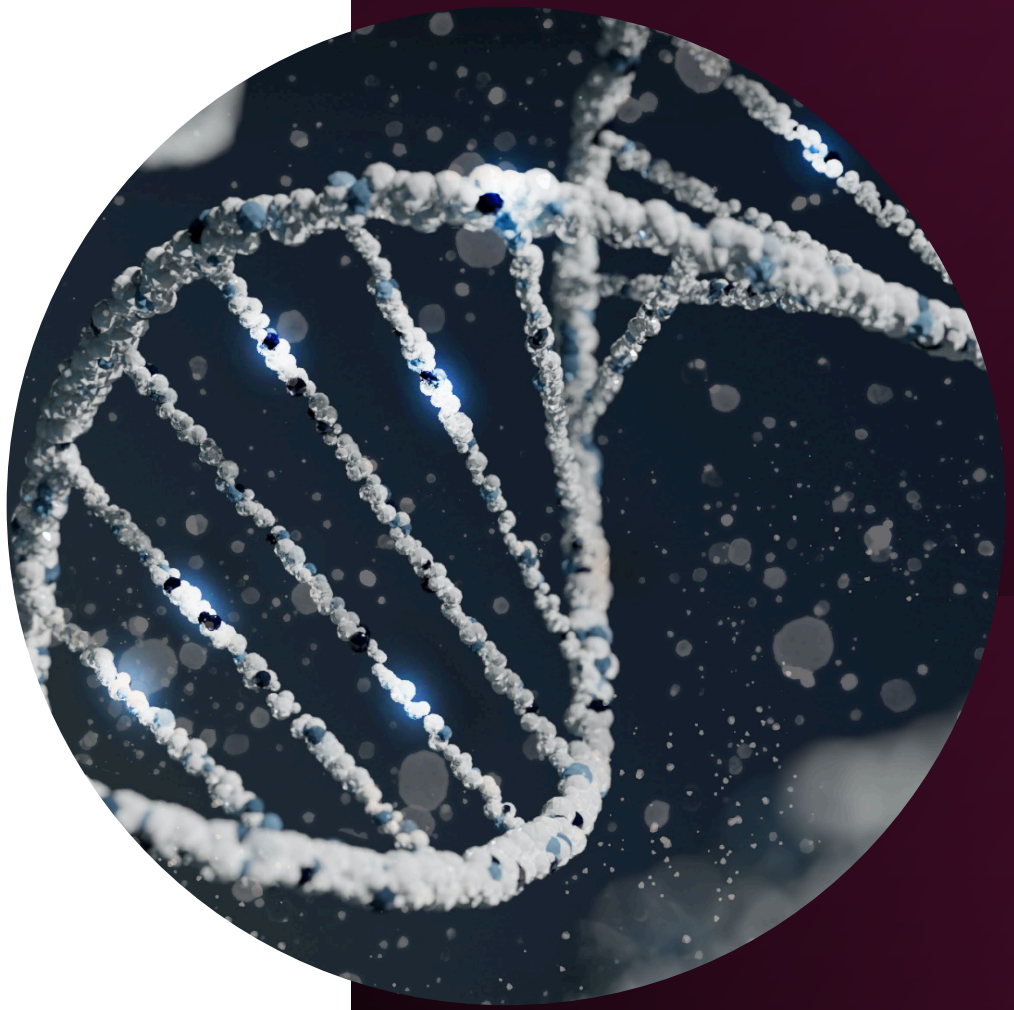
Alliance *for* Regenerative Medicine

CELL GENE

STATE *of the* INDUSTRY BRIEFING



Timothy D. Hunt – Chief Executive Officer, Alliance for Regenerative Medicine

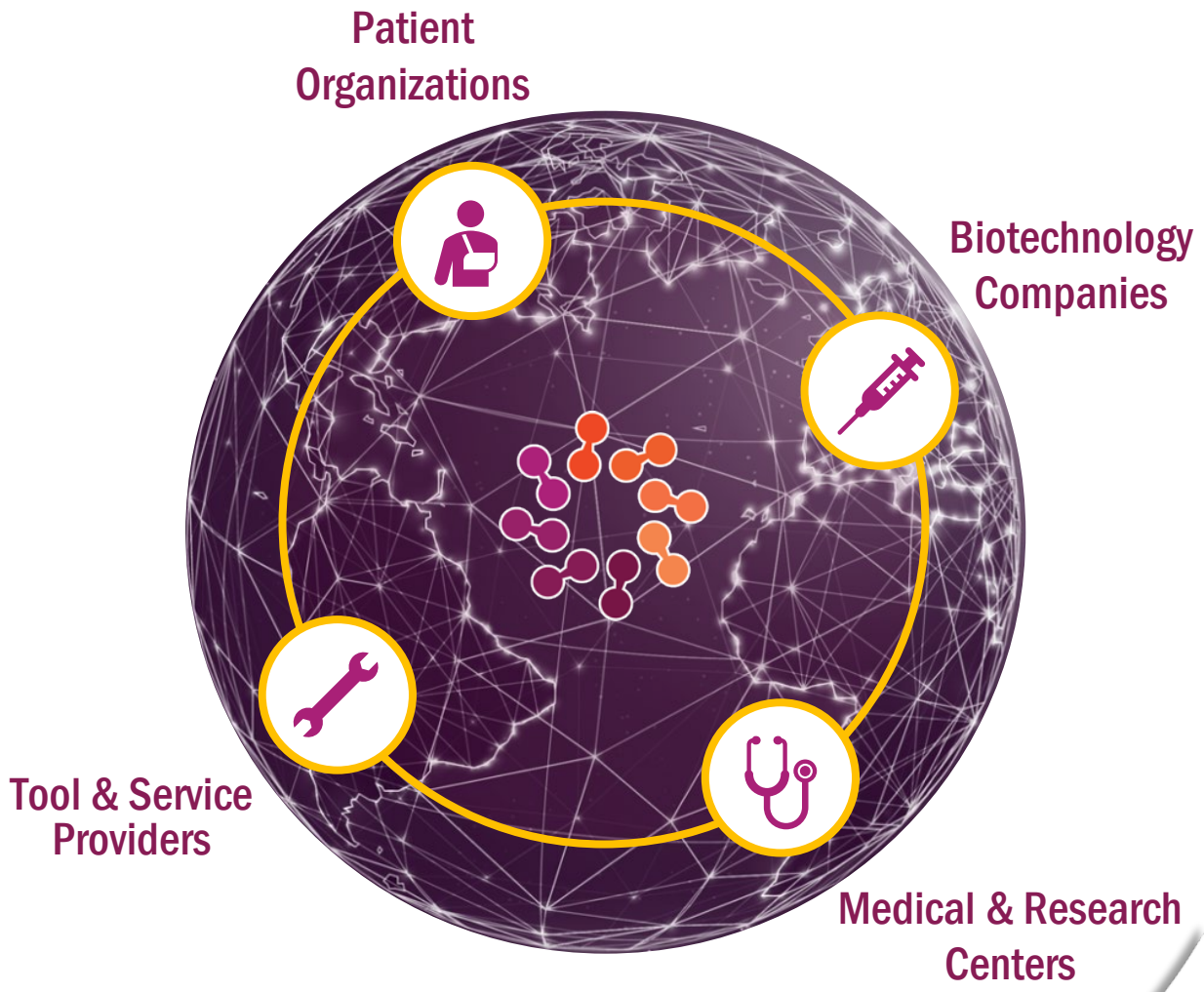
San Francisco, CA – 9 January 2023

ARM is the Global Voice of the Cell & Gene Therapy Sector

Representing 475+ members worldwide

Our focus:

- Convening the sector
- Providing data & analysis
- Engaging key stakeholders
- Enabling the development of advanced therapies
- Modernizing healthcare systems



Jimi Olaghere, Sickle Cell Disease Patient

“Being confident that I have the time and the health to properly take care of my children is a really, really good feeling.”

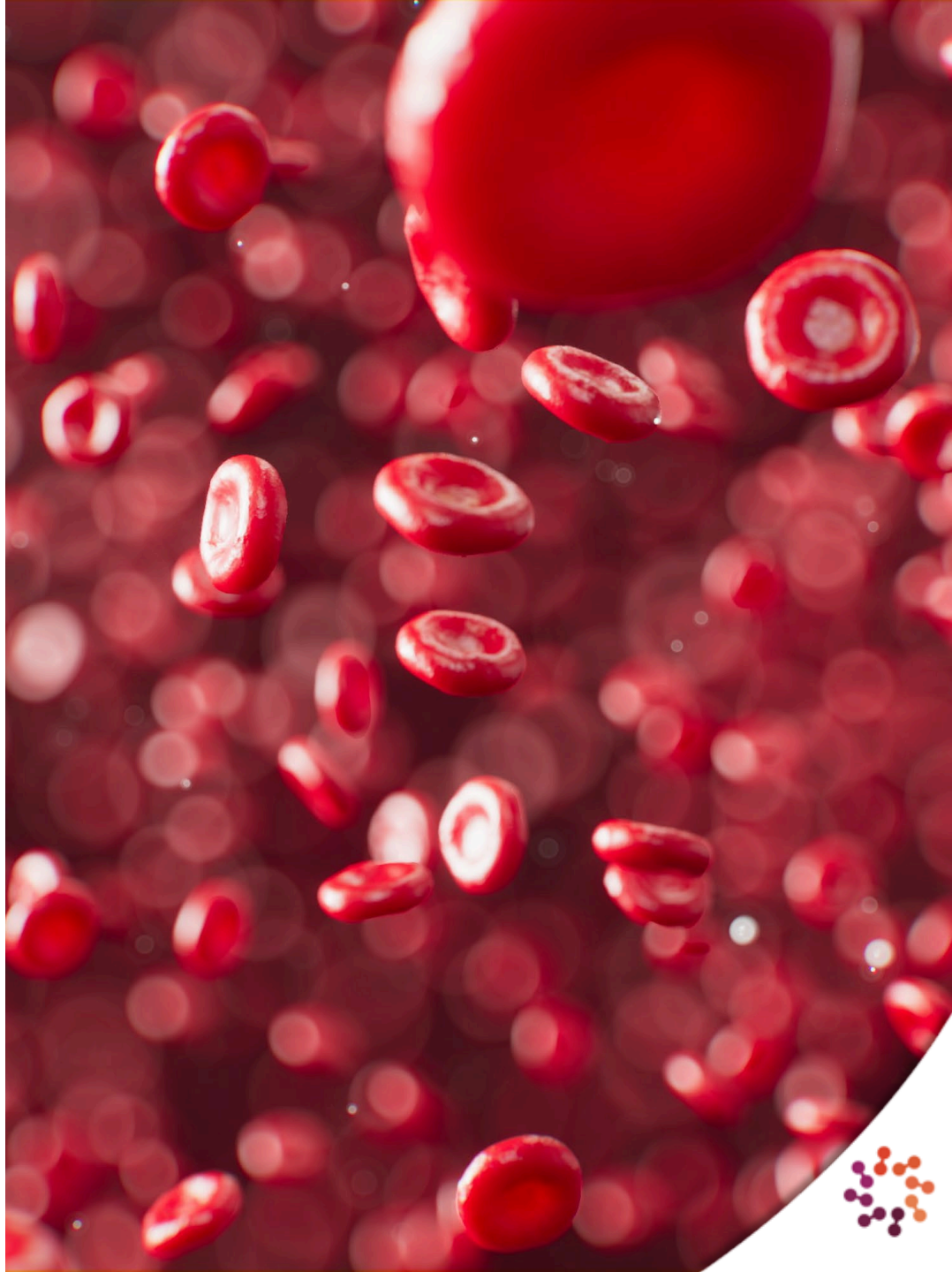
- Required frequent medical care and spent a considerable amount of time in the hospital
- Participated in the Vertex/CRISPR Therapeutics gene editing trial – treated in September 2020
- Outside of basic clinical trial follow-up, Jimi reports he no longer has any sickle cell care ongoing

Transformative therapies for SCD and hemophilia arrive

The science is advancing & the sector is continuing to mature

- Gene therapies for hemophilia A (BioMarin) and hemophilia B (uniQure/CSL Behring) approved/nearing approval
- 2 gene therapies for sickle cell disease poised for US approval in 2023 (bluebird bio and CRISPR Therapeutics/Vertex)

The era of larger patient populations has arrived – are healthcare systems ready?



Scientific Advances

Approvals and Clinical Milestones

2022: Another year of milestones

New Therapies Approved

Legend Biotech & Janssen	Carvykti - US and EU (CAR-T)
BioMarin Pharmaceutical	Roctavian - EU (Gene Therapy)
PTC Therapeutics	Upstaza - EU (Gene Therapy)
UniQure and CSL Behring	Hemgenix - US (Gene Therapy)
Ferring Pharmaceuticals	Adstiladrin - US (Gene Therapy)
Atara Biotherapeutics	Ebvallo – EU (Cell Therapy)

Therapies Approved in New Geographies or New Indications

Bristol-Myers Squibb	Breyanzi (CAR-T)
Novartis	Kymriah (CAR-T)
Kite Pharma (Gilead)	Yescarta (CAR-T)
bluebird bio inc.	Zynteglo (Gene Therapy)
bluebird bio inc.	Skysona (Gene Therapy)

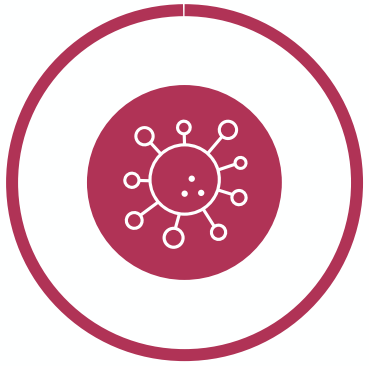
2023 regulatory outlook: notable ‘firsts' and milestones

Several potential milestones poised for regulatory decision(s) in the US and/or EU

Potential Milestones

US: At least 5 gene therapy approvals for rare diseases (5x5x5)

First CRISPR approval



First approval of adoptive cell therapy for solid tumor

First US approval of an allogeneic T-cell therapy

First approval for Duchenne Muscular Dystrophy

Anticipated regulatory decisions in 2023

United States Europe

Afami-cel (Cell Therapy)
Adaptimmune Therapeutics
Advanced synovial sarcoma

bb1111 (Gene Therapy)
bluebird bio
Sickle cell disease

CT-053 (CAR-T Therapy)
CARsgen Therapeutics
R/R multiple myeloma

fidanacogene elaparvovec (Gene Therapy)
Pfizer (formerly Spark Therapeutics)
Hemophilia B

HPC cord blood (Cell Therapy)
StemCyte
Unrelated Donor hematopoietic progenitor cell transplantation

Libmeldy (Gene Therapy)
Orchard Therapeutics
Metachromatic leukodystrophy (MLD)

Lifileucel (TIL Therapy)
Iovance
Metastatic melanoma

Omidubicel (Cell Therapy)
Gamida Cell
Hematological malignancies

Roctavian (Gene Therapy)
BioMarin
Hemophilia A

SRP-9001 (Gene Therapy)
Sarepta Therapeutics
Duchenne muscular dystrophy

Tab-cel (Cell Therapy)
Atara Biotherapeutics Inc
Epstein-Barr virus-associated post-transplant lymphoproliferative disorder (EBV+PTLD)

Upstaza (Gene Therapy)
PTC Therapeutics
Aromatic L-amino acid decarboxylase (AADC) deficiency

B-VEC (Gene Therapy)
Krystal Bio
Dystrophic epidermolysis bullosa

CTX001 (Gene Editing Therapy)
CRISPR Therapeutics & Vertex Pharmaceuticals
Sickle cell disease, β-thalassemia

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EtranaDez (Gene Therapy)
uniQure & CSL Behring
Hemophilia B

Lumevoq (Gene Therapy)
GenSight Biologics SA
Leber hereditary optic neuropathy (LHON)

As we enter 2023…

2,220 clinical trials active

- 43% w/sites in NA; 38% APAC; 18% EUR
- 254 new in 2022 (48% w/sites in APAC)
- 202 trials in phase 3
- More than 100 gene editing trials

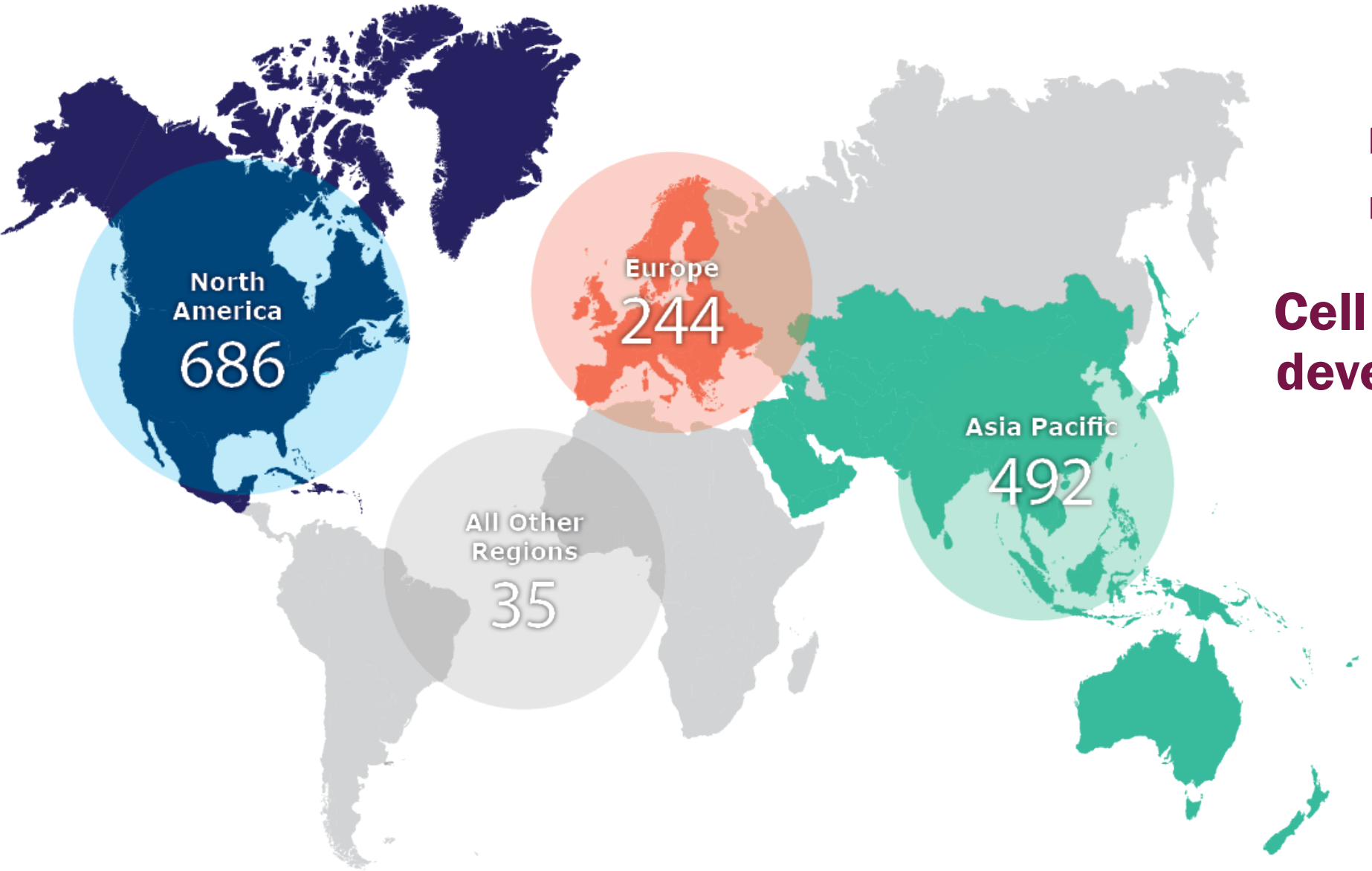
58% of trials have potential applications in a prevalent disorder

60% of trials focus on oncology

- Near equal representation of solid & liquid tumors

Cell and Gene Therapy Investment

Continued resilience in the face of significant macro headwinds

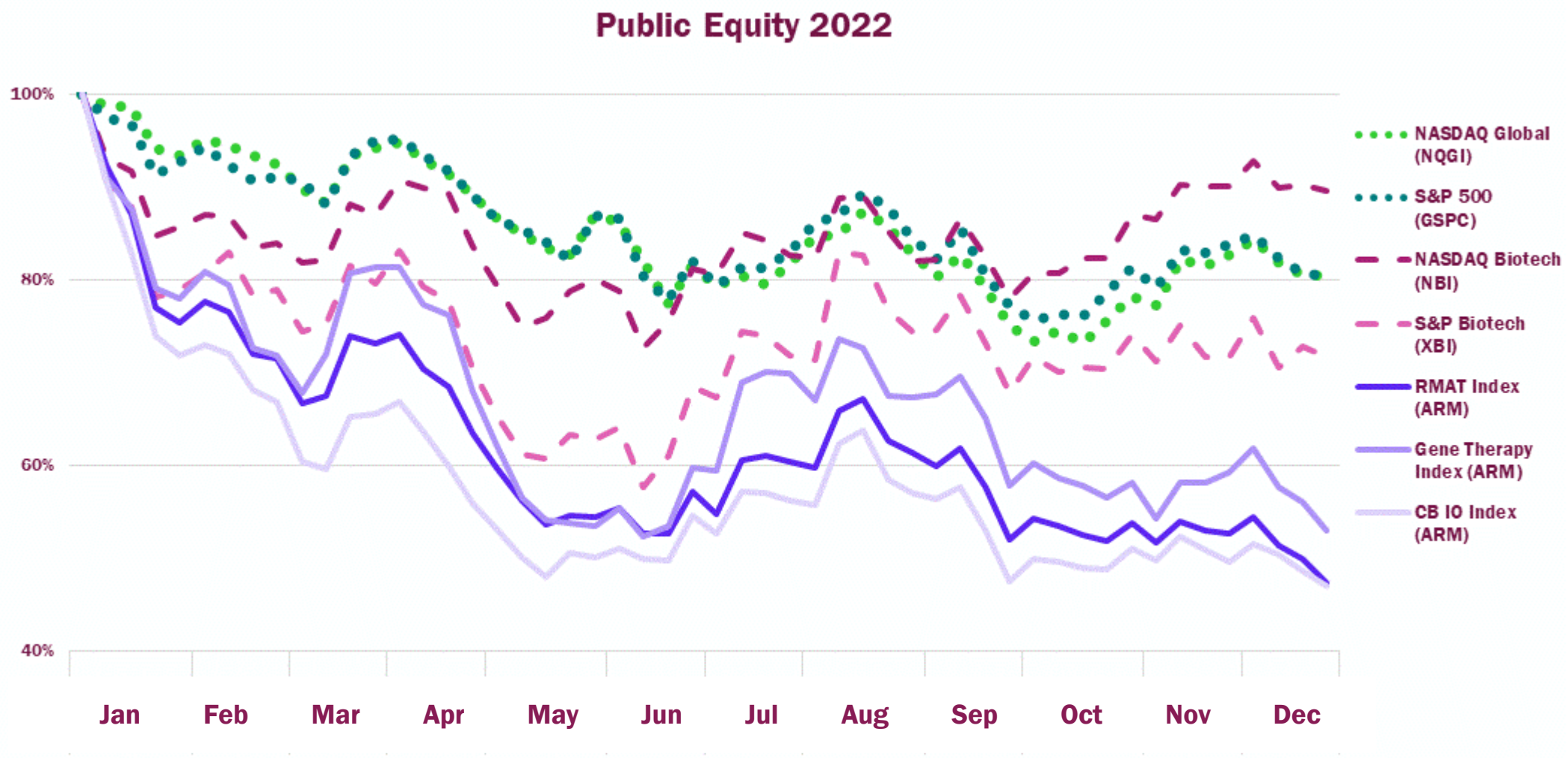


1,457

Cell and gene therapy developers worldwide

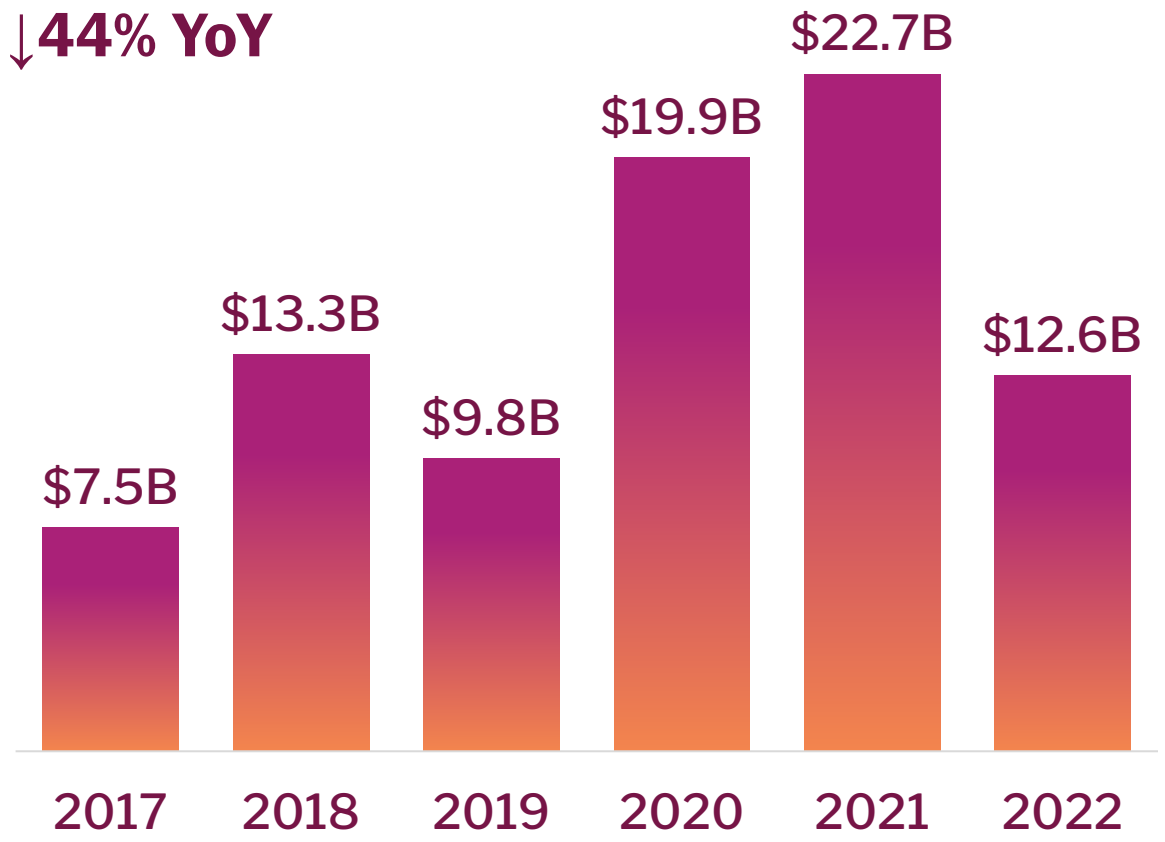
Up 11% YoY

Market Factors Depress Public Equity Performance



Investments “return to normal”

$12.6B raised in 2022



1. Includes upfront payments; excludes milestones, M&A, academic or government grants

Modernizing Healthcare to Ensure Patient Access

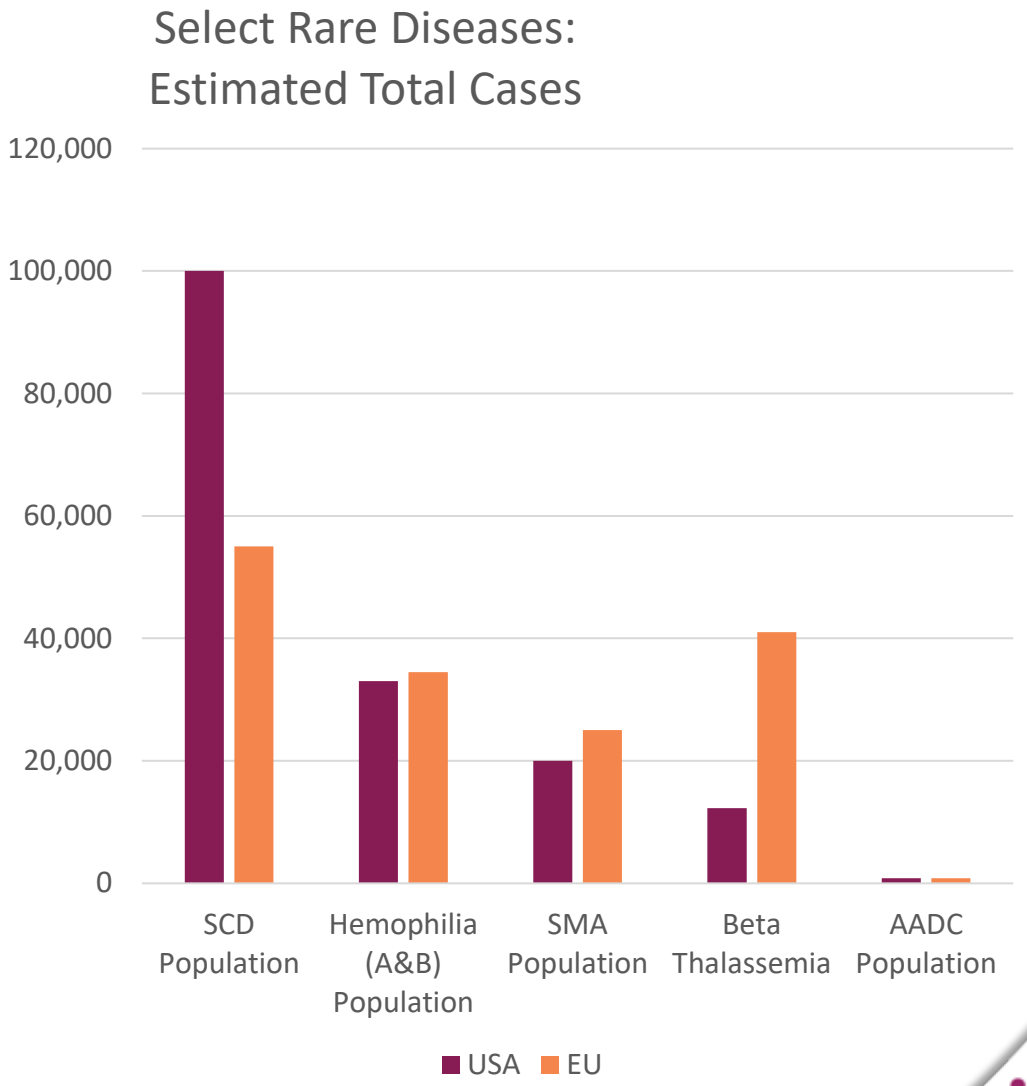
An opportunity we can't miss

2023+: The biggest test yet?

The science behind cell and gene therapies is progressing rapidly – to the immense benefit of patients

A highly dynamic time for healthcare systems – including payors and regulators

- Larger patient populations than with previous therapies
- Will new therapies be a “forcing function” for payers to adapt?
- Can they modernize to keep pace with the science?



US: The CGT wave arrives, to the benefit of patients

Up to 14 regulatory decisions expected

The FDA is evolving, by design, in order to keep pace

- Reorganization of OTAT to OTP ‘super office’
- Filling current vacancies
- PDUFA VII adding 100 new reviewers in next five years
- CMC: PDUFA readiness pilot & potency assay workshop

Questions linger about US payor readiness

- We need to modernize payment systems across Medicaid, Medicare and private insurers and expedite access to CGTs

EU: Urgent action needed to ensure patient access

Once a leader, the EU is now ‘a flashing yellow light of caution’ for patient access:

- Roadblocks in reimbursement have complicated patient access
- 7 of the 24 approved ATMPs have been pulled from the market
- Clinical trials and investment stagnating – only 3 new Phase 1 trials in 2022

However, a fork in the road exists with near term choices that will impact patients…

EU: Opportunity to choose a better path for patients

Once in a generation chance to reverse this trend

Revising the EU Pharmaceuticals Legislation

- Avoid one-size-fits-all approach – based on “pills of the past”
- Exempt ATMP clinical trials from GMO legislation
- Hospital exemption: Only for high unmet need and when there are no treatment alternatives

EU Health Technology Assessment

- Provide clear EU-wide guidelines for the use of real-world evidence (RWE); alternative to randomized clinical trials
- Leverage Health Data Space to collect RWE
- Continued collaboration with developers throughout Joint Clinical Assessment process

What will 2023 tell us about the future of CGTs?

Are healthcare systems modernizing…or clinging to the past?

How willing are patients to embrace new technologies?

- What will this signal for emerging therapies for prevalent diseases?

What are the implications for patients, developers, and investors?

2023 will send important signals…but where will we be in 2028?

Patient spotlight: Lucy Ellerker

“We think CAR-T should be the first line of treatment, not the last.” – Lucy Ellerker, Parent of CAR-T recipient

Patients are waiting for life-changing, life-saving treatments

We have an opportunity to build the future of medicine, together

In closing…

After walking for many years, CGTs began to jog in 2022

CGTs are poised to begin to run in 2023… but significant hurdles exist

Real running is attainable – but only if we modernize our approach to healthcare in the US and across the EU

Thank you.