Bluebird bio: What went wrong?

Presentation by Joanna Fernandes and Sophie Schmitz

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enlightened.thinking.applied

Partners4Access

Agenda

- **Bluebird bio: what happened?**
- Bluebird bio: what went wrong?
  - Was the problem with the European system?
  - Was the problem with the company's approach?
- What key learnings can we draw for the future?

After two years trying to gain access with Zynteglo™, bluebird bio exit Europe

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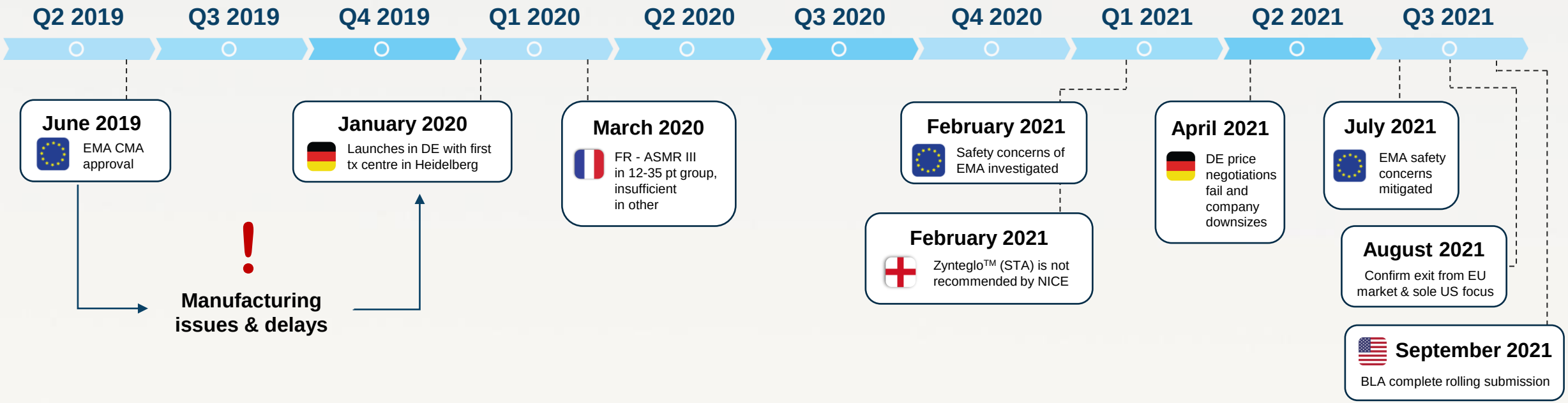
EU Access Timeline (select events)



ASMR: improvement in medical service; BLA: Biological license application; CMA: Conditional Marketing Approval; DE: Germany; tx: treatment; EMA: European Medicines Agency; EU: Europe; FR: France; NICE: National Institute for Health and Care Excellence; pt: patient; STA: Single technology appraisal; US: United States of America

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Why did the system let us down?

PRIME and accelerated access schemes do not align with evidence needed to satisfy HTA bodies

EUROPEAN MEDICINES AGENCY

Expedited Regulatory Schemes

YEAR	SCHEME
2006	Conditional marketing authorization (CMA)
2014	Adaptive pathways (pilot)
2016	PRIority MEdicines scheme (PRIME) Accelerated assessment Authorization under exceptional circumstances

Great in theory…

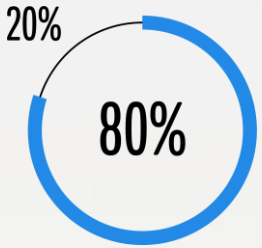
But not so great in practice:

- Evidence quality is lower
- Doesn't stand scrutiny to HTA assessments
- No alignment across HTA bodies
  (16% agreement on ATMP value in EU3)
- Price not aligned to evidence (comparator)

ATMP: Advanced therapy medicinal products; HTA: Health Technology Assessment; EU3: defined as Germany, France and England

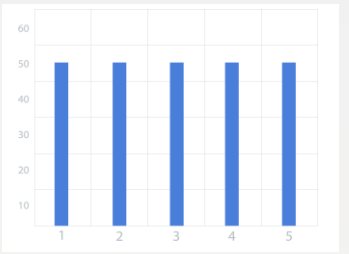
ATMPs offer unique durability benefits, which do not fit current EU financial infrastructures

We propose sharing risk with health care systems to create a sustainable model

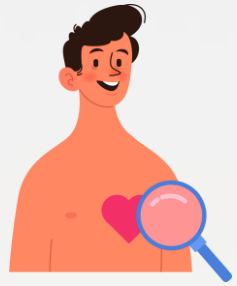


We are willing to put as much as 80 percent of the price at risk

After an initial payment of 20% annual milestone payments are made only if the treatment works. This is defined by easy-to-measure outcomes that assess meaningful patient benefits



A one-time treatment intended to have lifelong benefits, annual milestone payments would be capped at 5 years of equal installments



Fair value tied to direct patient benefit: living longer and quality of life improvements. Savings associated with treatment prior to therapy would be retuned to health system and society

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In summary

- **5 year** annuity model
- **We take the risk!**
- **Patients benefit**
- **The EU member states need to evolve their financial infrastructure**

Gene therapies are evolving the healthcare landscape not revolutionising it

Select historical events in gene therapy

1865

Mendel, **Father of Genetics** discovers the law of genetics

1953

Watson, Crick, Franklin & Wilkins discover **Double Helix Structure of DNA**

1976

First disease gene ever cloned: beta-globin gene at Cold Spring Harbor / Harvard University

Cold Spring Harbor Laboratory

1983

First human disease gene mapped with DNA markers (Huntington disease)

1990

Human Genome Project begins in **US and UK**

2000

Draft version of human genome sequence completed (end 2003)

2012

Glybera first gene therapy approved in the EU for patients with familial LPLD

Glybera®

2018

First CAR-T therapies approved in the EU

KYMRIAH® (tisagenlecleucel) YESCARTA® (axicabtagene ciloleucel)

The future of gene therapy remains largely unwritten

CAR-T: Chimeric antigen receptor T-cell; LPLD: Lipoprotein lipase deficiency

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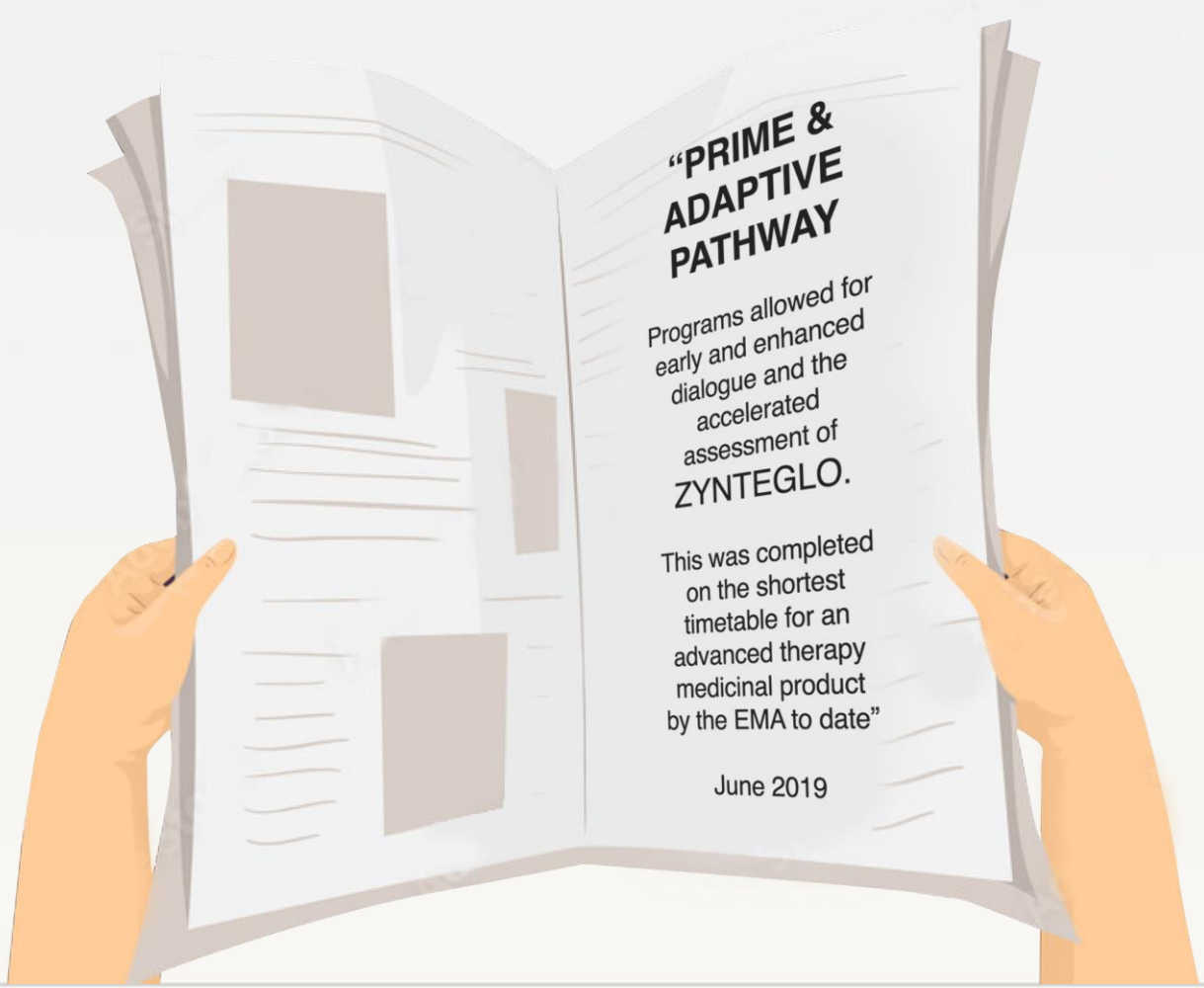
Why did bluebird bio fail with Zynteglo™?

Weak clinical value provided at time of EU launch



At time of regulatory approval, clinical value was based on two Phase I/II open-label single arm studies involving 14 patients across 2 years

HGB-204

(n=10) ages 12-35:

80%

reached the primary endpoint

HGB-205

(n=4) ages 5-35:

75%

reached the primary endpoint

https://investor.bluebirdbio.com/news-releases/news-release-details/bluebird-bio-announces-eu-conditional-marketing-authorization

Bluebird's access model was focused predominantly on affordability

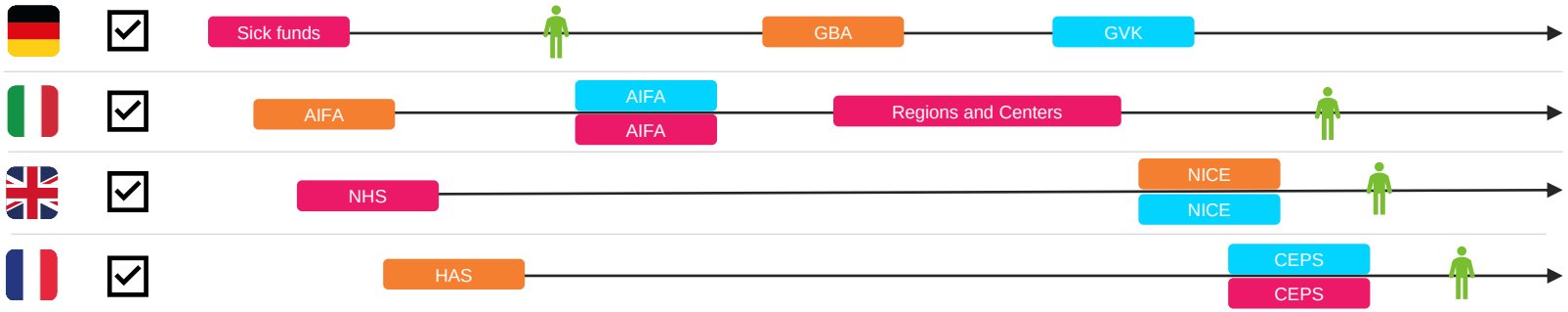
Bluebird *EU Launch strategy (June 2019)*

What are the next steps and how is launch readiness progressing?

EC Decision

- Team in place; completing set-up and working to activate QTCs
- Actively engaging payers
- Progressing forward with dossier submissions
- Working in collaboration with EMA to finalize commercial drug product specifications and manufacturing parameters

Each journey is different | Country-by-country recoding will play out over time



Milestone key

- Value based agreement (5yr)
- Health technology assessment
- Agree on price
- First patient infused

https://www.pmlive.com/__data/assets/image/0005/1291514/Bluebird_next_steps.png

Bluebird prioritised MEA in their strategic goals over patient benefit

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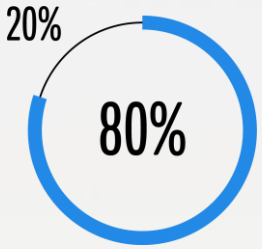

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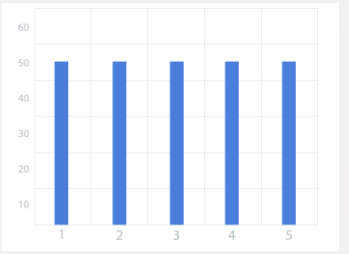

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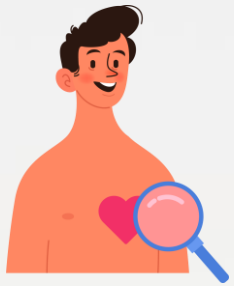

Fair value tied to direct patient benefit: living longer and quality of life improvements. Savings associated with treatment prior to therapy would be retuned to health system and society

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> “It is bluebird bio’s **goal to create a sustainable model to pay for one-time gene therapies** so that patients, health systems and society can realize the therapy’s potential lifelong value.”

https://investor.bluebirdbio.com/static-files/e4332043-0470-4633-ac65-7478f8d8acd5

Bluebird's official statement implied another company may be successful in Europe with Zynteglo™

> Bluebird's decision to focus on the U.S. market is driven by the **challenges of achieving appropriate value recognition and market access for ZYNTEGLO in Europe**, which makes bringing its transformative gene therapies like ZYNTEGLO and SKYSONA to patients and physicians in Europe untenable for a small innovative company at this time.*

> While European regulators have been innovative partners in supporting accelerated regulatory paths for these therapies, **European payers have not yet evolved their approach to gene therapy in a way that can recognize the innovation and the expected life-long benefit of these products**. We are committed to and hope to find a potential partner who can help us carry forward our therapies in Europe.*

> **There wasn't one smoking gun from one country**… There were multiple conversations going on across Europe. We had gotten far enough in multiple countries to see that the value recognition we were achieving in those countries was not going to be sufficient overall.

> Bluebird said it will be exploring options to ensure European patients can gain access to its gene therapies, including potentially out-licensing the ex-US rights to its three lead products to a company **with European experience and capabilities**

Andrew Obenshain, President, Severe Genetic Diseases, bluebird bio
https://investor.bluebirdbio.com/news-releases/news-release-details/bluebird-bio-reports-second-quarter-financial-results-and

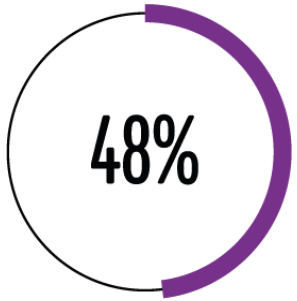
While bluebird blames European payers for its failure, Novartis' Zolgensma™ has seen success in the region

NOVARTIS

$315 million

in second-quarter sales for its spinal muscular atrophy gene therapy,

zolgensma®



increase at constant currencies

strong growth was **"driven by expanding access in Europe and ongoing geographic expansion."**

https://www.sandoz.com/news/media-releases/novartis-delivered-strong-q2-performance-driven-momentum-key-growth-brands-fy

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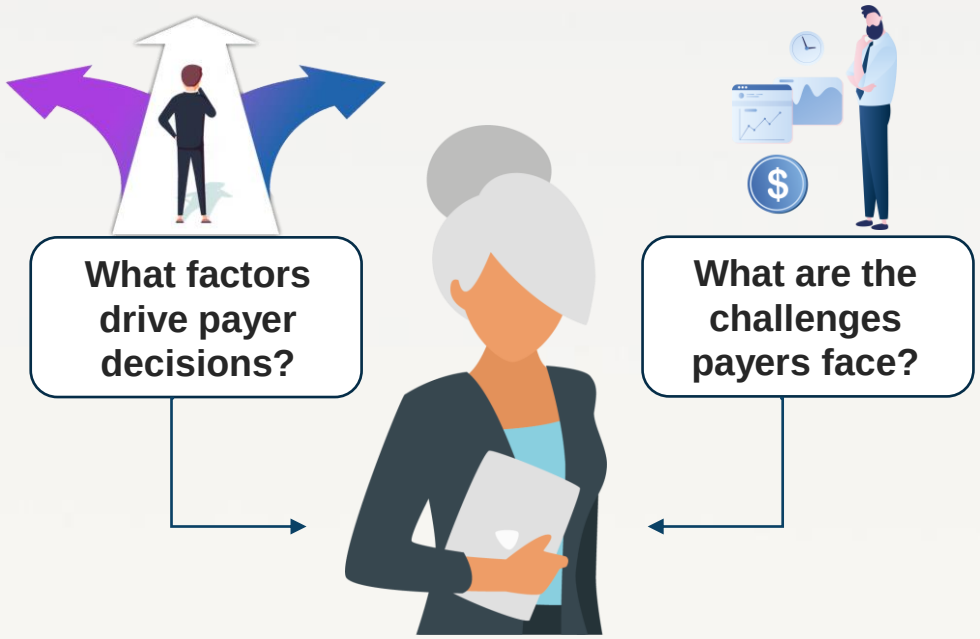
Changes in approach from companies and health authorities will be needed in the future for ATMP success

Understanding payers will support success!



Knowing this will greatly improve engagement and learning outcomes

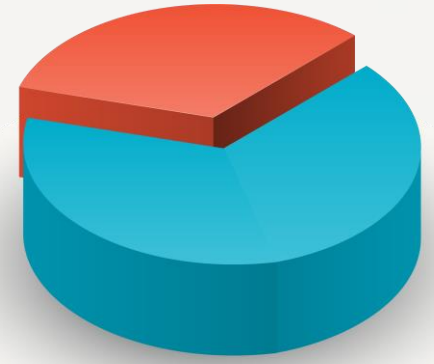
Alignment is needed across EU regulators and HTA bodies.

Consistency is needed across HTA process from different member states.

2,600

clinical studies on cell or gene therapies are ongoing

33% rare disease



67% in common diseases

Questions?