Addressing unique commercial challenges with gene therapy: *learnings from Strimvelis*

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WORLD OrphanDrug Congress Europe 2019

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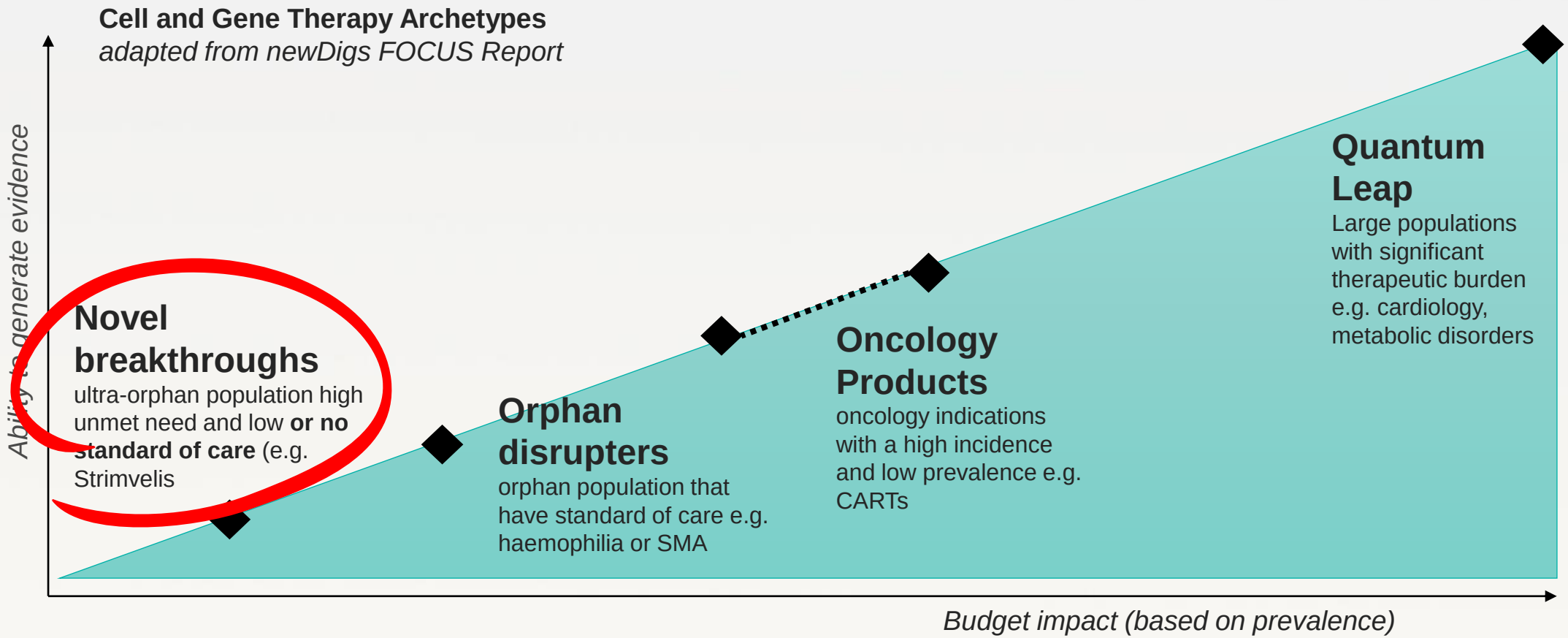
enlightened.thinking.applied

Partners4Access

Agenda

- **Introductions**
- The request
- The issues
- Working our way forward
- Q&A

Not all gene therapies are the same



https://newdigs.mit.edu/sites/default/files/NEWDIGS%20FoCUS%20Frameworks%2020180823.pdf

Agenda

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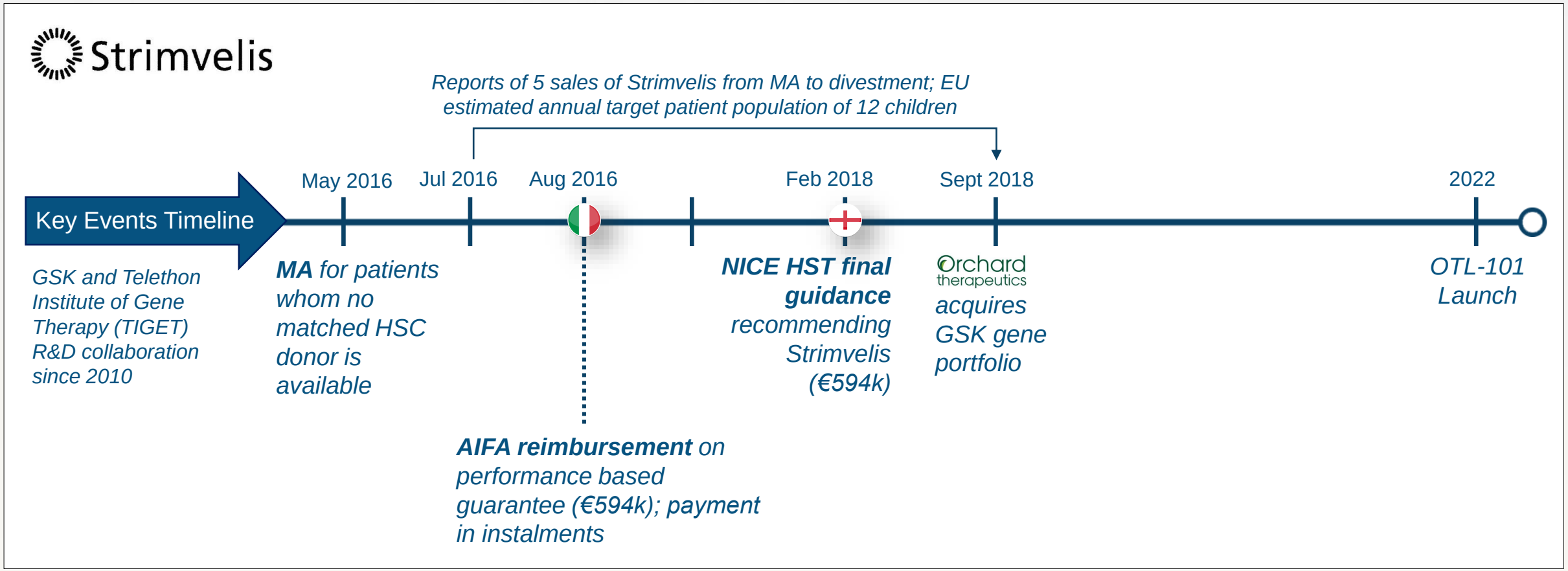
Orchard therapeutics

STRIMVELIS
(autologous CD34+ cells transduced to express ADA)

Strimvelis' had limited *commercial* uptake; Orchard were keen to understand how to help more children benefit



Orchard asked us to investigate options help more children and families benefit from Strimvelis therapy

Activity Timeline 2019

1

- **Understand goals for Strimvelis / ADA-SCID franchise**
- **Determine ‘state of play’**

2

- **Understand external (access and uptake) gaps and opportunities**
- **Understand internal gaps and opportunities**

3

- **Develop recommendations to manage priority gaps and opportunities**
- **Operational next steps**

We started with assessing three building blocks to assess the ‘state of play’

Building Block Assessment

Access

- Reimbursement pathways
- S2 / Cross Border Healthcare Directive
- Funding outside of therapy costs
- Legal access frameworks

KOLs/Tertiary Centres

- Specialist centres and leading KOLs
- Quality of relationship
- Treatment guidelines
- Treatment preferences

Patients

- Patient numbers
- New-born screening
- Patient registries
- Patients treated with Strimvelis or OTL-101

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Arriving via an assessment scorecard to quantify major opportunities that exist to benefit patients

Example Scorecards

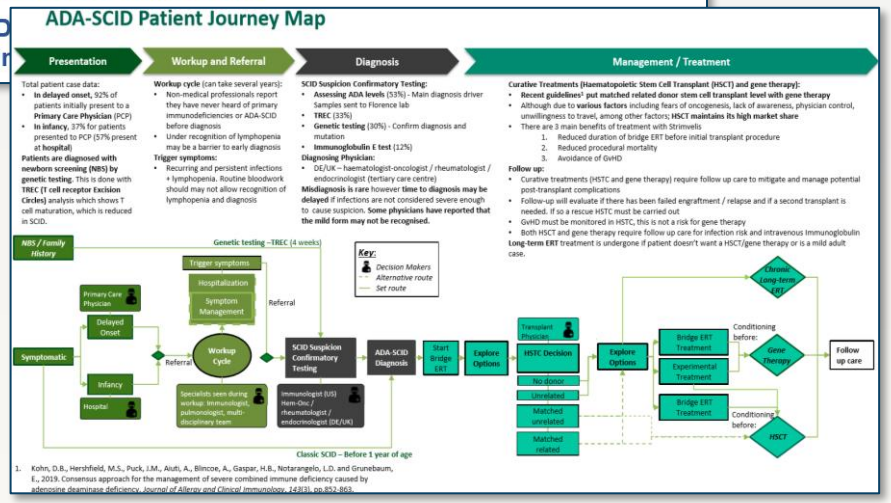
Where to place our resources to best benefit EU patients?

We then followed up with several expert interviews to better understand the landscape and patient journey

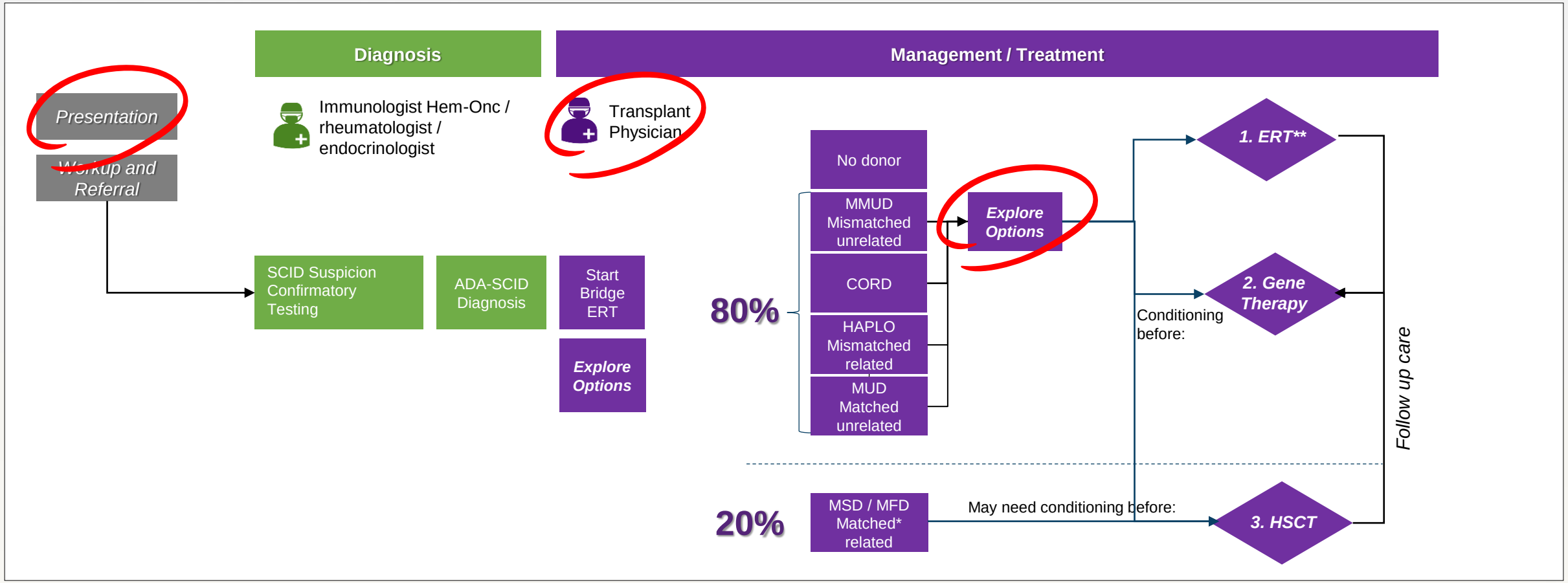
- **Co-developed** discussion guide
- Interviewed **EU KOLs in ADA-SCID**
- **Objectives:**
  1. Understand in detail **patient population and pathway**
  2. Understand **KOL opinions** on Strimvelis vs. HSCT and future gene therapy options
  3. Understand **current barriers and opportunities** in gaining reimbursement for Strimvelis as seen by KOLs in target countries

Partners Access

External Interviews



This is what we found



*First-choice treatment when a suitable HLA-matched related stem cell donor is available[1,4] applicable for <20% of patients[5] Can be given on a long-term basis;[1-3] not licensed in the EU although recommended in EU guidelines[2,6]

Let's explore inside their mind!

Transplant Physician

Need Recognition

Information Gathering

Evaluate Alternatives

Assess Evidence

Select Option

Implement Decision

Decision Review / Evaluation

Survival data in ADA-SCID *following transplant 1981-2009**

Treatment	MSD	MFD	MUD	Haplo	MMUD
Survival	86%	83%	67%	43%	29%
(n)	(36/42)	(10/12)	(10/15)	(13/30)	(2/7)

On <u>probing</u>, KOLs highlighted a few "unknowns"

- Lack of registries
- Long-term survival data
- Event-free survival data

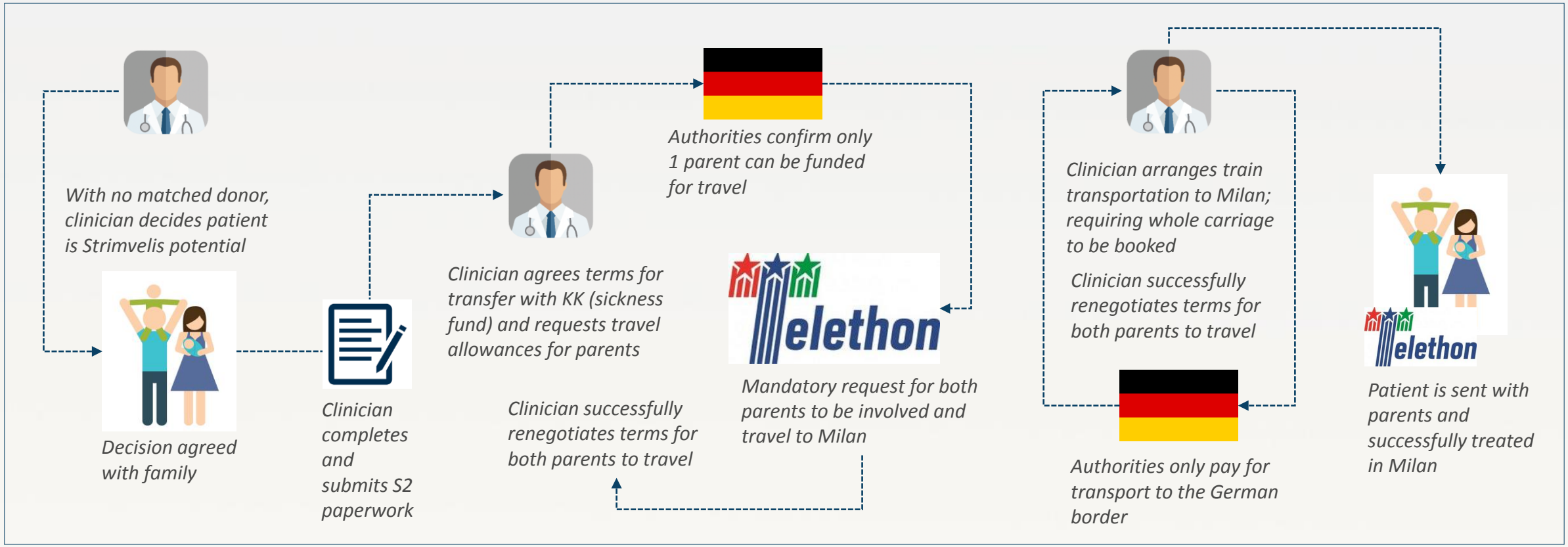
KOLs all considered **gene therapy to be the future**

Hassan, 2012

Even if they got to Strimvelis, the S2 process adds extra complexity

Clinician Strimvelis Journey *(Illustrative: does not include funding flow)*

~6 months



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In summary, we identified several barriers preventing children benefiting from Strimvelis therapy

Major Barriers *(Impacting Strimvelis access and uptake)*

1. *POSITIONING*
   KOLs are comfortable with transplant as the gold standard treatment option: GT is a distant second choice
2. *DIAGNOSIS*
   New-born screening programs not standard; negatively impacts diagnosis
3. *TRAVEL ABROAD*
   Travel to Milan and costs are a primary barrier influencing parents / caregivers choice
4. *S2*
   The S2 process (Cross Border Healthcare) is burdensome and unclear for all involved
5. *ENGAGEMENT & REFERRAL*
   Existing relationships with immunologists not transplant community (tight-nit)

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Orchard therapeutics

Learnings from Strimvelis

Darren Walsh

November 14, 2019

Global Fully Integrated Biotech Dedicated to Transforming the Lives of Patients with Rare Diseases Through Innovative Gene Therapies







Singular focus on *ex-vivo* autologous HSC gene therapy for rare diseases

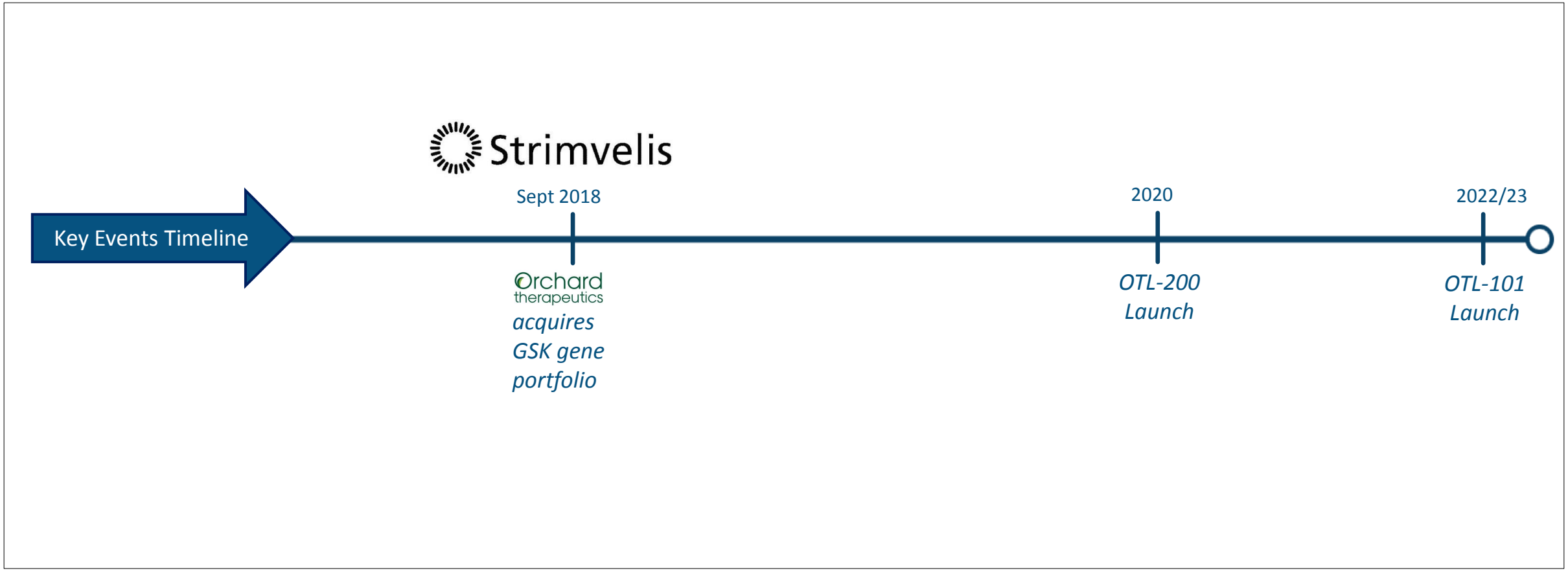
We are privileged to learn from Strimvelis and support our forthcoming launches - Over 160 Patients Treated with Orchard's Autologous *Ex Vivo* HSC Gene Therapies

Function	Program	Patients treated[1]	Longest patient follow-up (years)
Primary Immune Deficiencies	**Strimvelis®*** (ADA-SCID)	24	18
	OTL-101 (ADA-SCID)	62	6
	OTL-103 (WAS)	16	8
	OTL-102 (X-CGD)	10	3
Neurometabolic Disorders	**OTL-200** (MLD)	33	8
	OTL-203 (MPS-I)	6	1
Hemoglobinopathies	**OTL-300** (TDT)	9	3

Persistent, long-term effects across five indications with follow-up out to 8 years

[1] Patients treated in the development phase, including in clinical trials and under pre-approval access (defined as any form of pre-approval treatment outside of a company-sponsored clinical trial, including, but not limited to, compassionate use, early access, hospital exemption or special license). Data based on the most recent public data presentation for each program
Data include all patients treated with CD34+ hematopoietic stem cells transduced *ex vivo* with vector of interest.
Commercial patients excluded

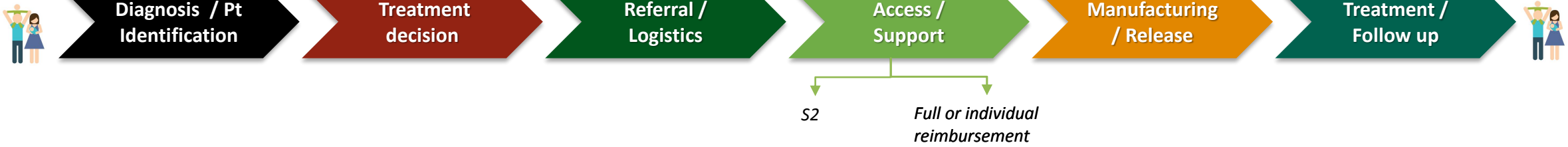
Since 2018 we have been working hard to improve access for Strimvelis and help us with planning across our future pipeline




WORK
TV
MIND
JOB
BUT
WORK
FUN
MOVE

Operationalising gene therapy successfully is complicated and requires partnership and collaboration with many interrelated stakeholders

Key Activities: Stages, Roles and Responsibilities



	Diagnosis / Pt Identification	Treatment decision	Referral / Logistics	Access / Support		Manufacturing / Release	Treatment / Follow up
Orchard therapeutics	Drive Widespread New Born Screening program* Patient story sharing Diagnostic support*	Stakeholders engagement strategy Strimvelis vs. HSCT event free survival data capture*	Positive experience sharing MoIMed scheduling	S2 concierge service for clinicians*	Develop / submit dossiers*	DP manufacturing QC/ Audits/ DP Logistics	Aftercare support, patient story sharing and long-term data tracking* LT Registry
SR-Tiget / I.R.C.C.S. Ospedale San Raffaele	Lobbying support for New Born Screening program* Patient story capture from prior families to share with parents of newly diagnosed children*	Peer to peer experience sharing Support patient's family needs	Eligibility assessment with clinician (and family as appropriate) Coordination and planning for treatment process	Funding verification Supports travel logistics / visa Meets family in Milan / ensures wellbeing throughout		Treatment coordination Ordering	Infusion of Strimvelis BM / engraftment evaluation Follow-up in clinic and/or day hospital

** Activities not yet in operationalisation*

We are working on a consolidated program of activities to address those barriers and help more children benefit from Strimvelis therapy

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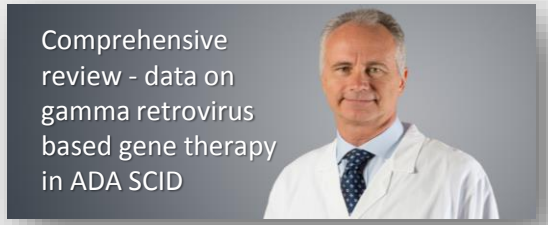
Addressing positioning barriers

1

POSITIONING
KOLs are comfortable with transplant as the gold standard treatment option: GT is a distant second choice

Key issues	Select Solutions
Gene therapy is too new	
'Transplanters' very comfortable with practice	
KOLs not as comfortable driving as limited experience	EBMT European Society for Blood and Marrow Transplantation — *Partnership long term HSCT safety data registry*

Ideal Outcome

Gene therapy is considered 1st choice within potential treatment options for ADA-SCID

Addressing diagnosis barriers

2

DIAGNOSIS
New-born screening programs not standard; negatively impacts diagnosis

Key issues	Select Solutions
Focus on diagnosis is important for ADA-SCID and other rare diseases	
Speed and challenge associated with ADA-SCID diagnosis	

Ideal Outcome

Improved diagnosis rates for Strimvelis and benefiting future assets

Addressing travel barriers

3

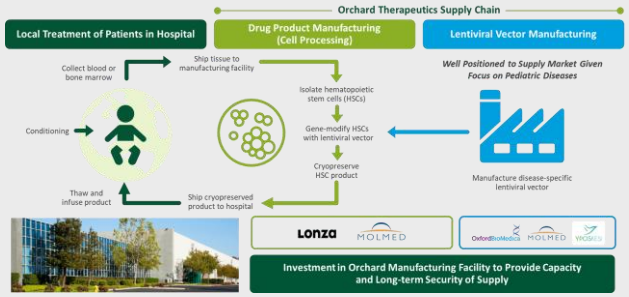
TRAVEL ABROAD
Travel to Milan and costs are a primary barrier influencing parents / caregivers choice

Key issues

Single site in Milan increased travel commitments and burden

Family fear of the unknown, new culture, language

Select Solutions



Investment in cryopreserved formulation

FONDAZIONE Telethon

Ideal Outcome

Increasing ability to treat localised patients and support given to parents to smooth the treatment journey

Addressing S2 barriers

4

S2
The S2 process (Cross Border Healthcare) is burdensome and unclear for all involved

Key issues	Select Solutions
Lack of KOL experience with S2 requests	
S2 paperwork is burdensome and complex	
Low / no awareness of cross-border directive	EUCOPE European Confederation of Pharmacists; Alliance for Regenerative Medicine

Ideal Outcome

Increased number of requests accepted for funding with minimal admin burden for KOLs

Addressing engagement and referral barriers

	Key issues	Select Solutions	Ideal Outcome
5 *ENGAGEMENT & REFERRAL Existing relationships with immunologists not transplant community (tight-nit)*	*Limited awareness of Strimvelis data from immunologists*	Published data review - Haplo HSCT in PIDs *(lower efficacy and safety when compared to Strimvelis)*	*Greater number of eligible children are able to benefit from Strimvelis*
	Eligible patients not always being referred		

We are adapting our commercial strategy across assets to effectively launch our pipeline globally

1 Geographic Footprint	• Teams in place in EU & North America – Expand as appropriate / possible • Focus on “launch countries” with highest unmet need • Build relationships with KOLs to drive engagement and appropriate referral
2 Patient ID and Diagnostics	• Expand newborn screening (NBS) for ADA-SCID • Assay selection & NBS pilot testing for MLD critical – takes significant time • Disease awareness and advocacy
3 Centers of Excellence	• Select leading centers with transplant & disease area experience • Ensure these centres match local payer expectations / requirements • Center qualification critical to increase patient choice / decrease travel
4 Market Access	• S2 process – Increase cross border options where possible • Gene therapy value determination for each program • Multi-stakeholder engagement - Option for flexible payment models
5 Global Supply Network	• Manufacturing hub(s) to ship cryopreserved product globally • Move towards a more sustainable “in-house” long-term model • Ensure distribution an logisitcs are seamless

When We Think about Value, It All Starts with the Child
and What Our Therapies, If Approved, Could Do for That Child and Beyond

Impact on Society

	From	To
The Child	Severely limited lifespan	Life free from symptoms & suffering
The Family	Immense financial & emotional toll	Lives of everyone in the family transformed
The Community	School, civic organization and employer resources engaged	Community resources re-deployed
The Health System	Chronic / costly interventions & palliative care	Deliver potentially curative therapy & save significant resources

A world where deadly diseases could potentially be stopped in their tracks

Any questions?