bridgebio

hope through
rigorous science

Incorporating Patient Experience Data into Drug Development and Regulatory

Adora Ndu, PharmD, JD

Chief Regulatory Affairs Officer;
Bridgebio Pharma

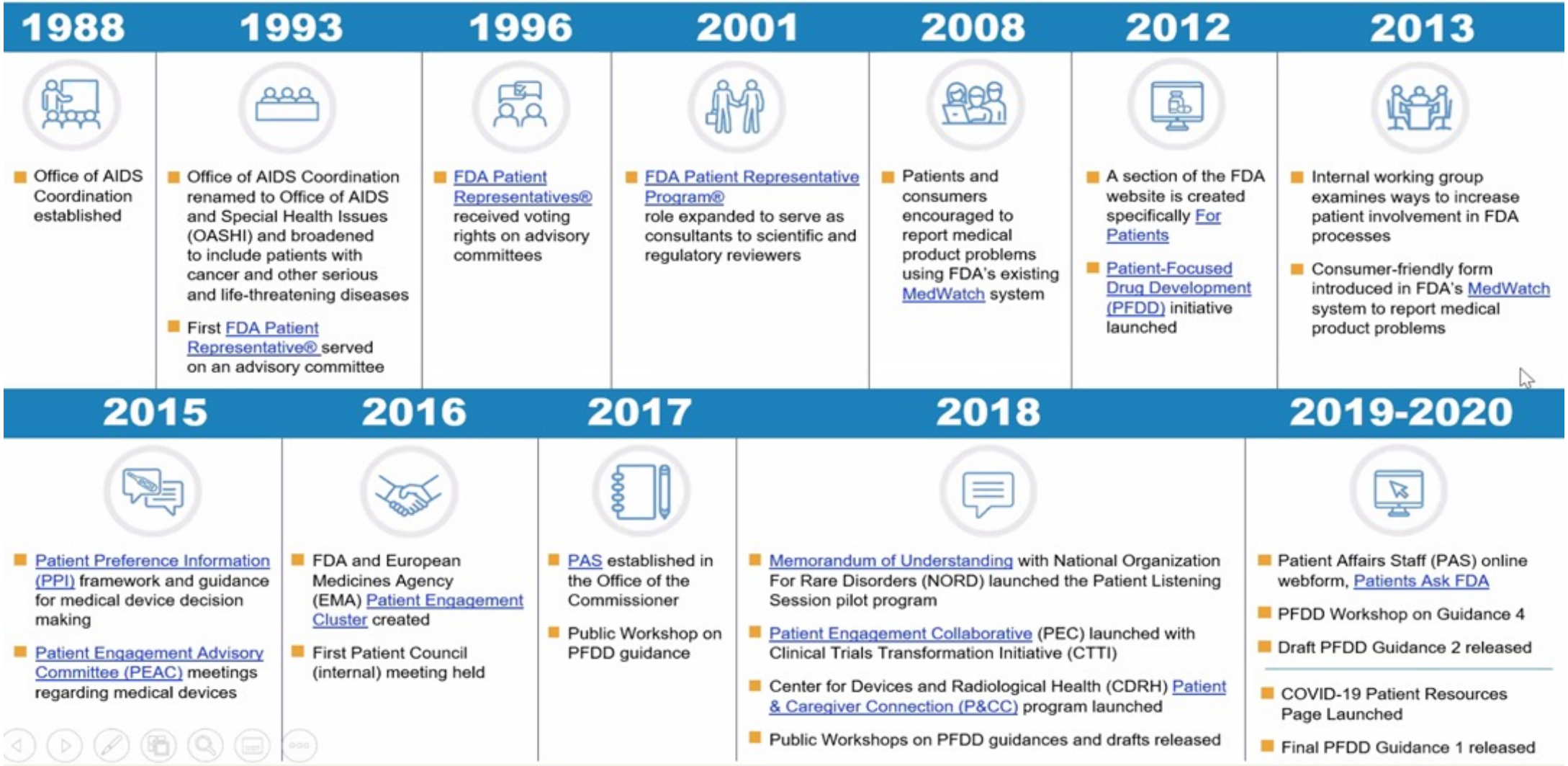
Contents

FDA's Patient-Focused Drug Development Program

- In 2012, **the FDA Safety and Innovation Act (FDASIA)** formally established a **Patient-Focused Drug Development (PFDD)** initiative to incorporate patient voice in drug and biologic development
- Patient-focused drug development (PFDD) is a systematic approach to help ensure that patients' experiences, perspectives, needs, and priorities are captured and meaningfully incorporated into drug development and evaluation.
- Primary goal of patient-focused drug development is to better incorporate the patient voice into drug development and evaluation, including but not limited to:
  - Approaches to collecting and utilizing robust and meaningful patient and caregiver input to more consistently inform drug development and regulatory decision-making
  - Best practices to facilitate patient enrollment and minimizing the burden of patient participation in clinical trials
  - Enhancing understanding and appropriate use of methods to capture information on patient preferences and the potential acceptability of tradeoffs between treatment benefit and risk outcomes
  - Identifying the information that is most important to patients related to treatment benefits, risks, and burden, and how to best communicate the information to support their decision making.

Source: CDER PFDD web page: https://www.fda.gov/drugs/development-approval-process-drugs/cder-patient-focused-drug-development

Foundation of Patient Experience Data (PED) Generation: Patient Focused Drug Development and Patient Engagement Initiatives



Source: Andrea Furia Helms, FDA – FDLI Annual Conference October 2020

21st Century Cures Act

- The 21st Century Cures Act (enacted in 2016) mandated FDA to:
  - After approving an application for a new medication, **publish a brief statement on any patient experience data** or related information that was part of the application.
  - **Issue guidance and report on its use of patient experience data** in regulatory decision-making.
- The PDUFA VII reauthorized in Oct 2022, mandated that FDA will "continue to strengthen capacity to **facilitate development and use of Patient-Focused methods to inform drug development and regulatory decisions**."
- The FDORA bill signed into law Dec 2022, directed FDA to convene at least one public meeting to address increased and **improved engagement with rare disease patients, rare disease patient groups, and experts on small population studies** to improve the understanding of patient burden, treatment options, and the side effects of treatments

PFDD – How Patients Engage with FDA

55+ EL-PFDD Meetings held to date

	Externally-led PFDD Meetings
Purpose	To allow patient organizations to identify and organize patient-focused collaborations to generate public input on other disease areas, using the process established through FDA-led PFDD meetings as a model
Topics Covered	FDA welcomes host organizations to have public meetings to discuss symptoms and daily impacts that matter most to patients, patient perspectives on current treatment approaches, and topics such as clinical trial considerations and meaningful benefit may also be explored.
Aims	Patient input from meetings and meeting summary reports can support FDA staff: 1. In conducting benefit-risk assessments for products under review, by informing the therapeutic context 2. Advising drug sponsors on their development programs

Source: https://www.fda.gov/patients/learn-about-fda-patient-engagement/fda-patient-engagement-overview

How Patients Engage with FDA (additional initiatives)

	Purpose	Topics Covered
FDA Patient Listening Session program	Informal patient community meetings that educate staff in multiple FDA centers about diseases, conditions, health experiences and unmet medical needs	Disease and symptom burden, treatment preferences, quality of life, unmet medical needs, FDA division-specific questions
Patient Engagement Collaborative (PEC)	A forum to discuss and share experiences on patient engagement in medical product development and regulatory discussions	Communication and education (assist sorting out topics of shared interest to the PEC, CTTI, and the FDA) & share information and experiences
Patient Engagement Advisory Committee (PEAC)	Provides advice to the Commissioner or designee, on complex issues relating to medical devices, the regulation of devices, and their use by patients in a public advisory committee meeting	Regulatory process and medical product review
Patient Representative Program (PRP)	Offers patients and caregivers the opportunity to provide critical advice to the agency as it regulates medical products through the drug development process and in advisory committee meetings.	Regulatory process and medical product review
Critical Path Innovation Meetings (CPIM)	CDER and investigators from industry, academia, scientific consortia, patient advocacy groups, and government discuss a methodology or technology proposed by the meeting requester and provide general advice	Includes: Biomarkers, Clinical Outcome Assessments, Natural history study, Emerging technologies, Innovative clinical trial design and analysis

Source: https://www.fda.gov/patients/learn-about-fda-patient-engagement/fda-patient-engagement-overview

PFDD – How patient advocacy groups can request meetings

	How to request	How to Prepare
Externally-led PFDD Meetings	Submit a Letter of Intent (LOI) that communicates • the importance of the meeting in the context of the disease area • important details regarding the meeting plan The letter of intent (LOI) should be brief (approximately 3 pages) and submitted approximately 1 year before the anticipated meeting date	• Joint, aligned effort by multiple patient organizations associated with the disease/condition, and other interested stakeholders • Review the meeting materials and discussion questions for a variety of the PFDD meetings
FDA Patient Listening Session program	Fill out form on FDA website with the following information: • the health condition, disease or your specific concern; • what you would like to share during the patient listening session; • a draft meeting agenda; and • what you hope to happen after the patient listening session	• Develop your meeting materials and refine your agenda • Identify and confirm the attendance of participants from the patient community • Plan your transportation to and from FDA (for in person)

Source: https://www.fda.gov/industry/prescription-drug-user-fee-amendments/planning-el-pfdd-meeting; https://www.fda.gov/patients/learn-about-fda-patient-engagement/fda-patient-listening-sessions

Recent externally-led PFDD Session: Limb Girdle Muscular Dystrophy

- EL-PFDD Meeting for LGMD – held on September 23, 2022
- 37 patients and and caregivers spoke at the session
- Key themes from patients:
  - LGMD affects multiple body systems
  - Many with LGMD are severely affected
  - All individuals with LGMD progress, but at different rates
  - LGMD is stigmatizing
  - There are currently no FDA approved treatments for any form of LGMD
  - Treatment approaches are palliative only and do not change the course of the disease
  - People living with LGMD urgently and desperately need better treatments
  - Individuals living with LGMD want to participate in clinical trials

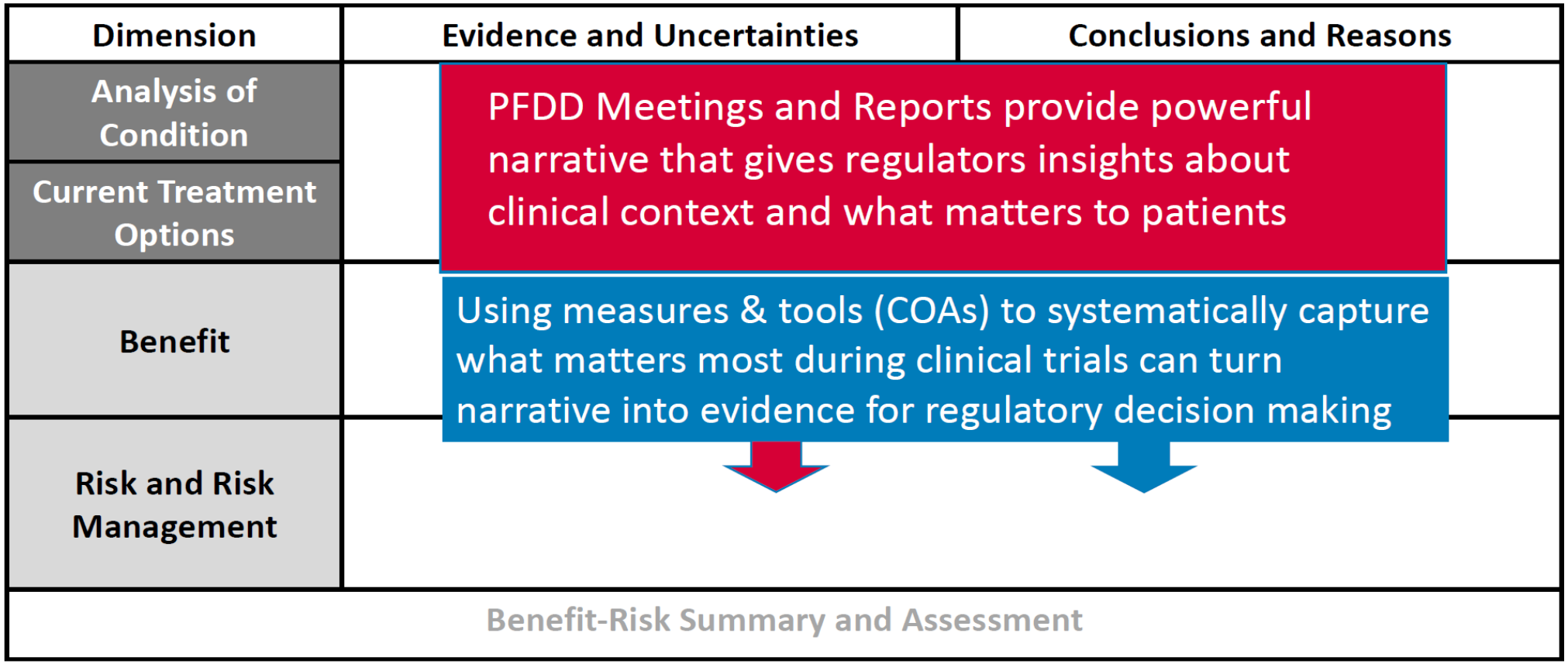
> The progressive nature of it leaves me feeling terrified about what my future holds, as I live alone and must face these challenges on my own. Any treatment or drug therapy that would even slow the progression of my condition would be considered a very major victory in my book.
> *—Dan, 57-year-old man living with LGMD2i*

EL-PFDD Meeting Recording; Meeting Report

Generation and Application of Patient Data in the Drug Development Process

Product Stage	Research and Discovery	Pre-Clinical Development	Clinical Development: Phase I	Clinical Development: Phase II	Clinical Development: Phase III	Pre-Market Review	Post Marketing
PED Data Considerations	**Identify outcomes that matter most to patients** • Burden of illness • Unmet medical need • Holistic disease experience (patient journey)		**Leverage methods to capture PED** • COA identification, selection, modification or development • Qualitative or quantitative PED generation • Patient Preference Information			**PED Data Integration** including collation of all PED (e.g., COA)	• Post-marketing COA data collection • Patient and HCP feedback
Relevant Decisions Made	○ Product design adaptation	○ Product design ○ Protocol design	○ Treatment arm selection ○ Subpopulation identification ○ Benefit-Risk (B/R) Assessment ○ COA Identification ○ Clinical Trial Design ○ Personalized Medicine/biomarkers ○ Development of drug development tools ○ Eligibility for expedited programs			○ Labeling Optimization ○ Advisory Committee Meetings	○ Healthcare Decision Aids ○ Label Expansion ○ Shared Treatment Decision Making ○ Personalized Medicine ○ Quality of Care

Patient Perspective Informs Benefit-Risk Assessment



Source: FDA CDER Presentation at the Conference Forum, May 2019

Use of Patient Experience Data is Documented in FDA Review Summaries
Table included in FDA's integrated review summary

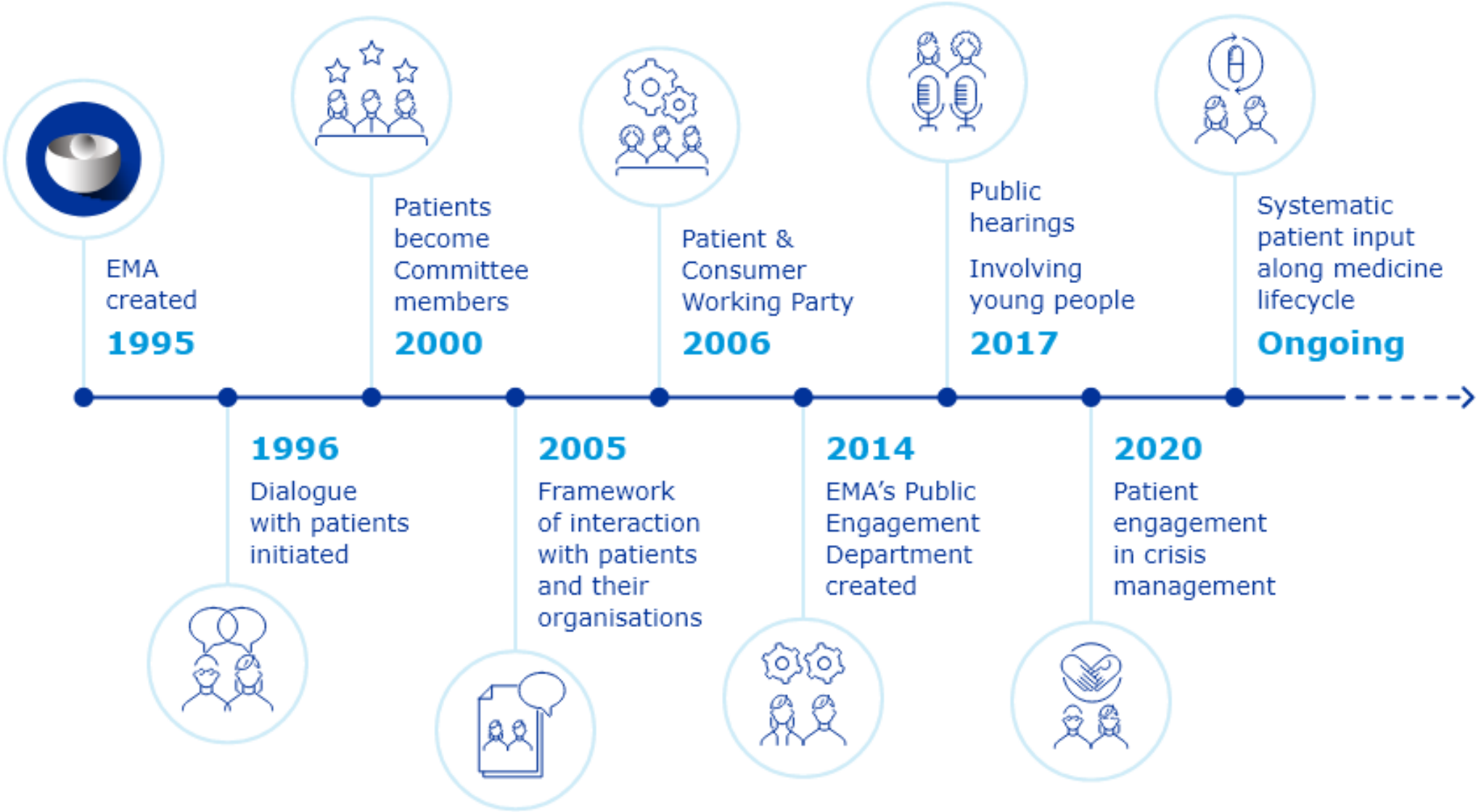
4. Patient Experience Data

Table 4. Patient Experience Data Submitted or Considered

Data Submitted in the Application		
Check if Submitted	**Type of Data**	**Section Where Discussed, if Applicable**
Clinical outcome assessment data submitted in the application		
☒	Patient-reported outcome	See Section 16.1
☒	Observer-reported outcome	
☐	Clinician-reported outcome	
☐	Performance outcome	
Other patient experience data submitted in the application		
☐	Patient-focused drug development meeting summary	
☐	Qualitative studies (e.g., individual patient/caregiver interviews, focus group interviews, expert interviews, Delphi Panel)	
☐	Observational survey studies	See Section 4 and 6.3.46
☒	Natural history studies	
☐	Patient preference studies	
☐	Other: (please specify)	
☐	**If no patient experience data were submitted by Applicant, indicate here.**	
Data Considered in the Assessment (But Not Submitted by Applicant)		
Check if Considered	**Type of Data**	
☐	Perspectives shared at patient stakeholder meeting	
☐	Patient-focused drug development meeting summary report	
☐	Other stakeholder meeting summary report	
☐	Observational survey studies	
☐	Other: (please specify)	

Source: FDA Integrated Review: Vosoritide

EMA has incorporated patient interaction since the creation of the Agency in 1995



Source: https://www.ema.europa.eu/en/partners-networks/patients-consumers

EMA's Patients' and Consumers' Working Party (PCWP) gives a voice to patients in regulatory matters

- Provides a platform for exchange of information and discussion of issues of common interest between EMA and patients and consumers.
- Mandate - The PCWP provides recommendations to the EMA and its Human Scientific Committees on matters of direct or indirect interest to patients in relation to medicines for human use and monitor the overall interactions between EMA and patients and consumers.

The PCWP consists of 30 members, of which:

- Twenty-two (22) are appointed from amongst the list of EMA eligible organisations by a Decision of the Executive Director;
- Six (6) are appointed by each of the EMA Human Scientific Committees (CAT, CHMP, COMP, HMPC, PDCO and PRAC);
- One (1) Chairperson is elected from its members (PCWP Co-Chair);
- One (1) Chairperson is nominated from amongst the EMA Secretariat by a Decision of the Executive Director (EMA Co-Chair).

Source: EMA's web site: https://www.ema.europa.eu/en/committees/working-parties-other-groups/chmp/patients-consumers-working-party

EMA's Engagement Framework acknowledges the necessity to further develop patients' capacities

The framework relies on EMA's broad network of patients and consumers organizations, its Patients and Consumers Working Party (PCWP) and the pool of disease-specific individual patient experts.

The framework establishes the basis for:

- supporting access to individual patients' real-life experiences
- promoting the generation, collection and use of evidence-based patient experience data for benefit-risk decision-making
- enhancing patients and consumers understanding of medicines regulation and their role
- contributing to efficient and targeted communication to patients and consumers to support their role

Source: https://www.ema.europa.eu/en/documents/other/engagement-framework-european-medicines-agency-patients-consumers-their-organisations_en.pdf

EMA Regulatory Science Strategy to 2025 Considers Patient Voice

EMA's Regulatory Science Strategy to 2025 and Joint EU Medicines Agencies Network strategy to 2025 - defines future direction of engagement - driving collaborative evidence generation to improve quality of regulatory evaluations and outcomes;

Includes two complementary elements:

1. Enhance generation and use of patient experience data
    - 2022 - Multi-stakeholder workshop: Patient experience data in medicines development and regulatory decision-making
        - EMA gathered input from patients, consumers, healthcare professionals, academia, regulators, health technology assessment bodies and industry

2. Expand methodologies for patient engagement during regulatory assessments

Source: https://www.ema.europa.eu/en/documents/presentation/presentation-progressing-concept-patient-centred-development-practice-n-bere-ema_en.pdf

Key Takeaways for EMA from the 2022 Patient Experience Data Workshop

- Continue multilateral stakeholder cooperation
- **Explore additional engagement opportunities (e.g. focus groups)** for key topics
- The Agency will publish a position paper to provide advice on the best EU approach to generate and collect PED
- EU regulators will explore how to better reflect in the assessment report the way PED is assessed as well as the rationale for acceptance/exclusion for Benefit/Risk decision-making in the adverse reports
- **The patient voice will continue to be gathered** and used in the European Health Data Space and the Big Data work plan
- The Agency will investigate different options to increase capacity and adequate training
- **Encourage collaboration and dialogue between different stakeholders and early involvement of patients**

Source: https://www.ema.europa.eu/en/events/multi-stakeholder-workshop-patient-experience-data-medicines-development-regulatory-decision-making

Approaches to Obtaining Patient Experience Data

- **Surveys, QOL tools, Discreet choice experiments, patient preference studies**
- **FDA-led PFDD Meetings**
  - 24 disease-specific PFDD meetings conducted by FDA from 2012-2017
  - Summary reports, transcripts, website recordings, and presentation slides maintained on FDA's web site
- **Externally-led PFDD Meetings**
  - FDA welcomes patient organizations to hold PFDD meetings as well, which FDA will typically participate in
  - Summary reports typically available
- **Other qualitative approaches**
  - **FDA Listening Sessions**
  - **Focus group summaries**
  - **Patient narratives**
  - **Participation in sponsor/ FDA meetings**

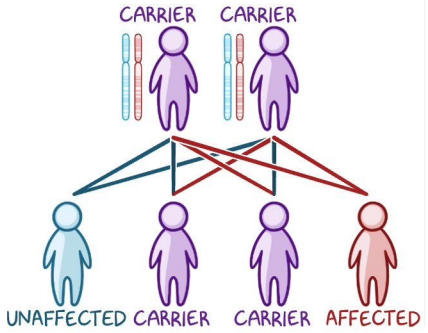
Information collected can and should be used to support rationale (e.g. lack of placebo arm, study duration, treatment outcomes) in regulatory interactions and submissions

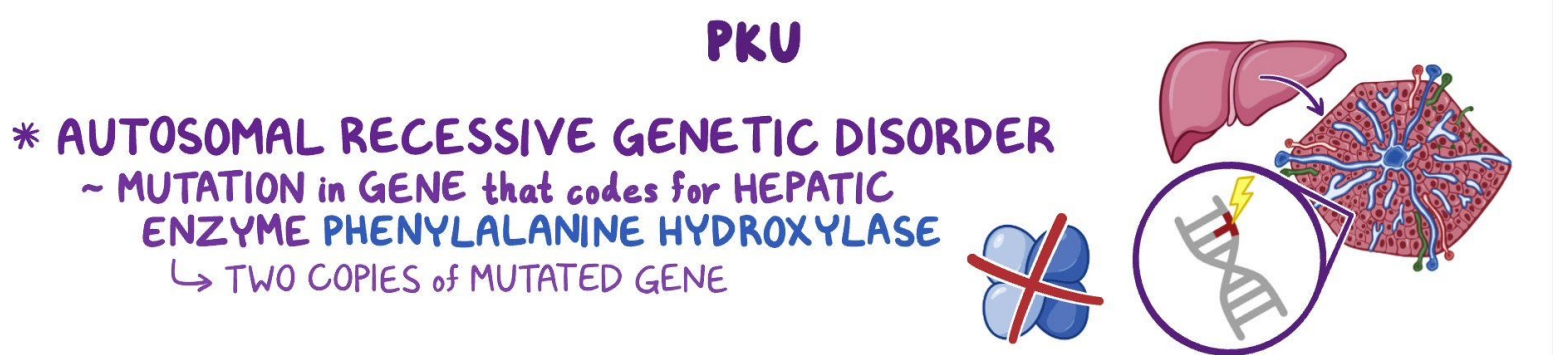
Case Studies

1insert source / footnote

Case Example – Palynziq
Patient Experience Data Informed Regulatory Decision-making

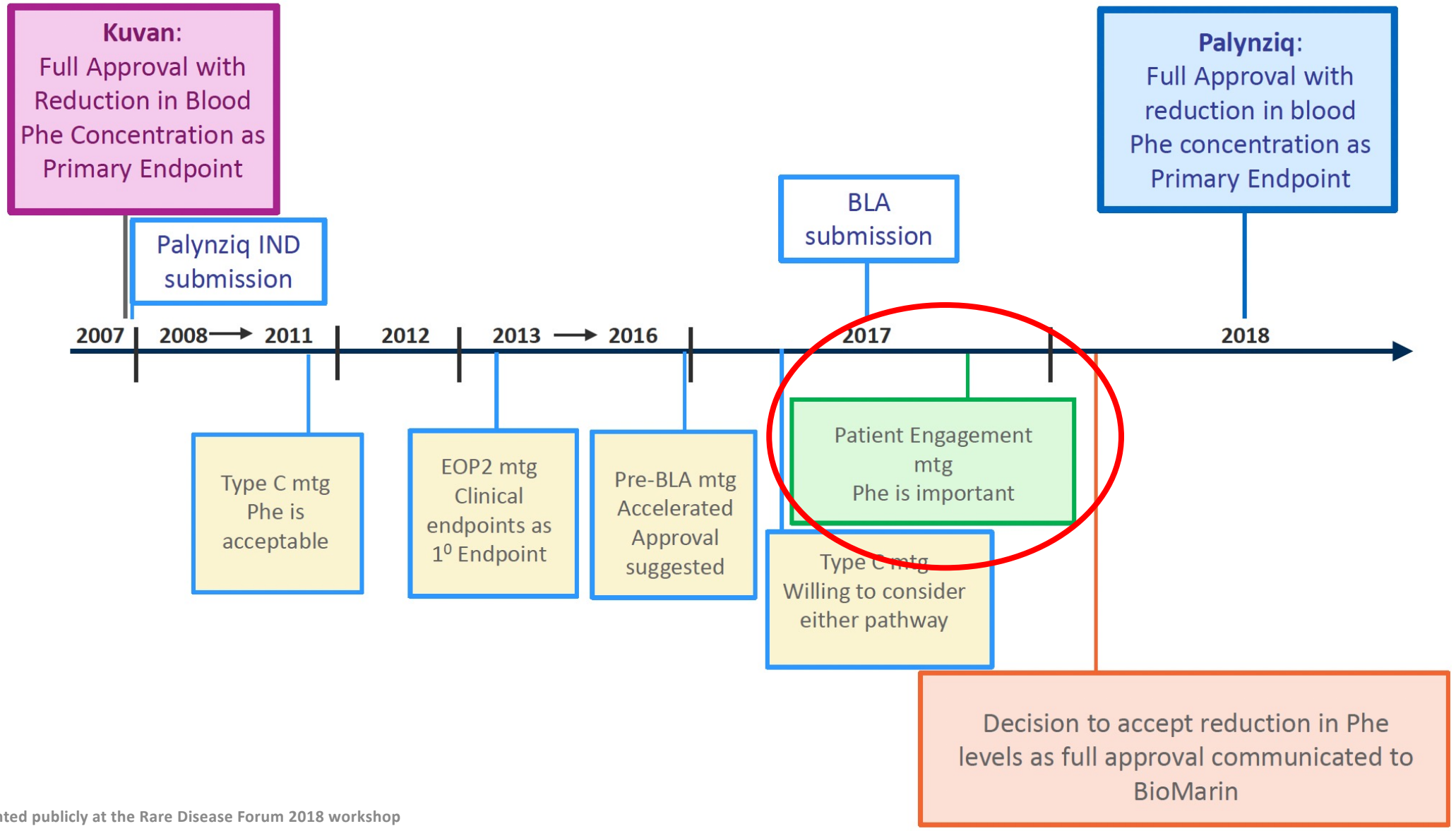
- Palynziq (pegvaliase-pqpz)
- BLA approved May 24, 2018 for Phenylketonuria (PKU)
- Patient experience data submitted and considered in the review.
  - FDA public meeting on Patient Focused Drug Development for neurological manifestations of inborn errors of metabolism, June 10, 2014.
  - Meeting between FDA and treated patients in pegvaliase clinical trials, with the National PKU Alliance in 2017
  - Benefit /risk survey





Source: FDA Review of Palynziq

Case Study: Palynziq



Case Study: Palynziq

Safety of Palynziq and Overall Benefit Risk

Challenge	Solution
Hypersensitivity Adverse Events (including Anaphylaxis) ✓ What is the mechanism? ✓ How to mitigate?	▪ Mechanism of action evaluated through immune complex (IC)-related AE's, circulating ICs, complement levels and drug-specific IgE ▪ HAEs are Type III hypersensitivity ▪ Critical evaluation of value of risk mitigations ▪ Safety meeting to share concerns and proposal ▪ Risk evaluation and mitigation strategies + ETASU to mitigate

Benefit Risk	▪ Patient survey data on willingness to take a drug like Palynziq
	▪ FDA sought patients' and clinicians' views on:
	  ▪ Unmet need
	  ▪ Willingness to accept benefits & risk of Palynziq

Case Study: Palynziq (FDA's version of the story)

Patient perspectives

- NPKUA meeting with FDA
- Patient meeting with DGIEP review team during BLA review
- Perspectives on both desired benefits and acceptable risks
  - What matters?
  - What is missing?
  - What degree(s) of (safety) risk are they willing to take to achieve what matters?

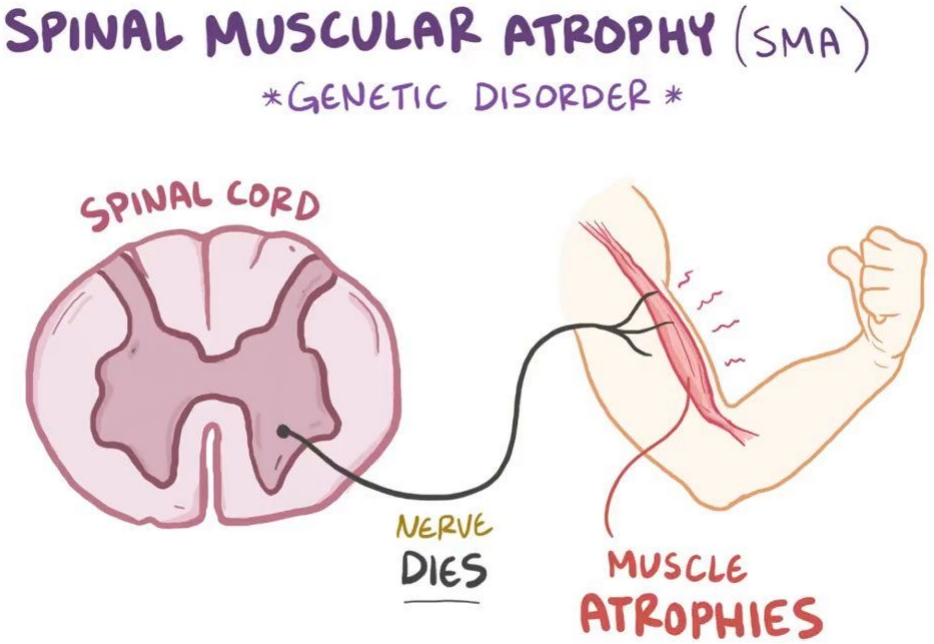
Case Study: Palynziq (FDA's version of the story)

Conclusions

- Quantitation of clinical benefit in PKU tightly linked to blood Phe concentration
- Remaining questions regarding degree of Phe reduction that leads to clinical benefit
- Important safety risks of Palynziq related to highly immunogenic foreign protein
- Patient input during drug development and regulatory review provided important insights to the review team
- Approval based on favorable benefit-risk assessment including assurance of safe use for the serious risk of anaphylaxis (REMS w ETASU), product labeling, and post-marketing required studies

Case Example – Evrysdi
Partnering with patients throughout drug development

- Evrysdi (risdiplam)
- NDA approved August 7, 2020 for spinal muscular atrophy (SMA)
- SMA Community helped shape the company's clinical development program in SMA and was central to ensuring faster and broader patient access and improving outcomes



Source: https://www.ema.europa.eu/en/documents/presentation/presentation-considerations-learnings-use-cases-m-muller-efpia_en-0.pdf

Case Example – Evrysdi

- Sponsor **partnered with the SMA community throughout development**
  - Patient Advocacy Groups advanced the sponsor's understanding regarding the existing unmet need, and what treatment effects were most relevant.
  - Members of the SMA Foundation were invited to regulatory meetings to provide the HA with insights from people living with SMA directly.
  - Patient views, published data from PAG-led surveys alongside the patient-reported outcome data from clinical trials, were included in regulatory applications to capture the unmet need and real-life value of SMA treatments.

- The sponsor conducted **patient and caregiver interviews to better understand the disease burden** in Type 2 and non-ambulant Type 3 SMA patients

- Sponsor **developed the SMA Independence Scale - Upper Limb Module** (SMAIS-ULM) for the SMA community with COA measurement experts
  - **Made the SMAIS-ULM available to the public** via the ePROVIDE platform to be used in clinical practice and future trials to monitor patients/assess benefit

Source: https://www.ema.europa.eu/en/documents/presentation/presentation-considerations-learnings-use-cases-m-muller-efpia_en-0.pdf

Summary

- FDA's PFDD Initiative acknowledges that patients, their families, caregivers, and associated patient groups are experts and are uniquely positioned to inform the understanding of the therapeutic context
- EMA has regularly incorporated the patient voice in regulatory decision making since its inception and continues to involve patients through the PCWP, workshops, frameworks, and internal strategies
- Patient experience is needed throughout the drug development process including identifying outcomes that matter most to patients and protocol design
- Patients can help reveal insights not known to health authorities and can provide invaluable experience to sponsors to create the best therapy possible

Questions?