# 19th DIA Japan Annual Meeting 2022

New “Quest for the future”

**October 9-11, 2022 | ※ Hybrid**

## Discussion with Patients about Rare Disease Drug Development to Improve Drug Lag in Japan (LS28) Development of Drugs for Rare Diseases; Regulatory Perspective

## 希少疾患治療薬の開発；規制当局の立場から

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DIA

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# Promotion of Development of Drugs for Rare Diseases: Orphan Drug Designation

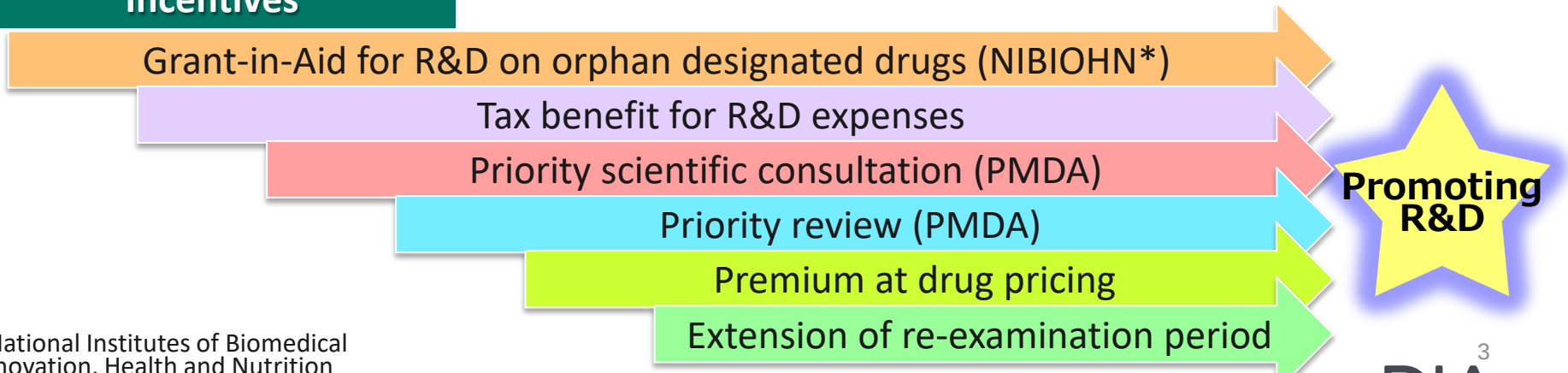
## Aim

✓ To promote R&D on products for rare diseases, aiming to provide the people with the safe and effective medicines/medical devices as early as possible

## Designation Criteria

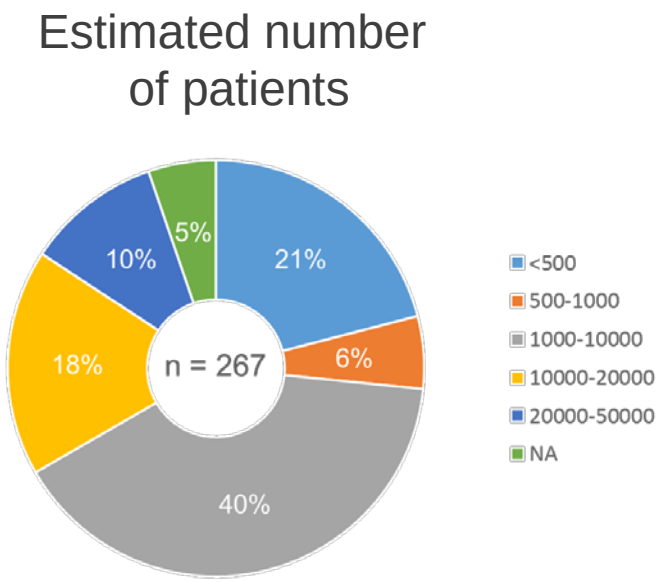
1. Number of patients (that any of the followings is satisfied)
   - Less than 50,000 in Japan
   - The target disease is one of the designated intractable disease
2. Medical needs
   - For serious diseases with high medical needs
3. Feasibility of development

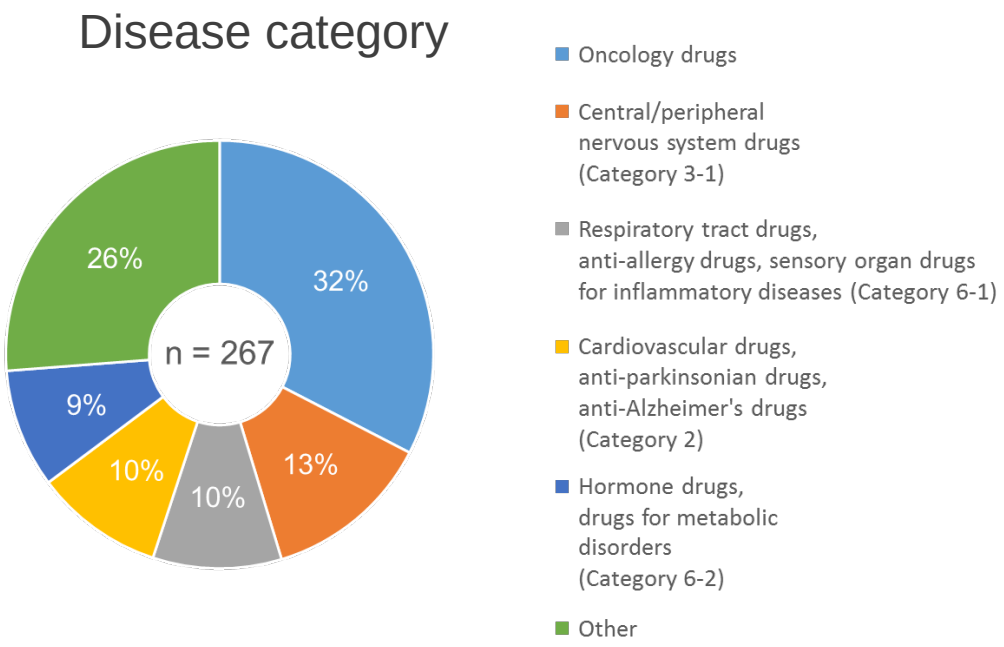
## Incentives




*National Institutes of Biomedical Innovation, Health and Nutrition

# Designation and Approval of Orphan Drugs




Distribution of the estimated number of patients for indications for which products received orphan drug designation from fiscal year (FY) 2004 to FY 2018. NA, not available, includes vaccine products for pandemic H5N1 influenza. b | Distribution of orphan drug designations from FY 2004 to FY 2018 by disease categories currently used in the regulation in Japan.

*Nat. Rev. Drug. Discov*. 2021, 20, 893-894

# Representative Examples of Orphan Drug Development

| Drug | Indication | Designation in Japan | Approval in Japan | Designation in EU/USA | Approval in EU/USA | Pivotal clinical trial (number of subjects) |
|---|---|---|---|---|---|---|
| **Edaravone** | Amyotrophic lateral sclerosis | 2005 | 2015 | EU: 2014<br>US: 2015 | EU: NA<br>US: 2017 | JCT<br>(Japanese 137) |
| **Leuprorelin** | Spinal and bulbar muscular atrophy | 2006 | 2017 | EU: ND<br>US: ND | EU: NA<br>US: NA | JCT<br>(Japanese 199) |
| **Mogamulizumab** | Adult T cell leukaemia/lymphoma | 2010 | 2012 | EU: ND<br>US: 2011 | EU: NA<br>US: NA | JCT<br>(Japanese 27) |
| **Nivolumab** | Malignant melanoma | 2013 | 2014 | EU: ND<br>US: 2013 | EU: 2015<br>US: 2014 | JCT<br>(Japanese 35) |
| **Mepolizumab** | Eosinophilic granulomatosis with polyangiitis | 2013 | 2018 | EU: 2013<br>US: 2011 | EU: NA<br>US: 2017 | MRCT<br>(total 136/Japanese 6) |
| **Canakinumab** | TRAPS, FMF, HIDS | 2014 | 2016 | EU: 2012 (TRAPS)<br>US: 2012–2013 | EU: 2017<br>US: 2016 | MRCT<br>(total 181/Japanese 8) |
| **Nusinersen** | Spinal muscular atrophy | 2016 | 2017 | EU: 2012<br>US: 2011 | EU: 2017<br>US: 2016 | MRCT<br>(total 121/Japanese 3) |
| **Patisiran** | Transthyretin-type familial amyloid polyneuropathy | 2016 | 2019 | EU: 2017<br>US: 2012 | EU: 2018<br>US: 2018 | MRCT<br>(total 225/Japanese 16) |

ND: Not Designated, NA: Not Approved, MRCT: Multi-Regional Clinical Trial, JCT: Japanese Clinical Trial
TRAPS: TNF-receptor associated periodic syndrome, FMF: familial Mediterranean fever, HIDS: hyperimmunoglobulin D Syndrome

# What Happens When Japan Misses a Chance to Participate in Pivotal MRCT

- MRCT will be a preferred option
  - Simultaneous development in Japan and other countries
  - Allow for an examination of the applicability of a treatment effect to diverse populations
- However, there are some cases missing a chance to participate in a pivotal MRCT
  - Domestic clinical trial in Japan may be needed to demonstrate the efficacy and/or safety of the drug in Japanese patients

# Why Does PMDA Require Efficacy Data in Japanese Patients

- Acceptability of foreign clinical data is decided based on existing data, on a case-by-case basis
  - Intrinsic/extrinsic ethnic factors
    - ADME
    - Receptor sensitivity
    - Disease definition
    - Therapeutic approach, etc.

# Clinical Trial Can Be a Therapeutic Option

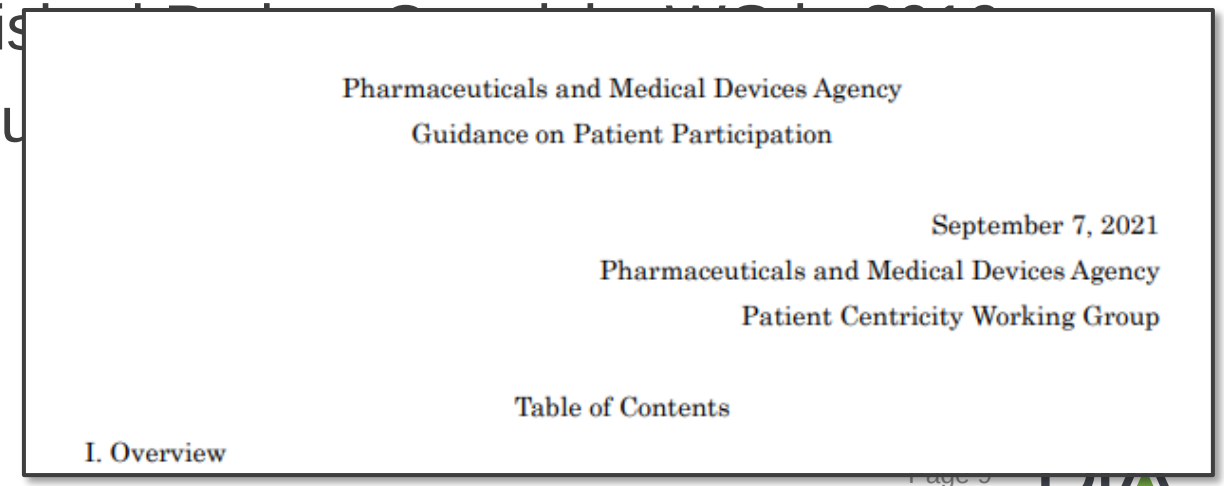
- Conducting a domestic clinical trial in Japan may lead to delay of the approval, but
  - Participating in a clinical trial can be a therapeutic option for patients in Japan
  - Conducting an expanded trial is encouraged for a drug with high medical need

✓"*If a high social demand for conducting an expanded trial … , it is desirable to consider conducting an expanded trial or preparing its protocol from the stage of preparing the protocol of its main trial.*"*

*: Clinical Trials Conducted on Ethical Grounds -Japanese Compassionate Use System- , PSEHB/ELD Notification No. 0122-7, January 22, 2016, Provisional Translation (as of December 2018)

# PMDA is Open for Discussion

- PMDA recognizes the importance of accountability for own decisions
- Scientific discussion is welcome
- Still we have limited channel for discussion with patients
- However, we are opening the door
  - PMDA establis
  - Released a gu
    2021



Pharmaceuticals and Medical Devices Agency

Guidance on Patient Participation

September 7, 2021

Pharmaceuticals and Medical Devices Agency

Patient Centricity Working Group

Table of Contents

I. Overview

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