Rare Disease Cures Accelerator-Data and Analytics Platform Virtual Workshop 2020
Role of integrated data and advanced analytics to accelerate medical product development:
A Case Study in Polycystic Kidney Disease

Pravin Jadhav
Global Development Leader
Otsuka Pharmaceutical Development & Commercialization
The opinions presented herein are those of the presenters, and are not necessarily the opinions of the presenters’ employers, or any affiliates of their employers, or of any collaborating companies.
Agenda

- ADPKD: Unmet Medical Need
- PKD Consortium: A Catalyst to ADPKD drug development
- Impact and Importance of Public-Private Partnership to Galvanize ADPKD Drug Development
Prevalence and Impact of ADPKD in the United States

The **most common** inherited renal disease¹

4th leading cause of ESKD
(after diabetes, hypertension, and glomerulonephritis)³;
~4.5% of ESKD cases⁴

ESKD = end-stage kidney disease

~140,000 patients currently diagnosed
Estimated prevalence is 4.3 per 10,000²,*

*Nearly 50% of all patients with ADPKD will reach ESKD by age 60⁵

¹. Torres VE et al. Lancet. 2007;369(9569):1287-1301

* Based on the National Ambulatory/Medical Care Survey (NAMCS)
Patients with ADPKD may remain asymptomatic for years while the disease progresses, likely due to compensatory hyperfiltration.

Up to 50% of the renal parenchyma can be lost before declines in renal function are clinically evident.

• cAMP
• Vasopressin
• mTOR
• AKT

2010: PKD Outcomes Consortium
Analyze patient data for qualification of TKV as a target endpoint for clinical trials

No therapies have been approved to treat PKD

Still waiting for treatments to slow or stop progression. Dialysis and transplantation remain the only options.
Otsuka—people creating new products for better health worldwide

ADPKD JOURNEY

2017
REPRISE Trial completed and Published in NEJM

2015-2016
TKV accepted as trial enrichment biomarker

2014-2015
Tolvaptan approved in three non-US regions for ADPKD

2013
NDA submitted for ADPKD, Complete Response Letter received

2007
First global pivotal trial in ADPKD

2006
TKV in ADPKD studies initiated

2004
Clinical dev. plan in ADPKD greenlighted

2003
Vaptans for ADPKD proposed at ASN

2002
NIH CRISP study begins

2001
TEMPO 3:4 Published in NEJM

2010
Tolvaptan approved in Japan for fluid retention in CHF

2009
Tolvaptan Approved for HN

2008
IND for tolvaptan in ADPKD filed in the US

2005
Otsuka People have committed decades of their lives and careers to bringing a treatment for ADPKD to patients and families with the disease. Where other companies might have given up, Otsuka has persevered for ADPKD patients.

Otsuka—people creating new products for better health worldwide

FOR INTERNAL USE ONLY. DO NOT DUPLICATE, DISTRIBUTE, OR USE IN DETAILING.
# Prognostic Biomarker Qualification: A Story of Perseverance

<table>
<thead>
<tr>
<th>Data Standards</th>
<th>Data Curation</th>
<th>Modeling</th>
<th>Model Refresh</th>
<th>Scientific Consensus</th>
<th>Regulatory Endorsement</th>
</tr>
</thead>
<tbody>
<tr>
<td>CDISC user guide</td>
<td>Data acquisition three patient registry datasets and two observational NIH studies</td>
<td>Developed, refined, and validated a joint model</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Received a Letter of Support from the FDA for the exploratory use of TKV in clinical trials for ADPKD

- FDA draft guidance (August, 2015) and EMA qualification opinion (October, 2015)
- Formal qualification of TKV as a prognostic biomarker (September, 2016)
PKD Consortium: A Catalyst to ADPKD drug development

**Patient Centric Mission**
To facilitate and accelerate drug development, leading to novel treatments reaching patients more quickly

**Scientific Rigor**
To evaluate TKV as a biomarker to predict progression of ADPKD
- Construct a quantitative biomarker dynamics and disease progression model to ascertain linkage between TKV progression and decline of kidney function (joint model)

**Regulatory Partnership**
To achieve the appropriate level of regulatory endorsement of TKV as a biomarker for use in ADPKD trials (patient selection and endpoint)

Streamlined ADPKD Drug Development
Impact and Importance of Public-Private Partnership to Galvanize ADPKD Drug Development

- **Regulatory acceptance**: Better understanding of disease and application of biomarkers across all stakeholders including health authorities.

- **Rapid implementation of biomarkers in clinical trials**: Accepted under IND vs qualified.

- **Patient stratification and disease monitoring biomarkers lead to efficient clinical trials, faster approvals**.

- **Change patient journey—precision therapeutic**.

- **Promoting diversity in clinical trials and supporting access for underserved populations**.
THANK YOU!

Don't forget to answer survey questions.

For more information, email rdcadap@c-path.org