Center for Orphan Drug Research (CODR)
College of Pharmacy
University of Minnesota

Reena Kartha, MS, PhD
Jim Cloyd, PharmD
Rare Diseases & Orphan Drugs

Rare Diseases
- Conditions affecting a small number of people
  - US FDA = prevalence of less than 200,000 (1 in 1650)
  - European Union = affects fewer than 1 in 2,000 people
- An estimated 25-30 million (1/11) in US (NIH)
- Majority (~2/3) affect children and 80% have a genetic origin
- Rare disorders are often devastating, life-threatening and difficult to diagnose
- ~7000+ distinct rare conditions (NIH) (and the # is growing)

Orphan Drugs
- Medications used to treat rare disease
- Only 5% of rare diseases have an approved therapy
- The Orphan Drug Act (1983) has resulted in # of FDA-approvals of orphan drugs: 26 of 52 novel drugs in 2021
Mission: To improve the care of individuals who have rare pediatric neurological disorders through research on new drug therapies; education of health professionals; and community engagement and advocacy relating to rare diseases and orphan drugs.

McGuire Translational Research Facility

Member of the University of Minnesota Rare Disease Center of Excellence
https://qa-cm.mhealthfairview.org/rare-diseases
CODR Personnel

Director: Jim Cloyd, PharmD

Associate Directors
Clinical Research: Robert Kriel, MD (Pediatric Neurology)
Translational Pharmacology: Reena Kartha, MS, PhD
Clin Pharm/Pharmacometrics: Lisa Coles, MS, PhD

Members
Dick Brundage, PharmD, PhD (Pharmacometrics)
Linda Krach, MD (Pediatric Rehab Medicine)
Jim White, MD (Adult Neurology)
Marie Kuker, RPh (Regulatory)
Sam Roiko, PhD (Pediatric Clinical Pharmacology)
Erica Barnes, MS (Ex Director, MN Rare Disease Advisory Council)

Laboratory Scientist: Usha Mishra, MS
Research Scientist: Marcia Terluk, PhD
Postdoctoral Fellow: Jaehyeok Roh, PharmD
ECP Administrator: Lori Endsley
CODR Research
CODR Areas of Research

Epilepsy Syndromes
- Infantile spasms
- Neonatal seizures
- Antiepileptogenesis
- Seizure emergencies

Spasticity
- Baclofen withdrawal

Neurologic/Psychiatric Disorders
- Adrenoleukodystrophy
- Gaucher Disease
- Parkinson’s Disease
- Non-suicidal Self Injury

Research Tools (humans & animals)
- Mechanisms of Action
- Biomarkers
- Formulations
- Pharmacokinetics & Metabolism
- Safety and Efficacy Studies
- Pharmacometrics
  - In-vitro (established cell lines)
  - Ex-vivo (patient-derived primary cells)
  - Animals (disease-specific)
CODR Model of Orphan Drug Development

- Preclinical Research (if required)
- Clinical Research
- Data Dissemination
- Commercialization (new molecules or formulations e.g. diazepam, topiramate and baclofen)
- Adopted into Clinical Practice
  - New uses: N-acetylcysteine;
  - Improved off-label use e.g. status epilepticus
- Product Approval
<table>
<thead>
<tr>
<th>Rare Disorder</th>
<th>Drug</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seizure clusters</td>
<td>Rectal Diazepam*</td>
<td>Approved</td>
</tr>
<tr>
<td>Seizure clusters</td>
<td>Intranasal diazepam prodrug</td>
<td>Pre-clinical studies</td>
</tr>
<tr>
<td>Status epilepticus</td>
<td>Intravenous allopregnanolone</td>
<td>Pre-clinical</td>
</tr>
<tr>
<td>Bridge therapy and neonatal seizures</td>
<td>Intravenous topiramate*</td>
<td>Phase I healthy volunteer study</td>
</tr>
<tr>
<td>Spasticity</td>
<td>Intravenous baclofen*</td>
<td>NDA submitted</td>
</tr>
<tr>
<td>Gaucher disease Type I</td>
<td>Oral N-acetylcysteine</td>
<td>Studies in healthy volunteers and patients</td>
</tr>
<tr>
<td>Neuronopathic Gaucher disease</td>
<td>Oral N-acetylcysteine amide</td>
<td>Pre-clinical studies</td>
</tr>
<tr>
<td>Adrenal insufficiency.</td>
<td>Rescue Therapy</td>
<td>Pre-clinical studies</td>
</tr>
<tr>
<td>Non-suicidal self-injury**</td>
<td>Oral N-acetylcysteine</td>
<td>Studies in patients</td>
</tr>
<tr>
<td>Adrenoleukodystrophy</td>
<td>Nervonic acid</td>
<td>Pre-clinical studies</td>
</tr>
</tbody>
</table>

*Designated by the FDA as an orphan product **not a rare disorder
CODR Education
CODR Education Activities

- Presentations at National and International Conferences
  - National Organization of Rare Disorders
  - European Infrastructure for Translational Medicine
  - Indian Society for Inborn Errors of Metabolism
  - American College of Clinical Pharmacy
  - FDA Workshops on Orphan Designation
  - Gaucher Community Alliance
- Center for Orphan Drug Research Weekly Seminars
- Lectures-Pharmacy students, Graduate Students
- Medical School, Healthcare Professionals
- Research Clerkships
  - Pharmacy and Graduate Students
- University of Minnesota Undergraduate Course
RARE DISEASES: WHAT IT TAKES TO BE A MEDICAL ORPHAN
Fall 2022, 3 Credits
Course Director: Reena Kartha, MS, PhD

Grand Challenge Curriculum
3 credit courses • Open to all students • Meet Liberal Education theme requirements

GCC 1906

Rare Disease: What it Takes to Be a Medical Orphan

What if you are born with a condition, which very few people know about and for which there are no cures? Or what if there is a cure, but it is very expensive and you have to take it throughout your

Course Details

Meeting Time: Spring 2020, TBD
Location: East Bank
Topics: economics, public policy, healthcare, business, pharmaceuticals
Credits: 3
Prerequisites: Freshman or first-year
Community Engagement and Advocacy

Interactions with Patient Advocacy Organizations
Annual Rare Disease Day Program
Rare Disease Play
Rare Disease Day Programs
Co-sponsors: UMN Stem Cell Institute and CODR

Past Program Themes
• Gene Therapy
• Telehealth
• Care Transition from Childhood to Adulthood
• Patient-focused Drug Development

3/2/2023, McNamara Alumni Center
University of Minnesota
Community Engagement and Advocacy

Rare: Stories of Dis-ease

The production and performance of a play done through a collaboration among the University of Minnesota Department of Theater Arts and Dance, CODR, and the Sod House Theater

Director: Luverne Seifert
Dramaturg: Sonja Kuftinec
Playwright: Kevin Kling