Welcome

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May 4, 2017
Agenda

• Opening Remarks
• Setting the context
  – Overview of FDA’s Patient-Focused Drug Development
  – Overview of Autism
  – Road from PFDD Meetings to Clinical Trial Endpoints
  – Overview of Discussion Format
• Discussion Topic 1
• Break
• Discussion Topic 2
• Open Public Comment
• Closing Remarks
Opening Remarks

Ellis Unger, MD
Director, Office of Drug Evaluation I
Office of New Drugs
Center for Drug Evaluation and Research
U.S. Food and Drug Administration

May 4, 2017
FDA’s Patient-Focused Drug Development Initiative

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Center for Drug Evaluation and Research
U.S. Food and Drug Administration

May 4, 2017
Patient-Focused Drug Development under PDUFA V

- FDA is developing a more systematic way of gathering patient perspective on their condition and available treatment options
  - Patient perspective helps inform our understanding of the context for the assessment of benefit-risk and decision making for new drugs
  - Input can inform FDA’s oversight both during drug development and during our review of a marketing application

- Patient-Focused Drug Development is part of FDA commitments under the fifth authorization of the Prescription Drug User Fee Act (PDUFA V)
  - FDA is convening 24 meetings on specific disease areas in FY 2013-2017
  - Meetings will help develop a systematic approach to gathering patient input
Disease Areas to be the focus of meetings for FY 2013-2017

<table>
<thead>
<tr>
<th>Fiscal Year 2013</th>
<th>Fiscal Year 2014</th>
<th>Fiscal Year 2015</th>
<th>Fiscal Year 2016-2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Chronic fatigue syndrome/myalgic encephalomyelitis</td>
<td>• Sickle cell disease</td>
<td>• Female sexual dysfunction</td>
<td>• Non-tuberculous mycobacterial lung infections</td>
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<tr>
<td>• HIV</td>
<td>• Fibromyalgia</td>
<td>• Breast cancer</td>
<td>• Psoriasis</td>
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<tr>
<td>• Lung cancer</td>
<td>• Pulmonary arterial hypertension</td>
<td>• Chagas disease</td>
<td>• Neuropathic pain associated with peripheral neuropathy</td>
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<td>• Narcolepsy</td>
<td>• Inborn errors of metabolism</td>
<td>• Functional gastrointestinal disorders</td>
<td>• Patients who have received an organ transplant</td>
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<tr>
<td></td>
<td>• Hemophilia A, B, and other heritable bleeding disorders</td>
<td>• Huntington’s disease and Parkinson’s disease Alpha-1 antitrypsin deficiency</td>
<td>• Sarcopenia</td>
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<tr>
<td></td>
<td>• Idiopathic pulmonary fibrosis</td>
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<td>• Autism</td>
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<td></td>
<td></td>
<td></td>
<td>• Alopecia areata</td>
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<tr>
<td></td>
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<td></td>
<td>• Hereditary angioedema</td>
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</table>

*To be announced*

- Alopecia areata
- Hereditary angioedema
“Voice of the Patient” Reports

- Following each meeting, FDA publishes a Voice of the Patient report that summarizes the patient testimony at the meeting, perspectives shared in written docket comments, as well as any unique views provided by those who joined the meeting webcast.

- These reports serve an important function in communicating to both FDA review staff and the regulated industry what improvements patients would most like to see in their daily life.

- FDA believes that the long run impact of this program will be a better, more informed understanding of how we might find ways to develop new treatments for these diseases.
Overview of Autism

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Deputy Director, Division of Psychiatry Products
Office of New Drugs
Center for Drug Evaluation and Research
U.S. Food and Drug Administration

May 4, 2017
Outline

• What is Autism Spectrum Disorder (ASD)?
• Who is at risk for ASD?
• What are the clinical manifestations?
• How many people are affected in the US?
• Treatment?
• Challenges in drug development for ASD
Autism Spectrum Disorder

• Persistent deficits in social communication and social interaction across multiple contexts

• Restricted, repetitive patterns of behavior, interests, or activities

Autism Spectrum Disorder

• Symptoms must be present in the early developmental period (but may not become fully manifest until social demands exceed limited capacities, or may be masked by learned strategies in later life).

• Symptoms cause clinically significant impairment in social, occupational, or other important areas of current functioning.

• These disturbances are not better explained by intellectual disability (intellectual developmental disorder) or global developmental delay.

Who is at Risk?

- Causes of ASD are unknown.
- Likely many causes for multiple types of ASD.
- Environmental, biologic and genetic factors likely play a role
- Individuals who have a sibling with ASD are at a higher risk of also having ASD.
- Common in certain genetic or chromosomal conditions (e.g., Fragile X Syndrome, tuberous sclerosis)
- Children born to older parents are at greater risk for having ASD.

www.cdc.gov/ncbddd/autism/facts.html
Clinical Manifestations

Children or adults with ASD might:

– not point at objects to show interest
– not look at objects when another person points at them
– have trouble relating to others or not have an interest in other people at all
– avoid eye contact and want to be alone
– have trouble understanding other people’s feelings or talking about their own feelings
– prefer not to be held or cuddled
– appear to be unaware when people talk to them, but respond to other sounds
– repeat or echo words or phrases said to them

www.cdc.gov/ncbddd/autism/facts.html
Clinical Manifestations (con’t.)

• Children or adults with ASD might:
• be very interested in people, but not know how to talk, play, or relate to them
• have trouble expressing their needs using typical words or motions
• not play “pretend” games
• repeat actions over and over again
• have trouble adapting when a routine changes
• have unusual reactions to the way things smell, taste, look, feel, or sound
• lose skills they once had (for example, stop saying words they were using)

www.cdc.gov/ncbddd/autism/facts.html
How Common is ASD?

### Identified Prevalence of Autism Spectrum Disorder

**ADDM Network 2000 – 2012**

**Combining Data from All Sites**

<table>
<thead>
<tr>
<th>Surveillance Year</th>
<th>Birth Year</th>
<th>Number of ADDM Sites Reporting</th>
<th>Prevalence per 1,000 Children (Range)</th>
<th>This is about 1 in X children...</th>
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</thead>
<tbody>
<tr>
<td>2000</td>
<td>1992</td>
<td>6</td>
<td>6.7 (4.5–9.9)</td>
<td>1 in 150</td>
</tr>
<tr>
<td>2002</td>
<td>1994</td>
<td>14</td>
<td>6.6 (3.3–10.6)</td>
<td>1 in 150</td>
</tr>
<tr>
<td>2004</td>
<td>1996</td>
<td>8</td>
<td>8.0 (4.6–9.8)</td>
<td>1 in 125</td>
</tr>
<tr>
<td>2006</td>
<td>1998</td>
<td>11</td>
<td>9.0 (4.2–12.1)</td>
<td>1 in 110</td>
</tr>
<tr>
<td>2008</td>
<td>2000</td>
<td>14</td>
<td>11.3 (4.8–21.2)</td>
<td>1 in 88</td>
</tr>
<tr>
<td>2010</td>
<td>2002</td>
<td>11</td>
<td>14.7 (5.7–21.9)</td>
<td>1 in 68</td>
</tr>
<tr>
<td>2012</td>
<td>2004</td>
<td>11</td>
<td>14.6 (6.2–24.6)</td>
<td>1 in 68</td>
</tr>
</tbody>
</table>

[www.cdc.gov/ncbddd/autism/data.html](http://www.cdc.gov/ncbddd/autism/data.html)
Treatment

• No FDA-approved drugs for the core symptoms of ASD
  – Drugs are approved for treatment of irritability associated with autism
• Mainstay of treatment is behavioral therapy
  – Applied Behavior Analysis (ABA)
  – Early Start Denver Model
  – Developmental, Individual Differences, Relationship-Based Approach (DIR; also called "Floortime")
  – Treatment and Education of Autistic and related Communication-handicapped Children (TEACCH)
  – Others

www.cdc.gov/ncbddd/autism/treatment.html ; www.autismspeaks.org/what-autism/treatment
Challenges to Drug Development

• Pathophysiology is unknown
• Likely many causes for many “autisms”
• Best endpoints for clinical trials unclear
• How long does it take to observe a change?
• Is there a developmental window for effective intervention?
• Where along the spectrum is intervention necessary?
Conclusions

• Prevalence of ASD has been increasing in the US, recently appears to have stabilized
• No FDA-approved drugs for core symptoms of ASD
• **Unmet** medical need
• Many challenges to drug development
The Road from Patient-Focused Drug Development Public Meetings to Clinical Study Endpoints

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Clinical Outcome Assessments Staff
Office of New Drugs
Center for Drug Evaluation and Research
U.S. Food and Drug Administration
Disclaimer

The views expressed in this presentation are those of the speaker, and do not necessarily represent an official FDA position.
But...
I need a valid assessment.
Pathways for FDA Clinical Outcome Assessment Review & Advice

1. IND/NDA/BLA Pathway
   - **Within** an individual drug development program
   - Investigational New Drug (IND) submissions to FDA
   - Potential to result in *labeling* claims

2. DDT COA Qualification Pathway
   - **Outside** of an individual drug development program
   - Development of novel COAs for use in multiple drug development programs addressing unmet measurement needs
   - Potential to result in *qualification* of COA

3. Critical Path Innovation Meetings Pathway
   - **Outside** of an individual drug development program
   - Potential for *general CDER advice* on specific methodology or technology (e.g., PRO) in its early stages of development

DDT = Drug Development Tool; COA = Clinical Outcome Assessment; PRO = Patient-Reported Outcome
NDA = New Drug Application; BLA = Biologics Licensing Application
Key Takeaways

- PFDD meetings are a “starting point” for developing patient-focused outcome measures and endpoints

- The outcomes of PFDD meetings will support and guide FDA risk-benefit assessments in drug reviews

- Individual and caregiver input ultimately helps determine:
  - **WHAT** is measured to provide evidence of treatment benefit
  - **HOW** best to measure concepts in a clinical study
  - **WHAT** a meaningful improvement is in treatment benefit
Relevant Resources

- FDA COA Staff Website: [http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm349031.htm#Endpoints](http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm349031.htm#Endpoints)


Overview of Discussion Format

Sara Eggers, PhD
Office of Strategic Programs
Center for Drug Evaluation
U.S. Food and Drug Administration

May 4, 2017
Discussion Overview

Topic 1: Health Effects and Daily Impacts of Autism
- What health effects are most challenging for you/your child?
- How do these health effects impact your/your child’s life day to day?
- How have your/your child’s experiences with autism changed over time?

Topic 2: Current Approaches to Treatment
- Are you/your child currently pursuing any interventions or treatments for autism? If so, what are your/your child’s goals for treatment?
- How well do your current treatments meet these goals?
- What would you consider to be a meaningful benefit of any treatment? What type and how much improvement would be impactful?
- What are the key things you think about when deciding whether to start a new treatment?
Discussion Format

• We will kick off our discussion with comments from a panel of individuals and family members
  – The purpose is to set context for a broader discussion with the audience
  – Panel commenters reflect a range of experiences with autism
  – Some panelists are affiliated with advocacy or support organizations

• We will then broaden the dialogue to include individuals and family members in the audience
  – The purpose is to build on the experiences shared by the panel
  – We will ask questions and invite you to raise your hand to respond
  – Please state your name before answering
Discussion Format, continued

• You’ll have a chance to answer “polling” questions
  – Their purpose is to aid our discussion
  – In-person participants, use the “clickers” to respond
  – Web participants, answer the questions through the webcast
  – Individuals or family members only, please

• Web participants can add comments through the webcast
  – Although they may not all be read or summarized today, your comments will be incorporated into our summary report
  – We’ll occasionally go to the phones to give you another opportunity to contribute
Send us your comments!

• You can send us comments through the “public docket”
  – The docket will be open until July 5, 2017
  – Share your experience, or expand upon something discussed today
  – Comments will be incorporated into our summary report
  – Anyone is welcome to comment


Or Search “autism FDA public meeting” on www.regulations.gov

And Click Comment Now!
Resources at FDA

A first stop for individuals and families:

- **FDA Office of Health and Constituent Affairs**
  - Contact: PatientNetwork@fda.hhs.gov, (301) 796-8460
  - Liaison between FDA and stakeholder organizations
  - Runs the Patient Network and Patient Representative Program

A first stop for advocacy and support healthcare providers:

- **CDER Professional Affairs and Stakeholder Engagement (PASE)**
  - Contact: CDERPASE@fda.hhs.gov
  - Facilitates communication and collaboration between CDER and stakeholders on issues in drug development, review, and safety.

**Check it out! May 12, 2017 Workshop: How to Navigate CDER**
(google Navigate CDER)
Discussion Ground Rules

• We encourage all individuals and family members to contribute to the dialogue

• FDA is here to listen

• Discussion will focus on autism health effects and treatments
  – Open Public Comment Period is available to comment on other topics

• The views expressed today are personal opinions

• Respect for one another is paramount

• Let us know how the meeting went today; evaluation forms are available at the registration table
Where do you live?

A. Within Washington, D.C metropolitan area

B. Outside of Washington, D.C. metropolitan area
I am:

1. A self-advocate - an individual with autism
2. A family member of an individual(s) with autism
Do you/your loved one with autism identify as:

A. Male  33%
B. Female  33%
C. Other  33%
What is your/your loved one’s age?

A. Younger than 5
B. 5 – 12
C. 13 – 17
D. 18 – 29
E. 30 – 39
F. 40 – 49
G. 50 – 59
H. 60 or greater
Discussion Topic 1
Health Effects and Daily Impacts of Autism

Sara Eggers
Facilitator

May 4, 2017
Topic 1 Panel Participants

• Nadine Morris
• Zoe Gross
• Sharrill Hemry
• Tom Frazier
• Sara Luterman
• Kiely Law
Nadine’s daughter Anna is 5 years old.
Topic 1 Panel Participants

• Nadine Morris
• Zoe Gross
• Sharrill Hemry
• Tom Frazier
• Sara Luterman
• Kiely Law
Sharrill’s children

SEPTEMBER 2009

THE LAST TIME ALL THREE CHILDREN HAD
RELATIVELY HEALTHY IMMUNE SYSTEMS
AT THE SAME TIME
Tom’s 13 year-old son
Topic 1 Panel Participants

• Nadine Morris
• Zoe Gross
• Sharrill Hemry
• Tom Frazier
• Sara Luterman
• Kiely Law
Kiely’s son Isaac is 24 years old
Which **health effects** of autism are most challenging to you/your loved one? 
*Please choose up to three health effects.*

A. Irritability or disruptive behaviors  
B. Cognitive impairment  
C. Social Impairments  
D. Communication difficulties  
E. Repetitive Behaviors  
F. Sleep Issues  
G. Depression or Anxiety  
H. Gastrointestinal symptoms  
I. Other health effects not mentioned
What aspects of your/your loved one’s daily life are most negatively affected by autism?

Please choose up to three impacts.

A. Ability to participate or perform daily activities (such as work, school, sports, drive, hobbies)
B. Ability to care for self or family
C. Risks to safety of self or others
D. Impact on relationships with friends and family
E. Stigma and social discrimination
F. Emotional impacts
G. Burden of medical care
H. Other impacts not mentioned
BREAK
Discussion Topic 2
Current Approaches to Treatment

Sara Eggers
Facilitator

May 4, 2017
Topic 2 Panel Participants

- Kathleen (Kit) Mead
- Brittany Reiger
- Susan Pannell
- Tom Hubbard
Susan’s son
Ben is 10 years old
Tom and Christine’s son
Ned is 29 years old
Have you/your loved one ever used any of the following to help reduce symptoms of autism? Check all that apply.

A. Prescription medications (such as anticonvulsants or psychiatric medications)
B. Psychotherapy and behavioral therapy (such as counseling or support groups)
C. Speech therapy
D. Physical therapy
E. Occupational therapy
F. Diet modifications
G. Other therapies not mentioned
H. I’ve never used any therapies
When considering treatment options, which of the following benefits would you/your loved one consider to be most important? Please choose up to three.

A. Reduced irritability and/or disruptive behaviors  
B. Reduced cognitive impairment  
C. Reduced social impairments  
D. Reduced communication difficulties  
E. Reduced repetitive behaviors  
F. Reduced sleep issues  
G. Reduced depression or anxiety  
H. Reduced gastrointestinal symptoms  
I. Other
When considering treatments, which ONE benefit would you/your loved one consider most important? Please choose one.

A. Reduced irritability and/or disruptive behaviors
B. Reduced cognitive impairments
C. Reduced social impairments
D. Reduced communication difficulties
E. Reduced repetitive behaviors
F. Reduced sleep issues
G. Reduced depression or anxiety
H. Reduced gastrointestinal symptoms
I. Other
Imagine that a new oral medication indicated to treat a core symptom associated with autism has recently been approved by FDA. Your doctor believes that you/your loved one may be a good candidate for this medication.

The medication requires administration every six hours and evaluation every eight weeks for dosage adjustment. The tablet can be crushed and mixed with food for ease of administration.

Common side effects of this medication include drowsiness, diarrhea, nausea and insomnia. Serious side effects such as respiratory tract infections and blood clots are rare, but possible.

What first thoughts come to mind as you hear this scenario?

What questions would you ask your doctor about this treatment?
Which **TWO** would you rank as most important to your decision about whether to use a medication to help manage autism?

A. How the medication is administered
B. The frequency and length of treatment
C. Your access to treatment (such as insurance coverage)
D. Whether the medication was studied in children
E. How much the medication showed benefit for a specific symptom
F. Common side effects
G. Rare, but serious side effects
H. You/your loved one’s previous response to a similar treatment
I. Whether other treatment options are available
Closing Remarks

Mitchell Mathis, MD
Director, Division of Psychiatry Products
Office of New Drugs
Center for Drug Evaluation and Research
U.S. Food and Drug Administration

May 4, 2017