Outline

• What’s been happening?
• Who is involved?
• What do I need to know?
• What can I expect?
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Process

May-Aug 2019
Design Study

Sept 2019
Radiation Safety Review

Oct 2019
Scientific Review

Nov 2019
Pre-IRB Review
Process

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Design Study

Sept 2019
Radiation Safety Review

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Scientific Review

Nov 2019
Pre-IRB Review

Jan 2020
Respond to pre-IRB comments
• FDA submission

Jan-Feb 2020
Submit to IRB

Feb-Mar 2020
Respond to IRB/FDA comments

Mar-Apr 2020
Enroll patients
Process

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Design Study

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Radiation Safety Review

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Nov 2019
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Jan 2020
Submit to IRB

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- FDA submission

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May-Aug 2019

Sept 2019

Oct 2019

Nov 2019

Jan 2020

Feb-Mar 2020

Mar-Apr 2020
AKT Inhibitor Miransertib in Proteus Syndrome
Trial support

- Databases – keeping track of information
  - Safety information (side effects)
  - Procedures and evaluations
  - Results
- People and things
  - Research coordinator
  - Drug supply
  - Sample kits
  - Quantificare camera
Outline

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Who is involved?

MOSAIC Clinical Trial - ArQule - ArQule
https://www.arqule.com › mosaic-clinical-trial
Genetic mutations can lead to many different diseases. At ArQule, we're currently conducting the MOSAIC clinical trial (Miransertib in Overgrowth Syndromes in ...}

ArQule Announces First Patient Dosed in ... - ArQule, Inc.
investors.arqule.com › news-releases › news-release-details › arqule-annou...
Oct 2, 2019 - The MOSAIC trial represents the first registrational trial of its kind for patients suffering from these rare genetic conditions characterized by ...
Who is involved?

ArQule, a wholly-owned subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA (known as MSD outside the United States and Canada)

CLICK TO VISIT MERCK.COM

www.MERCK.com
Who is involved?

- ArQule → Merck
  - Support and collaboration
  - Working on way to see MOSAIC patients for NIH-specific tests
- NIH
  - IRB (ethics board)
  - Safety monitoring board
  - Regulatory monitoring
  - Data management
  - Clinicians and departments
  - Our team
Eligibility

• Cohort 1:
  • 3-16 years old
  • CCTN on the bottom of the foot

• Cohort 2:
  • 3-25 years old

• Cohort 3:
  • 3-25 years old
  • Have taken miransertib before
Person with Proteus syndrome

26 or older
- Not eligible

25 or younger → with measurable disease
- Already taken Miransertib → Cohort 3
  - With foot CCTN
  - Without foot CCTN → Cohort 2
  - 17-25 years old

- 3-16 years old
  - With foot CCTN → Cohort 1
    - 25 or younger
AIM Proteus vs. MOSAIC

AIM Proteus
• ONLY Proteus
• 4 months longer
• Measuring CCTN in two ways
• Systematic measurement of other things

MOSAIC
• Proteus and PROS
• Measuring CCTN one way
• Measuring other things if possible
CCTN

Quality of life

Lung cysts and function

Bony overgrowth

MOSAIC

AIM Proteus

Targeted therapy at the NIH
Outline

• What’s been happening?
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• **What do I need to know?**
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What is involved?

• Trial length
  • Planned for 4 years

• Dosing
  • Daily pill
  • “Cycles” = 28 days
  • First 3 cycles = 15mg/m²
  • Cycle 4 until end = 25mg/m²
What is involved?

• NIH visits for
  • Safety visits
  • Efficacy measurements
    • “Is it working?”

• Symptom and medication diaries at home

• Side effects
  • Increased blood sugar
  • Tummy troubles
  • Rash
  • Dry mouth
How many visits are we talking about?

• Cycle 1-14 (year 1) → 9 visits
• Cycle 15-27 (year 2) → 4 visits
• Cycle 28-40 (year 3) → 4 visits
• Cycle 41-52 (year 4) → 4 visits
How long is each visit?

- Most visits are just one day
  - Exam
  - Short tests
  - Blood draw
- One 3-5 day visit every 6 months
  - Exam
  - Blood draw
  - More and longer tests
Who can come? Will I need to pay?

- Both parents at first and annual visits
- Siblings welcome but may not have flights paid for
- Flights, lodging, most meals covered
- Merck may offer additional support

→ Tell us what you need and we will try to help
Which tests will you do?

Short visits
• Physical exam
• Blood tests
• Urine tests
• Count pills, new prescription
Which tests will you do?

Short visits
- Physical exam
- Blood tests
- Urine tests
- Count pills, new prescription

Every 6 months
- Photos
  - Routine
  - Special camera
- MRIs
- CT scans
- Lung function tests
- X-rays

Tests not exactly the same for each person
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For now…

- NIH will continue working
- We will update Kim, the PSF, and individual families as needed
- Call us with questions

301-443-3962
proteustrial@nih.gov
In the future…

- Results will be reported as soon as possible
- Results will inform next steps
  - Maybe another drug might work better
  - Maybe different dose needed
From trial to approval

- Collect Data
- Enroll patients
- Analyze Data
- Interim analysis
- Approval
- Marketing