Showcasing biotech success stories: digital endpoints in clinical trials

DIGITAL MEDICINE SOCIETY

Tuesday, January 28, 2025

11:00 AM - 12:00 PM ET

Lauren Alani
Director, Digital Innovation
Seuss+

Prashant Bansal
Senior Director, Imaging & Digital Biomarkers
Dyne Therapeutics

Peter Fernandes
Former CEO
Bellerophon Therapeutics

Sarah Valentine
Partnerships Lead
Digital Medicine Society (DiMe)
Moderator

81 Sponsors have collected **505** digital endpoints

Primary, Secondary or Other/Exploratory

Source: Library of Digital Endpoints

Last updated November 7, 2024

But first, housekeeping

- Please note: **today's session is being recorded**
    - Slides and recording will be available on DiMe's webinar page after the session
- To ask a question for discussion during live Q&A, please either:
    - **'Raise your hand'** in the Reactions and the moderator will unmute you to ask your question live, or
    - **Type your question** into the chat box

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Cut Slides - Prashant Case Study

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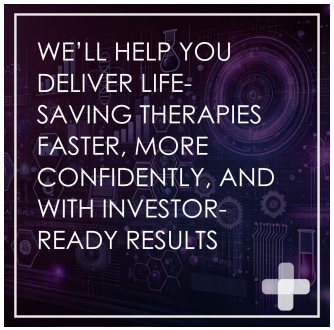
Introduction: Seuss+



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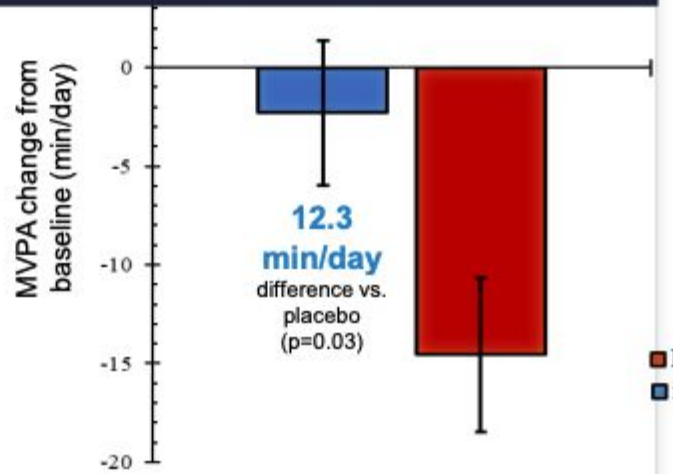
"Innovate with Regulators – Taking the plunge with Actigraphy in the US"

Peter Fernandes – Former Chief Executive Officer & Chief Regulatory, Safety & Quality Officer
Bellerophon Therapeutics

- A 5-year Journey with obtaining FDA (CDER's) acceptance and implementation of a DHT measure - Actigraphy as a single primary endpoint for Phase 3 registration study with a significantly reduced sample size.
  - Saving is Both Cost and Time
  - Actigraphy Exploratory Anchoring Analysis:
    - PGIS/PGIC – a preliminary read

Phase 2 data supports use of MVPA measurement as primary endpoint for Phase 3 trial

Moderate to vigorous physical activity (MVPA; min/day) maintained on iNO45 while placebo patients deteriorate



MMRM analysis based on change from Month 1 to Month 4; data points and error bars = LS mean and standard error; p-value not adjusted for multiplicity

14.6 min/day decline in MVPA on placebo; 2.3 min/day decline in MVPA on iNO45 at month 4

- 12.3 min/day (~21%) difference in time spent in MVPA as compared to placebo
- 10-20% change in actigraphy parameters estimated to be clinically relevant in diseased populations (fILD, COPD, heart failure)‡

Similar trend seen in overall activity

- iNO45 group remained stable
- ~6% placebo adjusted difference (89.4 counts/min)

King et al., Annals of American Thoracic Society, 2022, 19, 4, 594-602, https://doi.org/10.1513/AnnalsATS.202107-864OC; †. Rivera-Lebron, Advances in Pulmonary Hypertension, 2013, 12:127-134; "IPF Voice of Patient", FDA Meeting and Report, 2015; ‡ Hur, et al, 2019; Teylan et al., Chron Respir Dis., 2019, 16:1479973118816424; Demeyer et al., PLoS One. 2016;11:e0154587; Shoemaker MJ, World Journal of Cardiovascular Diseases; 2012., 129-35

FDA Discussion and Agreement (reached April 2019) on MVPA as a Primary Endpoint in Phase 3 IPF Study

Question 2:

Is FDA in agreement with the proposed Pivotal Phase 3 study with **Physical Activity** parameters as measured by **Actigraphy** as the Primary Endpoint?

FDA Response to Question 2:

Yes, we agree with your study design.

Additional FDA recommendations: Carefully specify the primary endpoint "change (%) in minutes of moderate activity (MVPA) measured via actigraphy from baseline to week 16".

Cohort 2 Re-analysis Based on Final REBUILD Compliance Criteria for Actigraphy

- **Initial trial size of 300 patients** was initially powered to achieve a p-value of 0.01
- Actigraphy Primary and first secondary endpoint now **powered (>90%) with just 140 patients**

Endpoint	Significance Level	Estimate of treatment effect	Sample size for 90% power	N=140 patients N=70/arm	N=300 patients N=150/arm	Reference Table (available in the Appendix)
MVPA (REBUILD Primary endpoint)	0.05	0.735 SD=1	N=80	99%	99%	Analysis based on Cohort 2 actigraphy data 8-2 Criteria Bi-Week 4 (weeks 7-16)
	0.01		N=114	95%	99%	
Overall Activity (REBUILD 1st Secondary endpoint)	0.05	0.591 SD=1	N=122	93%	99%	Analysis based on Cohort 2 actigraphy data 8-2 Criteria Bi-Week 4 (weeks 7-16)

Bi-weekly compliance defined as 8 days of which 2 are weekends, with wear-awake minutes of 600 or more minutes (10 hrs/day in a compliant day)

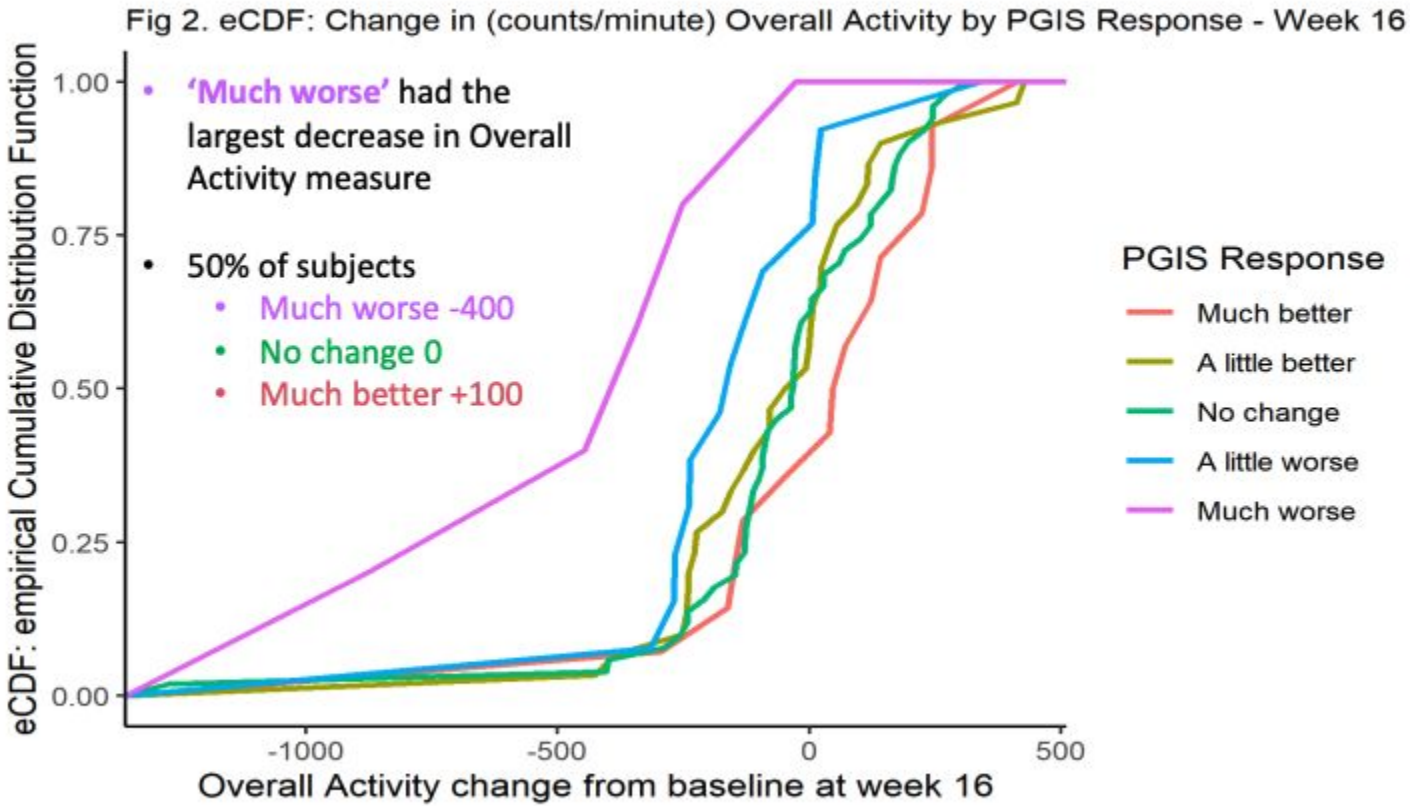
Cytel Report, Sample Size Considerations for PULSE-PHPF-001 (REBUILD study), July 20, 2022

REBUILD Trial Options June 2022 Capital Raise Needs

Options	Based US Current Sites		Considerations
300 pts	**$29.7M (78% dilution)** • **Topline Results by LR: Jun-2024**		• Highly powered for primary and secondary PRO endpoints • Potential for significant challenge in large capital raise under current market conditions
140 pts	**$0M (0% dilution)** • **Topline Results by May-23**		• Well powered for primary endpoint; secondary endpoints supportive • Submit FDA amendment on size reduction to 140 • Will need FDA agreement prior to implementation

Dilution based on fully diluted share count as of 5/31/22 and assumes 25% discount to market based on 6/22/22 close

Overall Activity (Actigraphy) vs PGIS Response Categories (All 145 subjects)



Lesson Learnt

- The history of innovations has taught us that the first iteration of progress is rarely perfect
    - But it shows us what can be possible

&

    - Gives us the opportunities to learn and iterate

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Breaking Barriers with Digital Health Technologies: Advancing CRS Risk Prediction

WEBINAR

Thursday, February 13

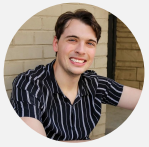
11 am - 12 pm ET

DATAcc

Digital Health Measurement Collaborative Community

by DiMe

Chris Medberry
Director, Global Regulatory Affairs Digital Health
The Janssen Pharmaceutical Companies of Johnson & Johnson



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Matt Ream
Executive Vice President, Marketing and Innovation
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Matt Wilkes
Senior Medical Director
Best Buy Health

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