Miami Investigator Meeting
Opening Presentation
Ben Zimmer, Priovant CEO

Priovant Background

Rarer High Morbidity/Mortality Indications Have Been Historically Neglected By JAKi Drug Development

JAK inhibitors approved or in industry-sponsored P3[1]

- Rheumatoid arthritis: **8**
- Psoriatic arthritis: **4**
- Ulcerative Colitis: **4**
- Myositis, uveitis, scleroderma, Behcet's, sarcoidosis, IgG4-RD, polychondritis, polymyalgia rheumatica: **0**

Brepocitinib Is Distinctively Optimized For Highly Inflammatory Conditions With High Morbidity/Mortality

- Optimal suppression of type I IFN
- Suppression of type I IFN, type II IFN, IL6, IL12, IL23 with single asset
- Oral once-daily administration
- Success in 6 pbo-controlled P2 studies across rheumatic, dermatologic, and GI indications

Priovant Created To Address This Need / Opportunity

- Dedicated to rarer autoimmune disease with higher morbidity/mortality and few available therapies of any mechanism/modality
- Initial focus on developing and commercializing brepocitinib for these indications
- Initial indication: dermatomyositis
  - ✓ Large unmet need
  - ✓ Strong clinical and mechanistic rationale
  - ✓ No approved targeted therapies of any modality; no other oral therapies in P3 development
- Strategy of moving directly into single P3 study to get an approved therapy as quickly as possible, given unmet need and strong rationale
  - ✓ VALOR: Largest interventional clinical study ever undertaken in dermatomyositis (N=225)

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1. Includes approvals / industry-sponsored development programs in any geography; excludes brepocitinib

Timeline & Key Priorities To Achieve Desired Brepocitinib Approval In DM

Enrollment Completion Tracking Mid-2024 → **VALOR Top-Line Readout (Mid-2025)** → **New Drug Application (End-2025)** → **Potential FDA Approval (End-2026)**

Subjects Enrolled = 155
Subjects In Screening = 30
Screenings Scheduled = 22
(As of Feb 29)

Tracking to wrap up screening sometime in May or June – please make effort to identify additional subjects to screen in March/April

Many clinical trials for investigational medicines that "should" work fail for reasons related to study design and/or execution

- We all need to work diligently to make sure that doesn't happen

Large focus of today's meeting: generating high quality data & set up study for success

We are now potentially less than 3 years away from potential approval of a once-daily oral treatment for DM in U.S.

Submission and potential approval timelines in other regions to follow shortly behind U.S.

Enrollment By Region

Region	Subjects Enrolled As Of Feb 29
United States	67 Subjects
Americas, ex-US	18 Subjects
Europe, Middle East	60 Subjects
Asia	10 Subjects

Shout-Out To Our Highest Enrolling Sites

Sites in countries represented at Miami IM that have enrolled at least 3 subjects (as of Feb 29)

Site/Institution Name	Country	Principal Investigator	Subjects Enrolled
Austin Neuromuscular Center	USA	Yessar Hussain, MD	7
Neuromuscular Clinic and Research Center, Arizona	USA	Kumaraswamy Sivakumar, MD	5
Mayo Clinic – Scottsdale	USA	Aaron Mangold, MD	5
Centro Internacional de Estudios Clinicos	Chile	Francisca Bozan Perez, MD	5
Hospital Angeles Clínica Londres	Mexico	Gabriel Medrano Ramirez, MD	4
Emory University	USA	Prateek Gandiga, MD, FACP	4
Rheumatology Associates of Oklahoma	USA	Latisha Heinlen, MD	4
Mayo Clinic – Jacksonville	USA	Jason Sluzevich, MD	3
Marietta Rheumatology Associates	USA	Roel Querubin, MD	3
University of Chicago	USA	Iazsmin Bauer Ventura, MD	3
Arthritis Center of North Georgia	USA	Brent Flickinger, MD	3
University of California, San Francisco	USA	Anna Haemel, MD	3

Enrollment Summary Thoughts

- Please make a concentrated effort coming out of this meeting to identify additional subjects for screening over next two months
- We ask that all sites work hard to try to get to at least 2 patients, but the most important priority is to only enroll eligible/appropriate patients (even if that means you don't get to two)
- Enrollment is not capped at any site; even if you already have 2, 3, or more subjects enrolled, please continue working to find additional patients
- We are here to help – some high-enrolling sites have found patients mostly on own, but in many cases high enrolling sites have benefited from very close involvement from Priovant team
  - Presentations this afternoon from Drs. Mangold and Gandiga, and Scott Jones from Priovant team
- Focus for remainder of morning is making sure we generate high-quality data
  - Detailed presentations from Drs. Aggarwal, Vleugels
  - Four broader themes: right patients, accurate assessments, steroid taper, appropriate use of rescue medication

Priority 1: Enrolling Right Patients

Risk Factor

It is difficult to demonstrate a drug effect over placebo for patients who are too mild or too severe

What We Can Do About It

Understand ***spirit & rationale*** of inclusion/exclusion criteria around disease severity and background medications; use your judgement as a clinical researcher around whether each patient is truly the right fit

Patients with mild skin & muscle disease*:* degree of improvement (i.e. TIS score) is capped for these patients → less opportunity for drug to show an effect, so especially important to manage risk of placebo response

- Make sure patient is not in the midst of a self-limiting flare that could resolve on its own
- Make sure there is no risk of a new background medication/dose still taking effect
- Pay extra attention to accuracy of ratings at screening and baseline
- Mild patients on background steroids that can be tapered during study are stronger candidates for inclusion

Patients with severe muscle disease: Risk of irreversible muscle damage limiting ability for drug to demonstrate benefit

- Even for patients who technically meet protocol cutoff (MMT8 > 80), use your independent medical judgement around degree to which muscle disease is driven by inflammation versus permanent damage

If you are not sure about whether a borderline patient is a good candidate for the study, we encourage you to consult with Priovant team in advance of screening

Priority 2: Accuracy Of Assessments

Risk Factor

DM endpoints are subjective clinical assessments subject to noise/variability

What We Can Do About It

1. Make sure to allocate appropriate investigator/rater time to thoughtfully conduct each assessment

2. Help us reduce variability across sites/patients (presentations by Drs. Aggarwal & Vleugels)

3. Help reduce variability within sites/patients by aiming to have a consistent rater throughout study

    - Same rater should perform screening, baseline, primary endpoint, and majority of assessments in between

Priority 3: Steroid Taper

Risk Factor

Steroid taper is most meaningful tool at our disposal to manage risk of placebo response during study; it also is valuable to demonstrate steroid-sparing effect of brepocitinib → if too many patients fail to successfully taper, jeopardizes our ability to generate a positive study

What We Can Do About It

1. In advance of week 12, proactively come up with a taper plan for each subject on background OCS
   - Subjects on >5mg/day: required taper to 5mg between weeks 12 and 36 (stable after week 36)
   - Subjects on ≤5 mg : optional taper (as investigator deems appropriate) to 0mg/day between weeks 12 and 36 (stable after week 36)

2. Help patients understand the importance of the taper for the study, as well as potential benefits for their own health given side effects of chronic steroid use

3. Make strong effort to successfully complete required taper; for more challenging cases, consult early with Priovant team to jointly come up with appropriate plan

Strong Taper Success Rate In Study So Far (87.5%) – Appreciate Continued Prioritization Of This Feature Of Protocol

Data as of Feb 29, 2024

155 Subjects enrolled

115 Subjects (74%) on OCS at Baseline

36 Subjects on OCS ≤ 5 mg

Optional taper; preferred goal where appropriate: taper to zero

Completed Taper Window	**4**
Achieved 0	2
Between 0 and 5mg	2
In Taper Window Now	**17**
In progress	4
Not Started	13
At 0	0

79 Subjects on OCS > 5 mg

Mandatory taper to ≤ 5 mg

Completed Taper Window	**18**
Achieved ≤5mg	16
In Taper Window Now	**33**
In progress	18
Not Started	2
At ≤5mg	13

Priority 4: Rescue Therapy & Prohibited Meds

Risk Factor

Must balance need to care for wellbeing of patients over 52-week pbo-controlled trial with fact that initiation of rescue medication or other new medications during study can drive placebo response and confound study results

What We Can Do About It

1. Take care that prohibited meds are not used unintentionally by patients
   - Remind patients not to use prohibited medications on their own that are OTC or where they may have leftover supply from previous prescription **(particular focus on topical steroids & oral steroids post-taper or beyond stable study dose)**
   - Remind any other physicians who see patient (e.g., PCP, referring physician) to consult with you before prescribing new medication, since patient is in a clinical trial

   Key area where study coordinators can play a big role – remind patient at each visit (and explain importance) and help remind investigators to remind patient

2. If you do feel that rescue therapy or a medical intervention not allowable under the protocol is needed, please consult with medical monitor before initiating treatment so that we can jointly determine the course of action that best serves the patient and the study (unless a medical emergency)
   - We have invested in having medical monitor be a senior member of the sponsor team who brings a partnership, rather than clerical, mindset

Dr. Ade Adeboye

Use Time Today To Continue To Get To Know The Priovant Team

~20 % of our company is in attendance!

Ade Adeboye

Whitney Holmes

Paul Mudd

Courtney Cupples

Noriko Iikuni

Lindsey Rios

Sergey Pavlenko

Scott Jones

Matt Ackermann

Sabrina Pogrebivsky

Drew Webster

Daniel Herz-Roiphe

David Tromblay

Ben Zimmer

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