



THE FORUM

For Collaborative ResearchSM

Berkeley's Hub for Regulatory Science

LF RLSE Project Overview

LF19 – Paris, France

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LF RLSE Project Timeline



-LF15
 - Continuous efforts to assess status of NIT data as “fit-for-purpose” for accelerated approval
 - “Show us the data”
- LF16 – Washington, DC
 - Standardizing NASH NITs
- LF17 – Paris, France
 - Forum RLSE Proposal Presentation 1
- LF18 – Washington, DC
 - Presentation 2
- LF19 – Paris France
 - Presentation 3

Multiple interactions with regulators

Clear signals that FDA DHN is prepared to consider NITs

What is new since LF18

- FDA DHN Publication
- BQP LOI (Echosense)



- Until clinical benefit confirmed, drugs are not SOC
- Demonstrating that NITs correlate with histology (or histologic response to therapy) may also be useful to support the mechanistic rationale by showing that the NIT may reflect the primary causal pathway(s) in MASH pathogenesis.
- A description of the mechanism of action of the drug, and how that relates to the understanding of the disease and the attributes measured by NITs should also be described
- Use of NITs to identify progression to cirrhosis could also be considered for development as a VSE.



Drug Approval (CDER)

- RLSE
- VSE
- Generally Accepted
- Qualified (BQP)

IVD (CDRH)

- Assay validation
- Clinical validation
- Clinical utility
- Cleared or approved (PMA)

For DRUG DEVELOPMENT



Accelerated Approval

- RLSE
- Qualification RL

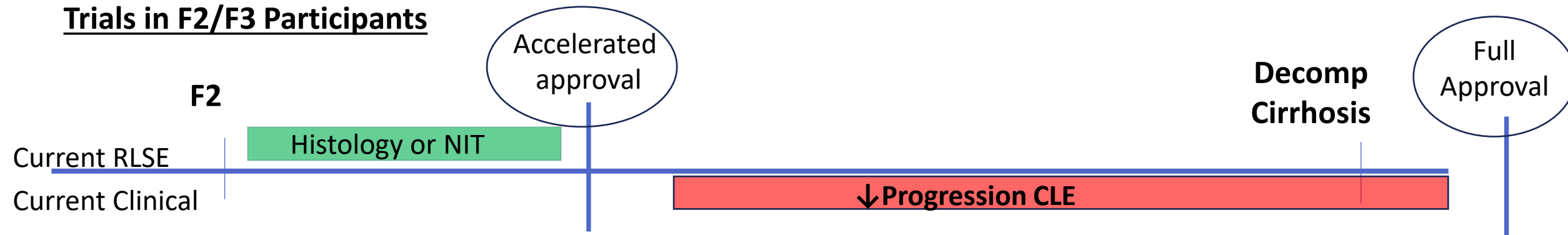
Full Approval

- VSE
- Generally accepted SE
- Qualified SE



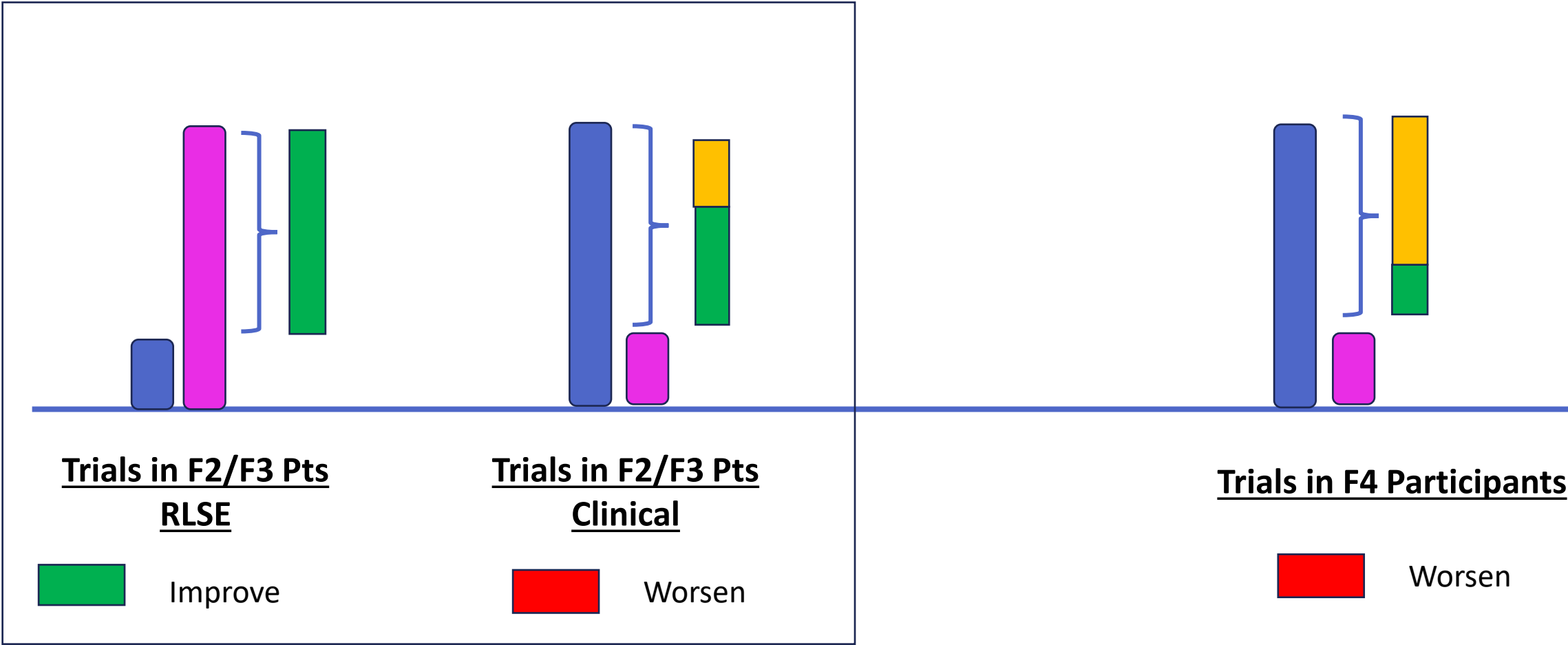
-  Improve
-  Stable
-  Worsen

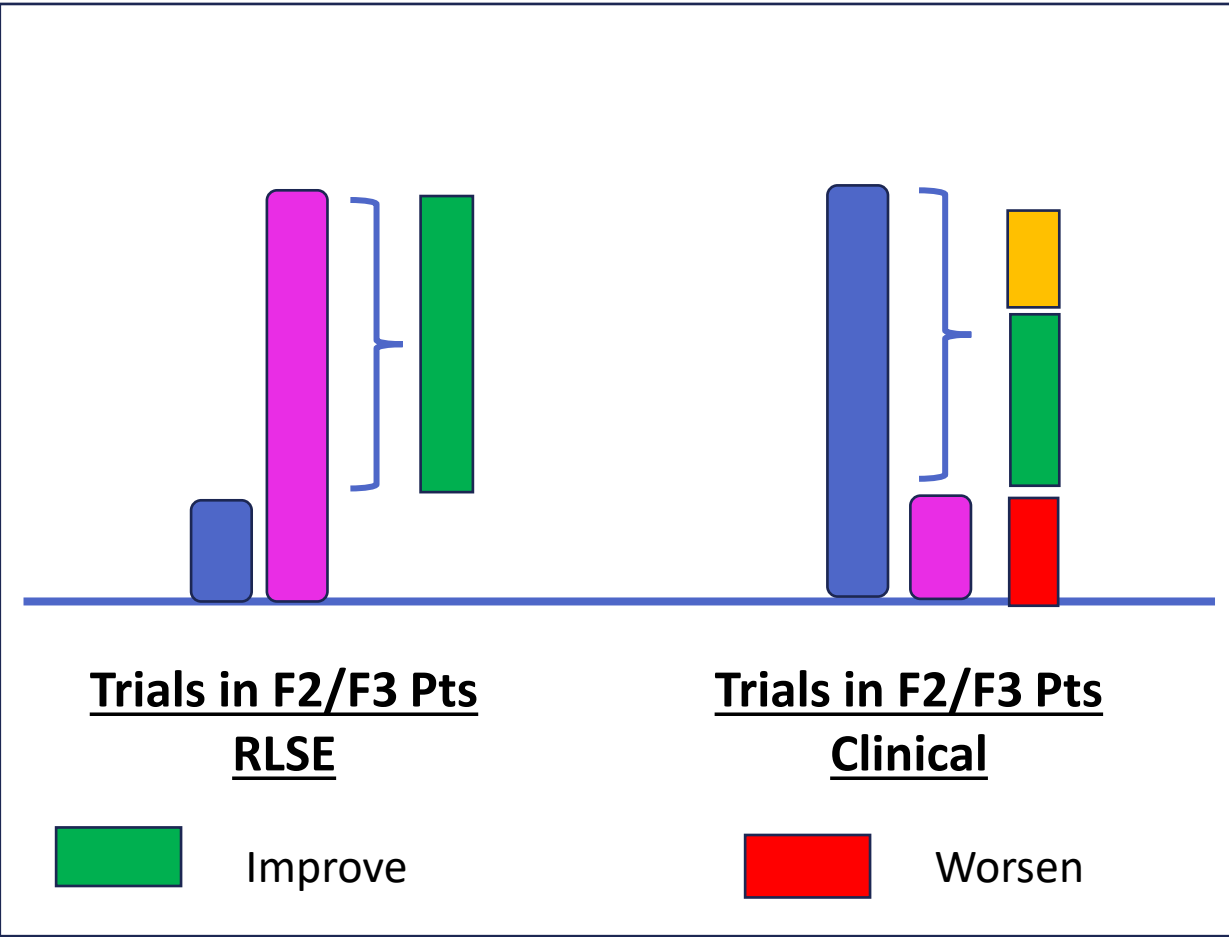
Trials in F2/F3 Participants



Trials in F4 Participants







**RLSE = improvement only
Correlate with
Disease improvement
AND
Disease stability**

TODAY

- Update on VCTE LOI
- Update on LF Project for F2/F3
 - Literature review
- Statistics
- NITs for progression to cirrhosis

