



Precision medicine: a whistle-stop tour before designing a trial with a biomarker threshold optimization!

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Once upon a time, on a mission to find a new bike...



One-size-fits-all?

Does not work for bikes, does not work for medicines either.

The 5Rs of **precision medicine**:

The Right patient

The Right medicine

The Right time

The Right dose

The Right route



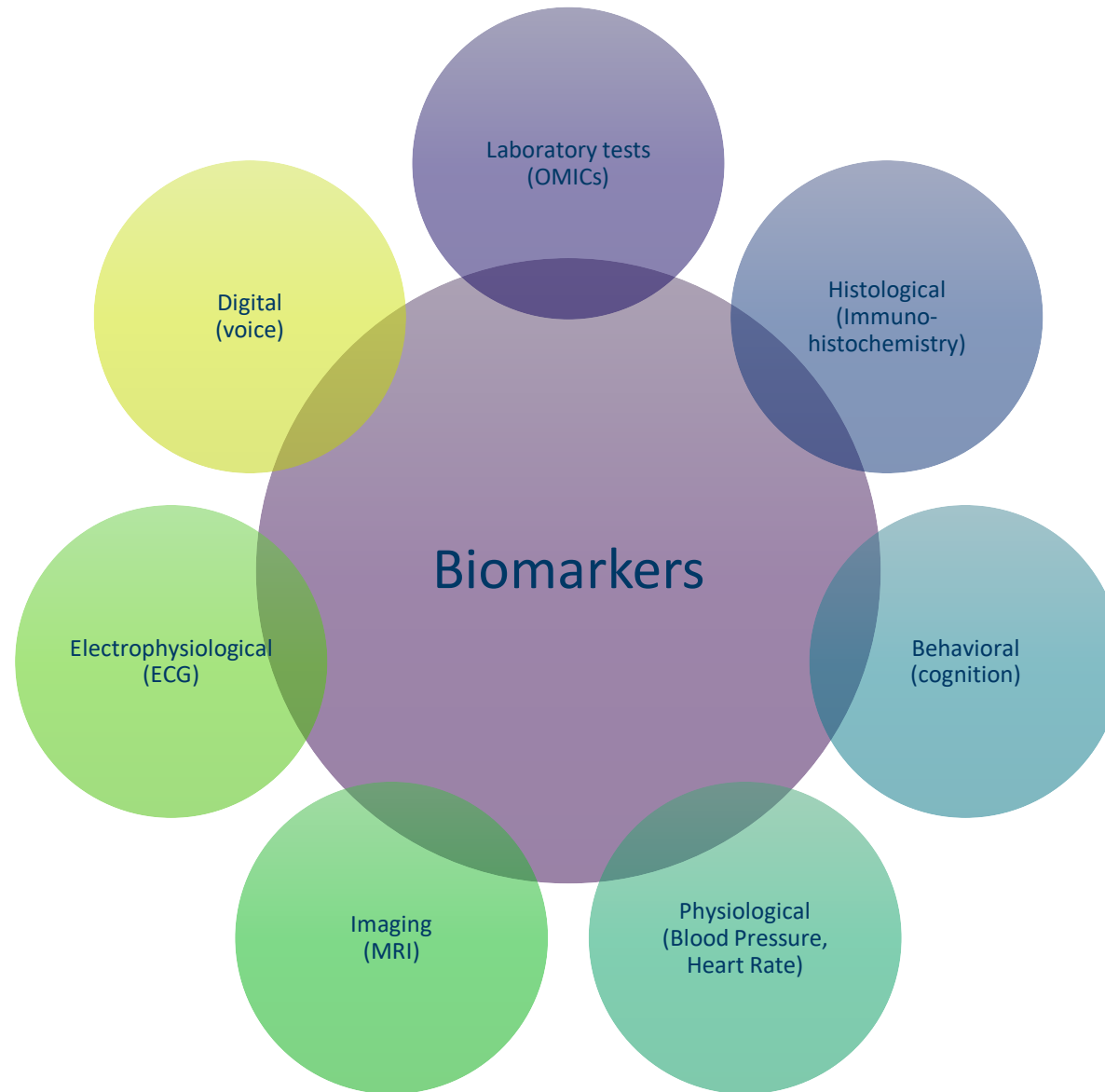
Biomarkers: an umbrella definition

“A defined characteristic that is measured as an indicator of normal biological processes, pathogenic processes, or biological responses to an exposure or intervention, including therapeutic interventions.”

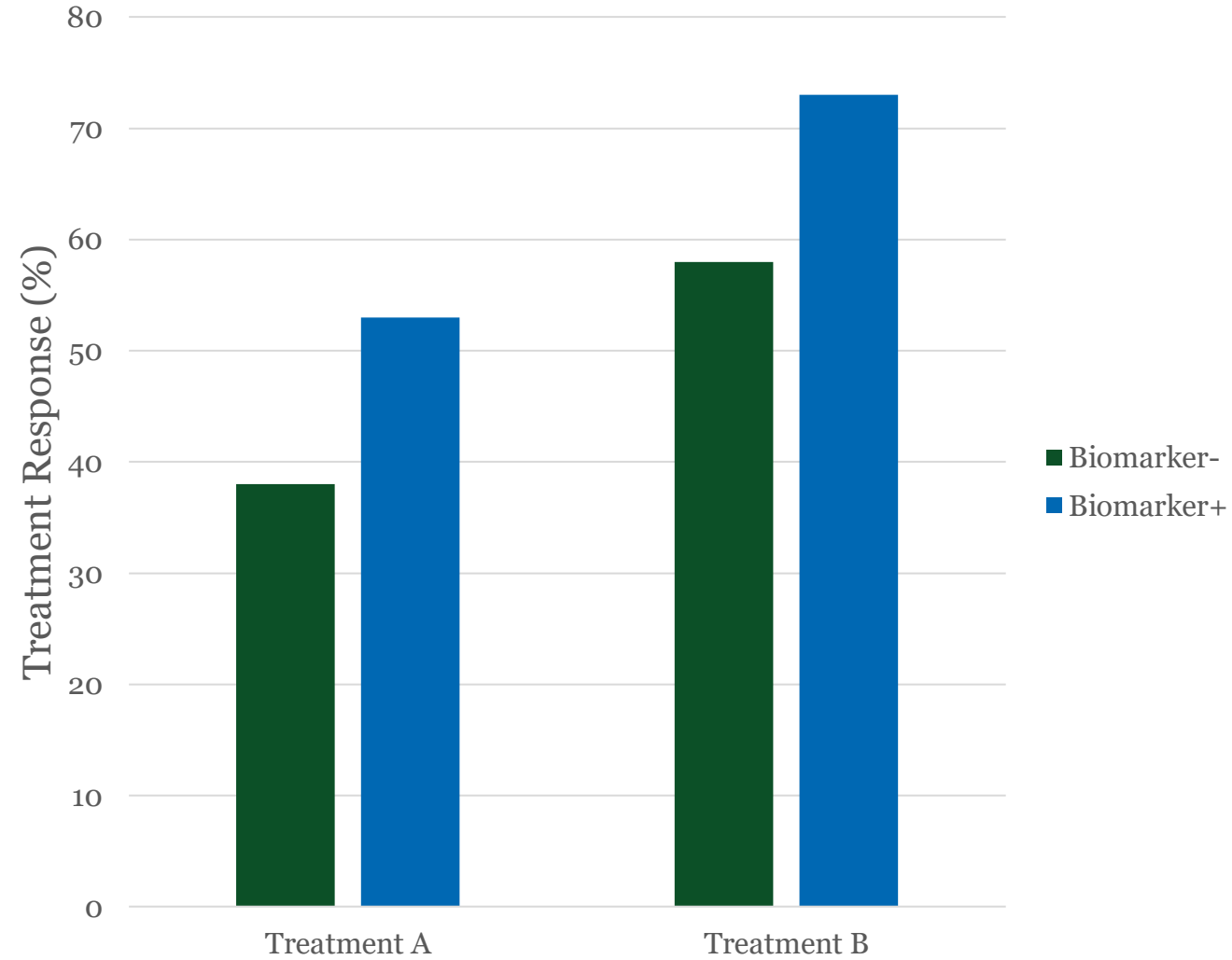
BEST (Biomarkers, EndpointS, and other Tools), FDA – NIH, 2016



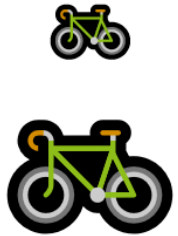
Biomarkers: very diverse kinds of data



A biomarker can be prognostic



Biomarker:
Bike size

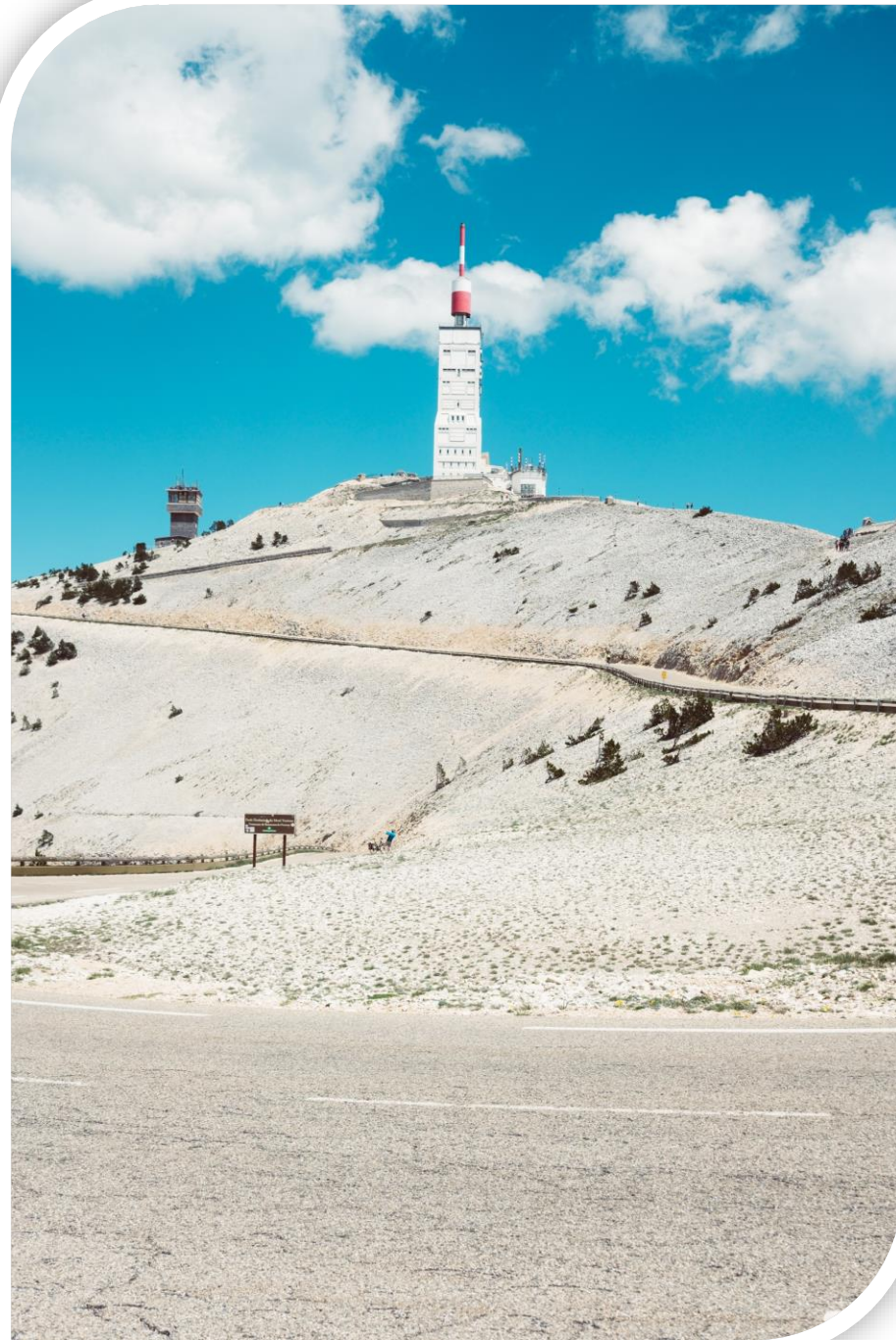


Treatment:
Training

Do not train
Train 1 hour a month
Train 4 hours a day

Objective:
Climb Mont
Ventoux
under 1.5 hour

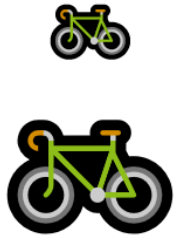




Size of your bike?

A prognostic biomarker of climbing Mont Ventoux under 1.5 hour

Biomarker:
Bike size



Treatment:
Training

Do not train

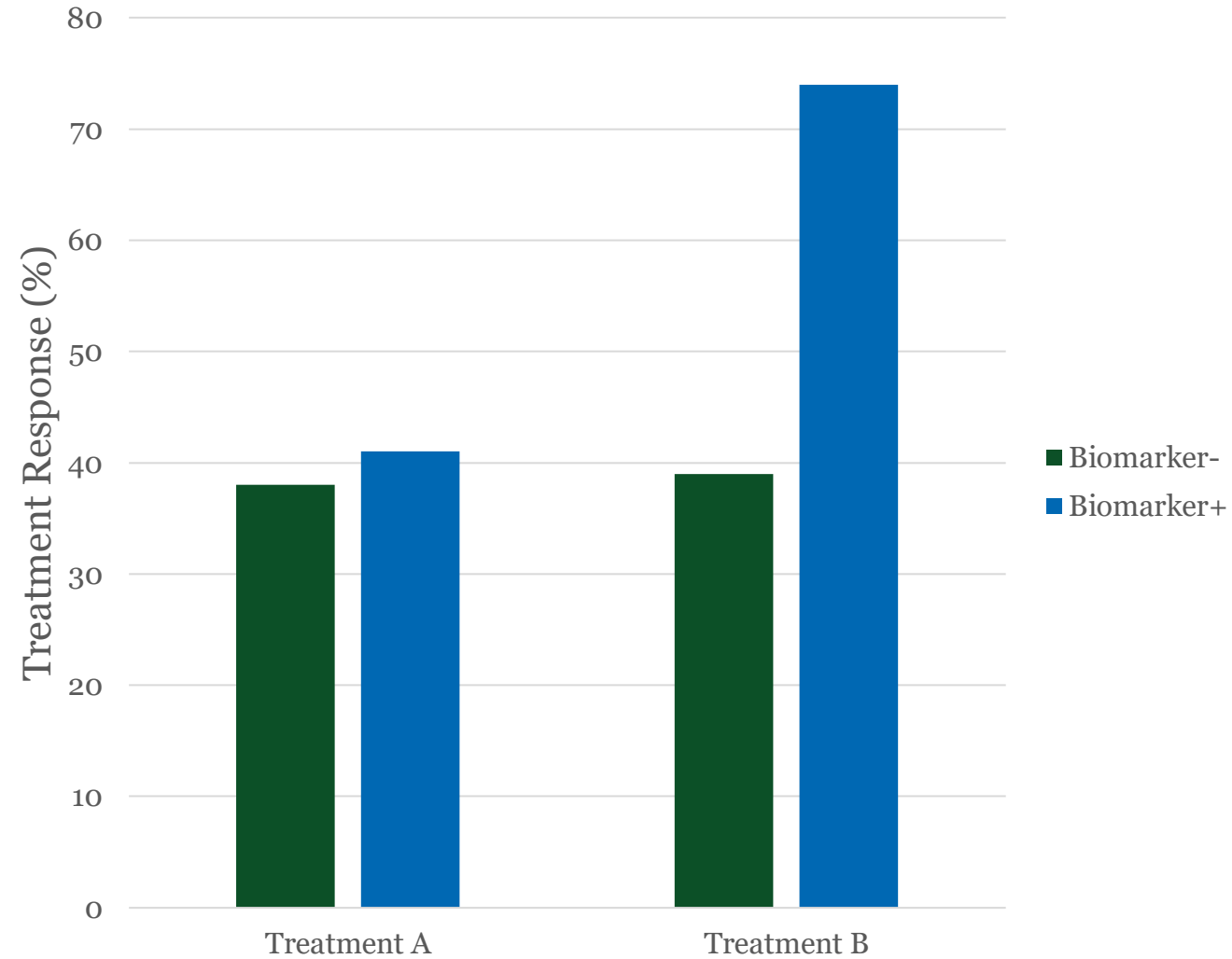
Train 1 hour a month

Train 4 hours a day

Objective:
Climb Mont
Ventoux
under 1.5 hour



A biomarker can be predictive



Biomarker:
Bike model



Treatment:
Training

Do not train

Train 1 hour a month

Train 4 hours a day

Objective:
Climb Mont
Ventoux
under 1.5 hour



The bike model?

A biomarker predictive of your treatment response!

Biomarker:
Bike model



Treatment:
Training

Do not train

Train 1 hour a month

Train 4 hours a day

Objective:
Climb Mont
Ventoux
under 1.5 hour



So, what is a biomarker already? 🤯

A biomarker can be many things and can play many roles.







A summit attempt with 1 key question



Compound efficacious?



This sounds easy-*ish*, let's go for a Phase IIa!





You Should *Play To Win*



A summit attempt with 2 key questions



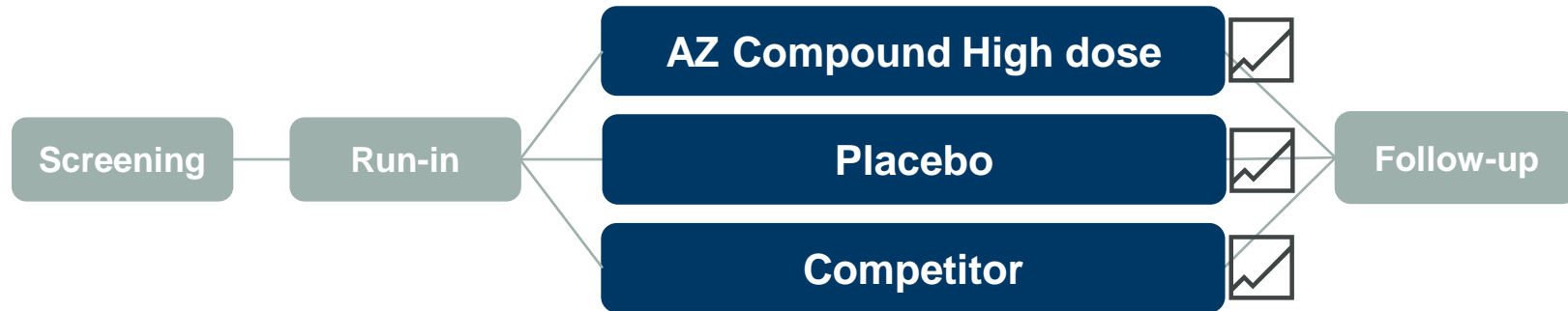
Superior to the competition?



Compound efficacious?



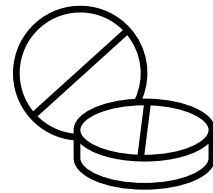
Ok, let's go for a PhIIb with a dual primary endpoint then!



A summit attempt with 3 key questions



Superior to the competition?



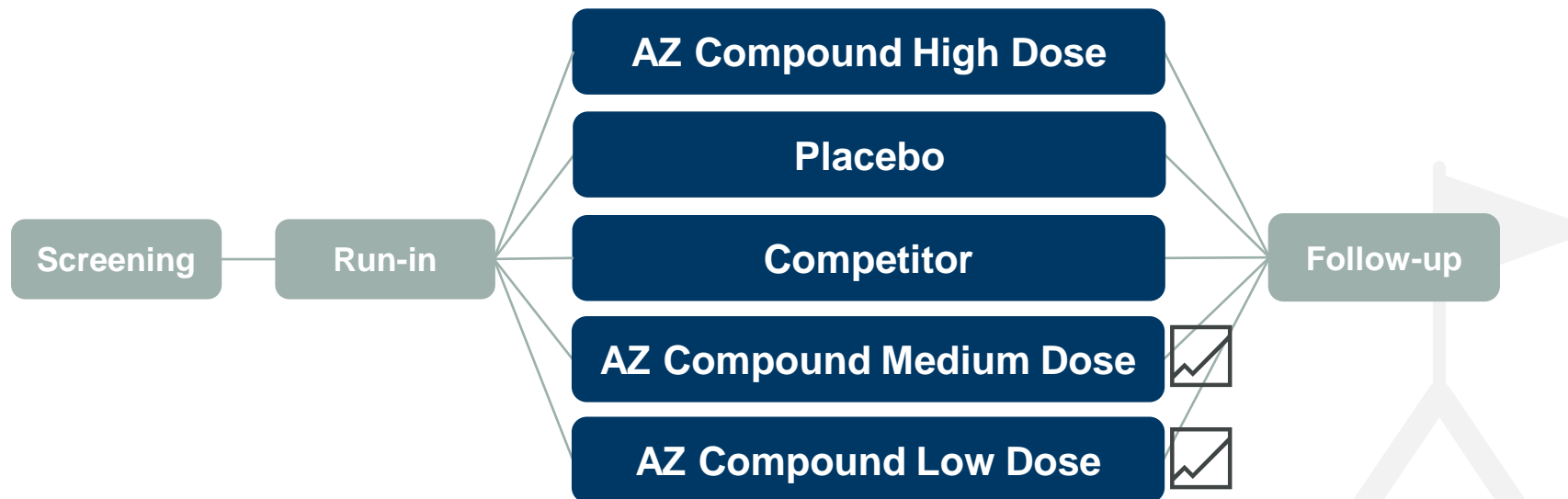
Right dose?



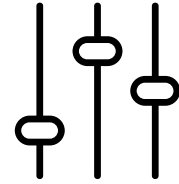
Compound efficacious?



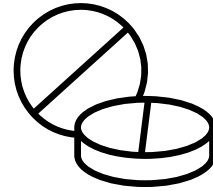
Ok, let's go for a larger PhIIb then!



A summit attempt with 4 key questions



Biomarker threshold?



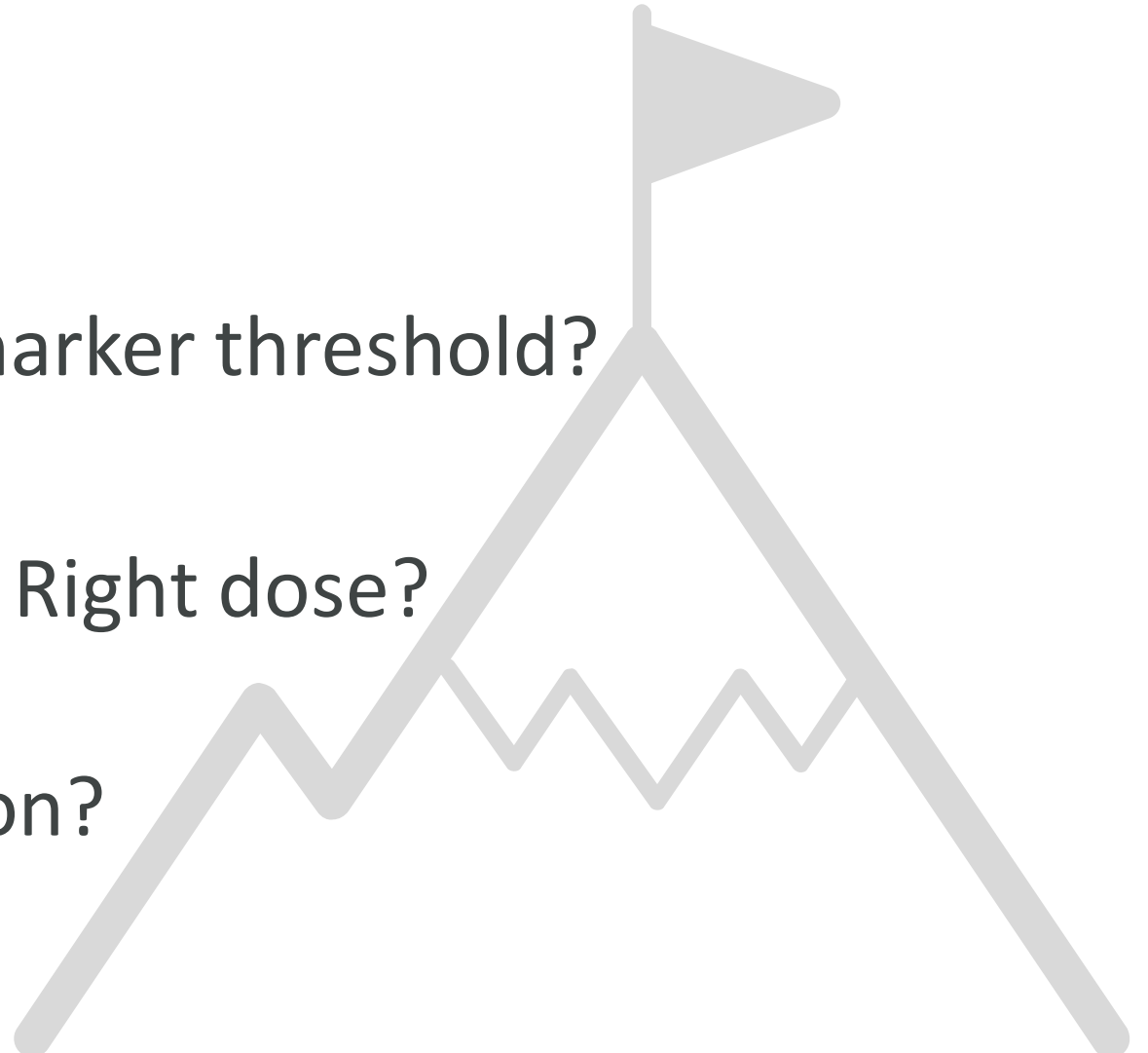
Right dose?



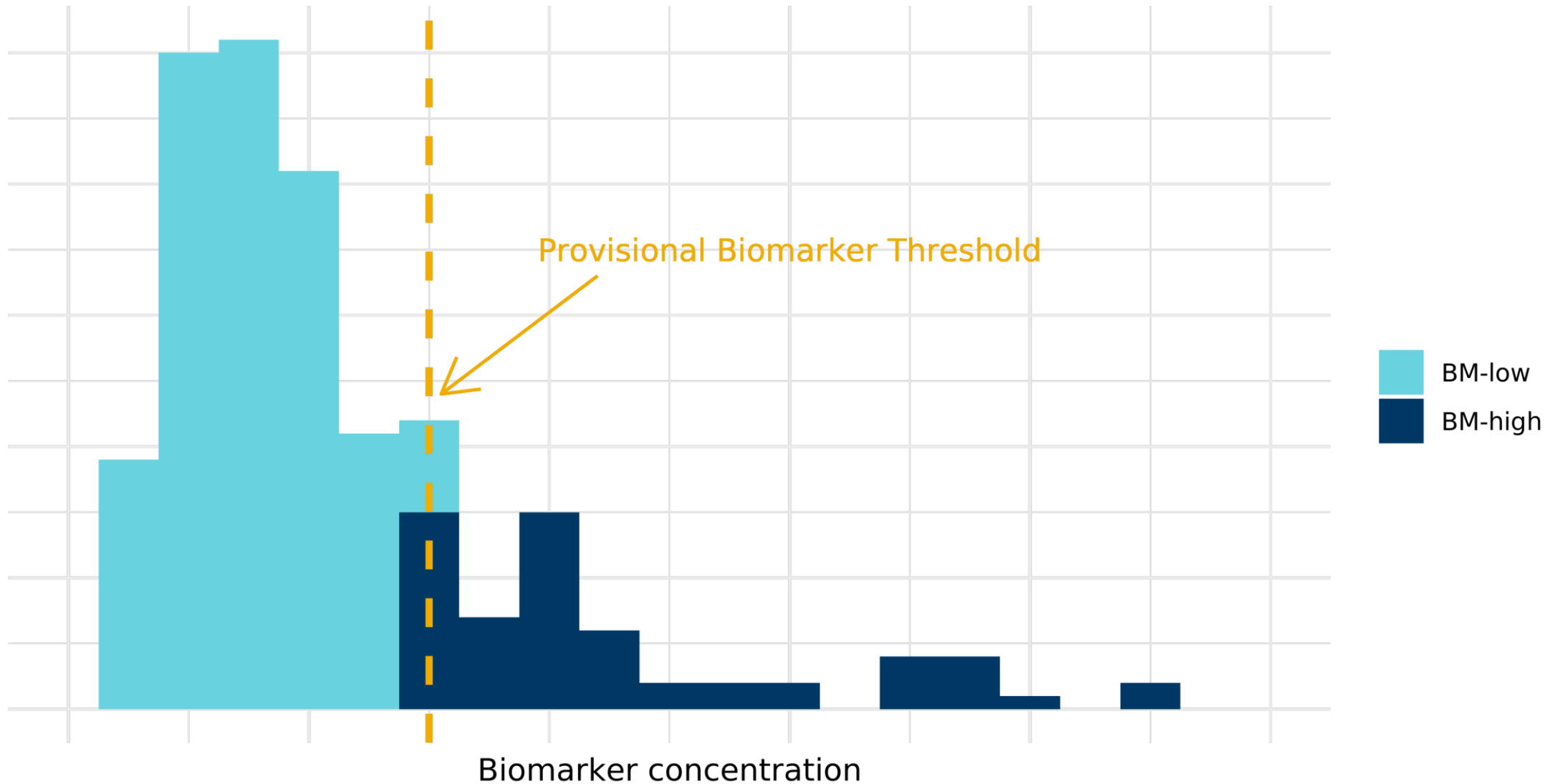
Superior to the competition?



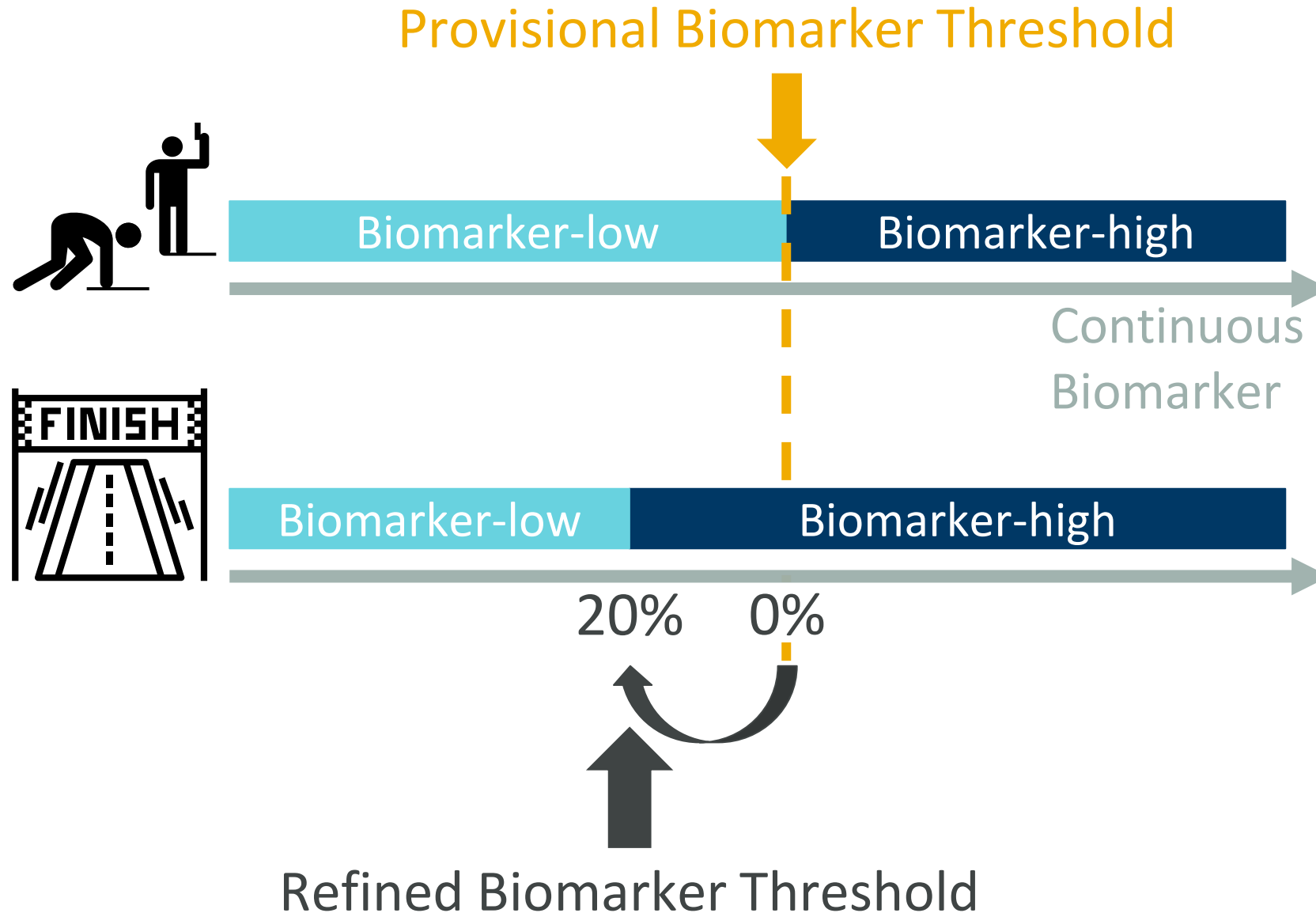
Compound efficacious?



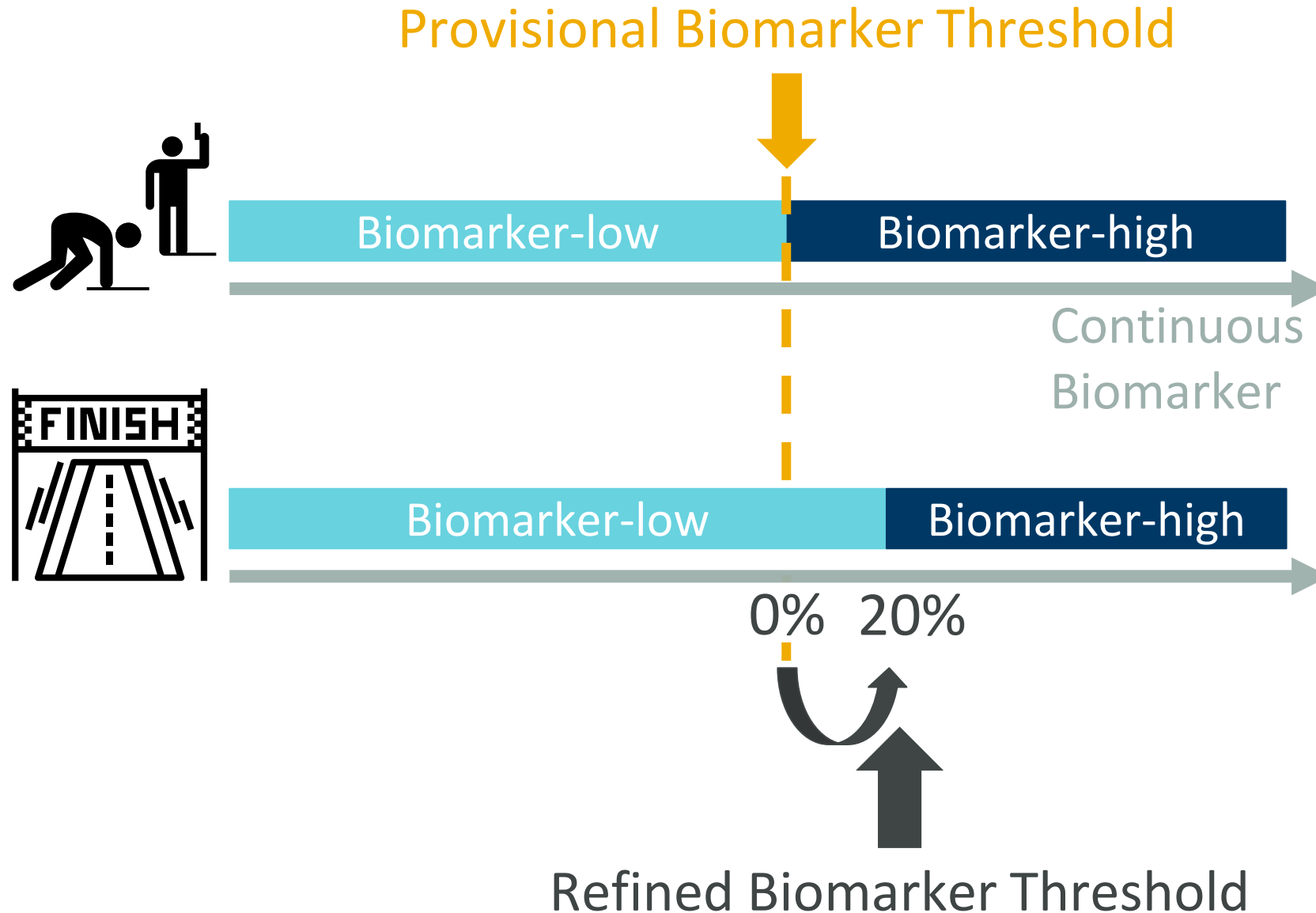
Provisional biomarker threshold defined with real-world data



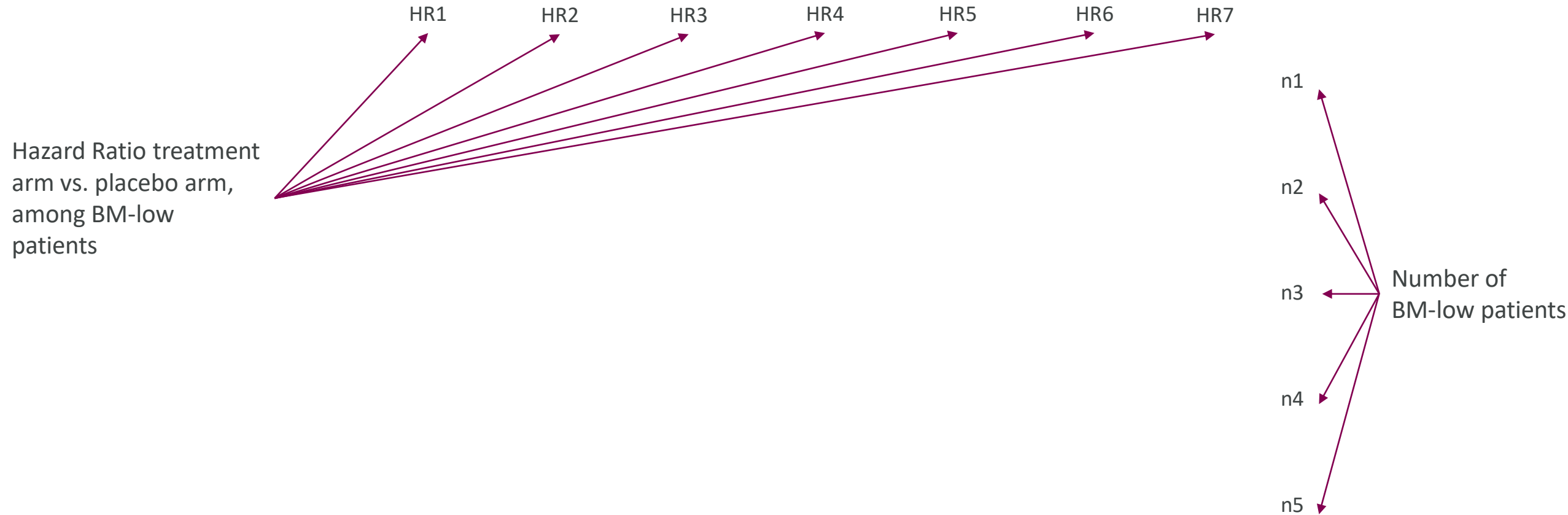
Biomarker threshold refinement, moving it lower



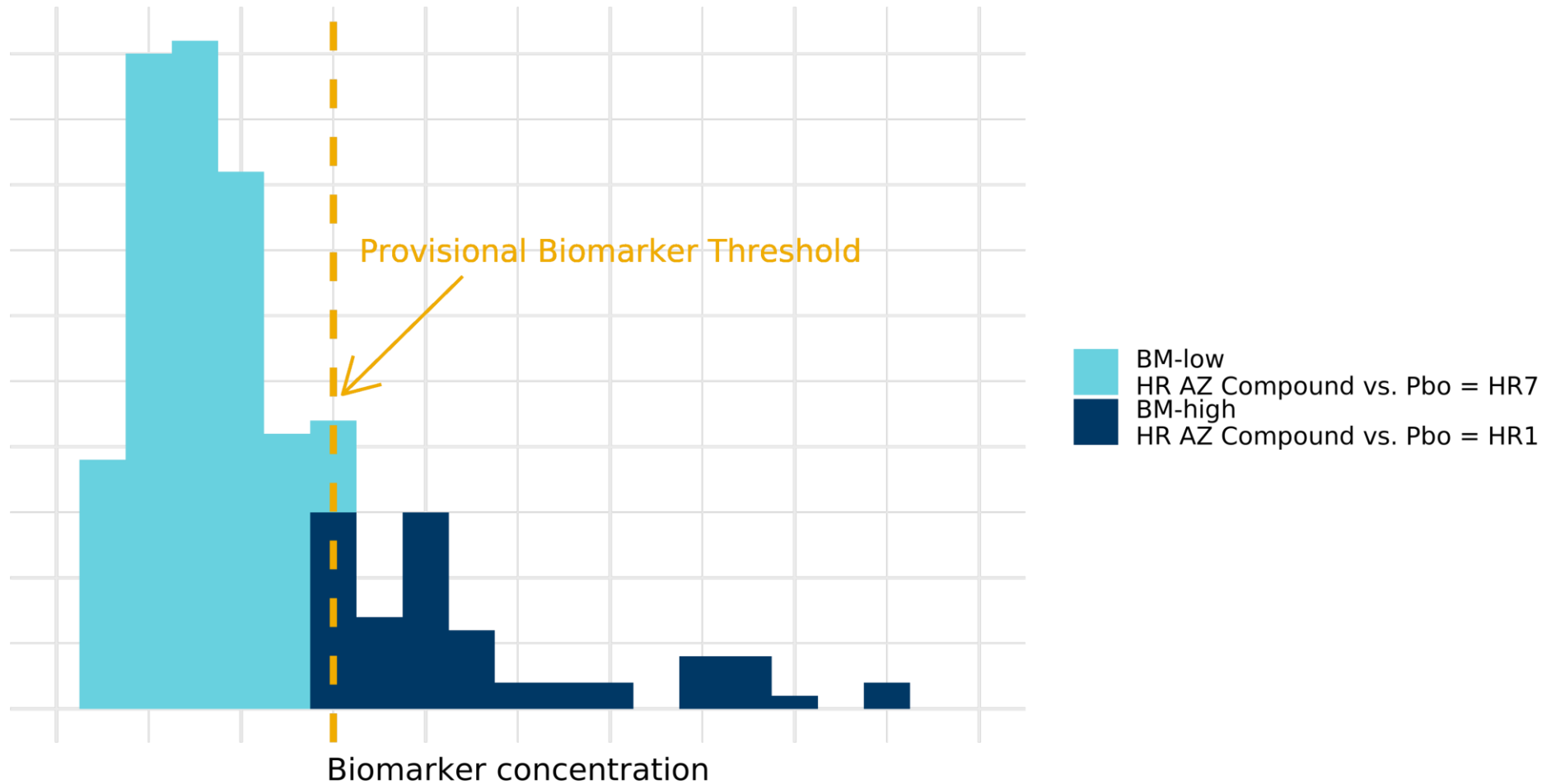
Biomarker threshold refinement, moving it higher



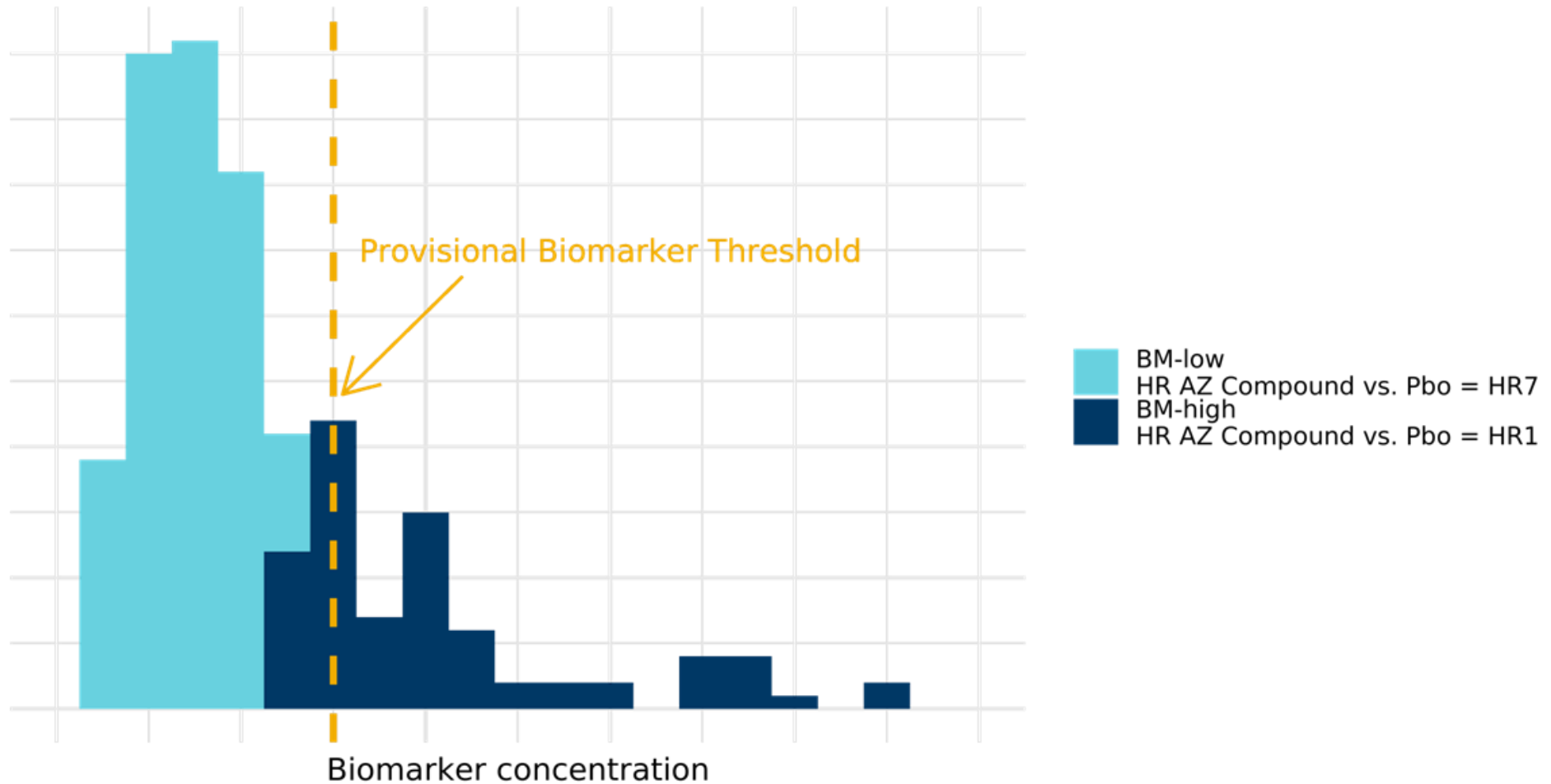
Let's add some biomarker-low patients, but how many?



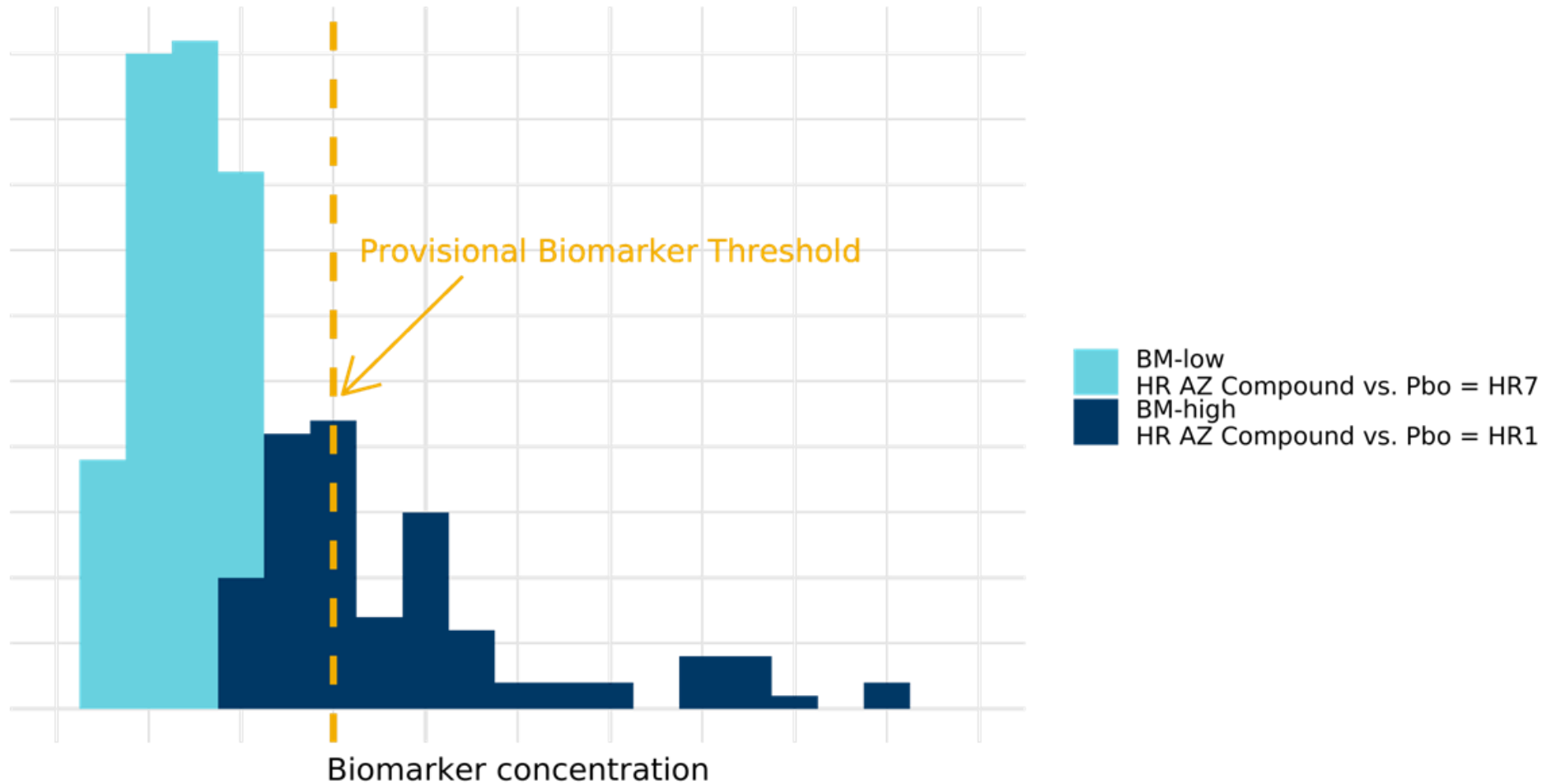
Simulating what the reality could look like



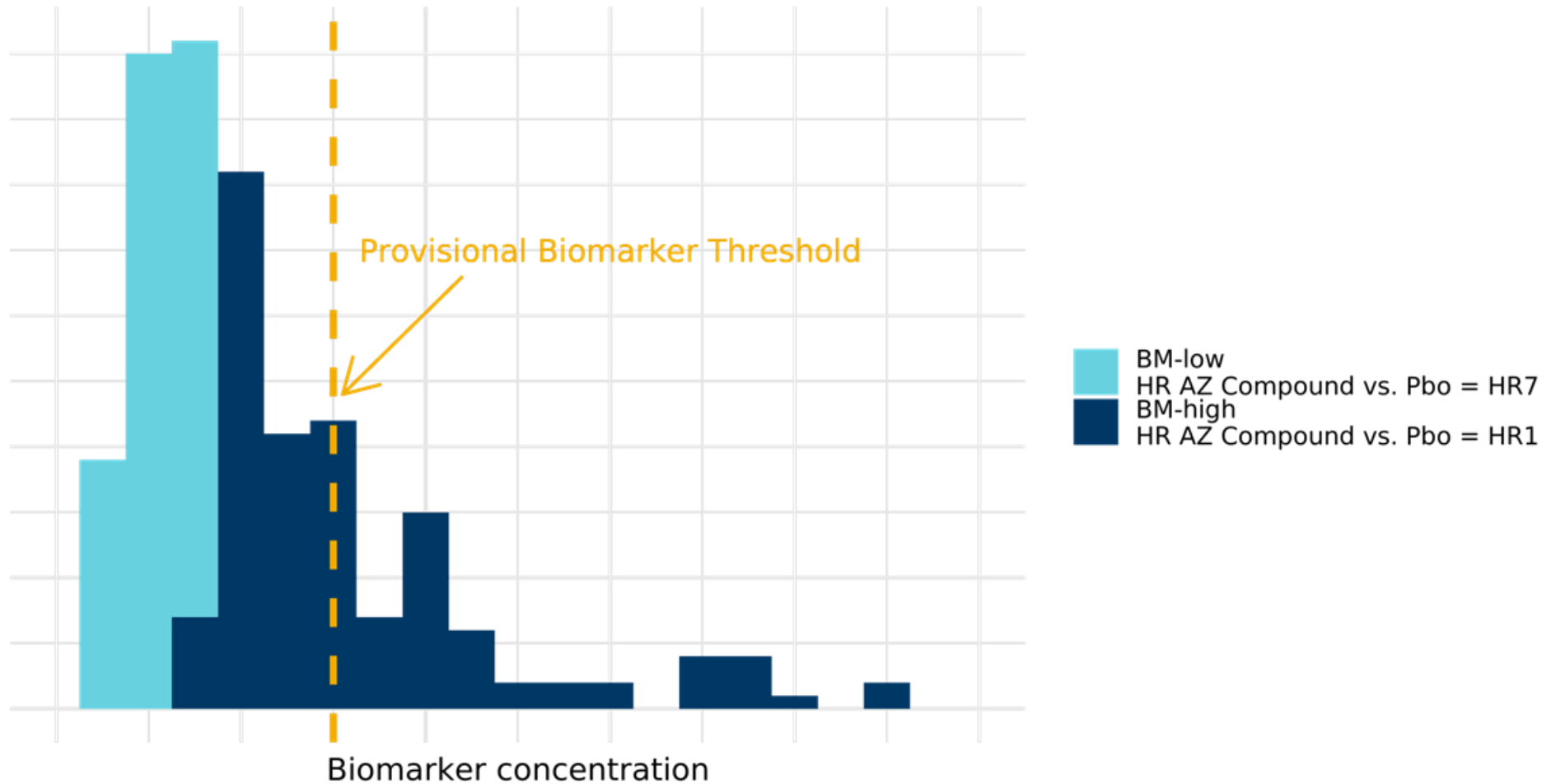
Simulating what the reality could look like



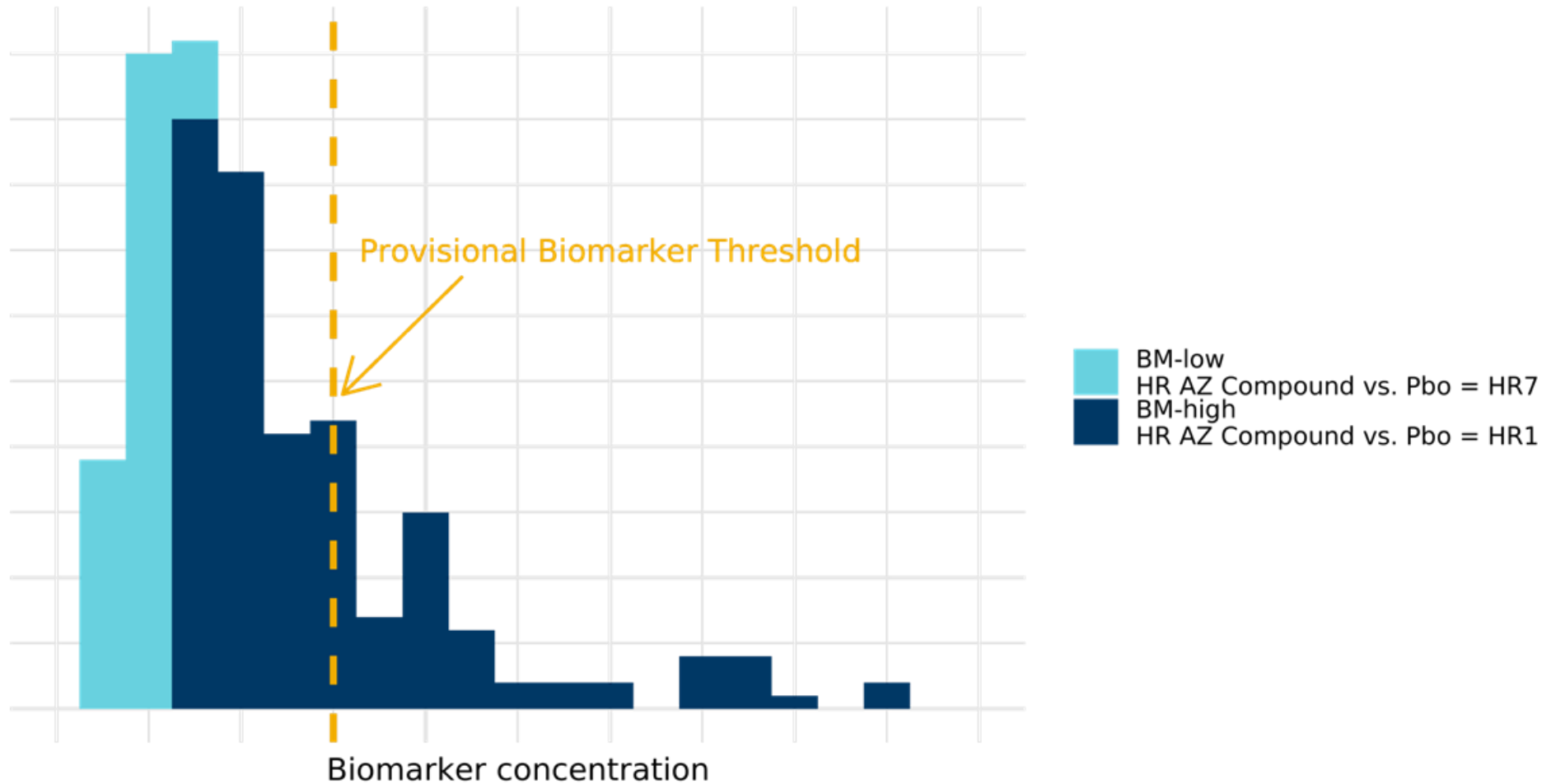
Simulating what the reality could look like



Simulating what the reality could look like



Simulating what the reality could look like



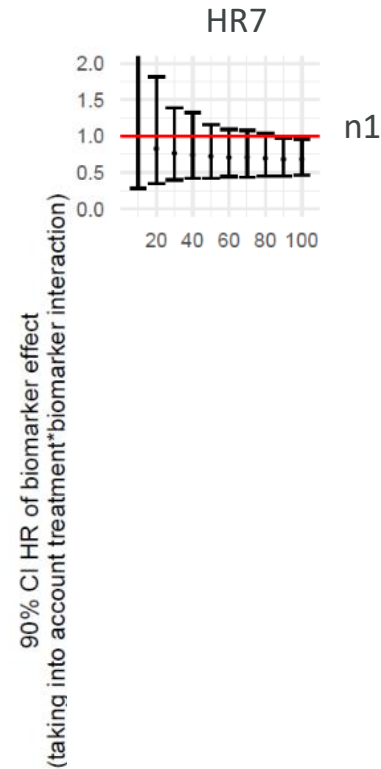
Let's add some biomarker-low patients, but how many?

Hazard Ratio BM-high vs. BM-low, taking into account the treatment*biomarker interaction



Let's add some biomarker-low patients, but how many?

Hazard Ratio BM-high vs. BM-low, taking into account the treatment*biomarker interaction

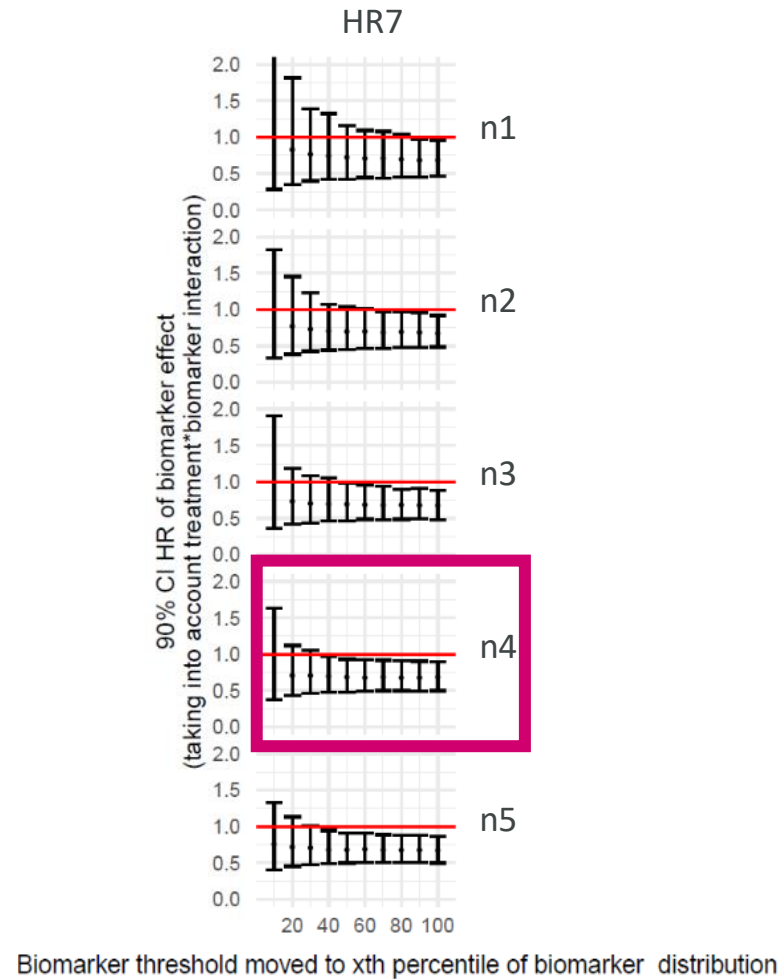


Biomarker threshold moved to xth percentile of biomarker distribution

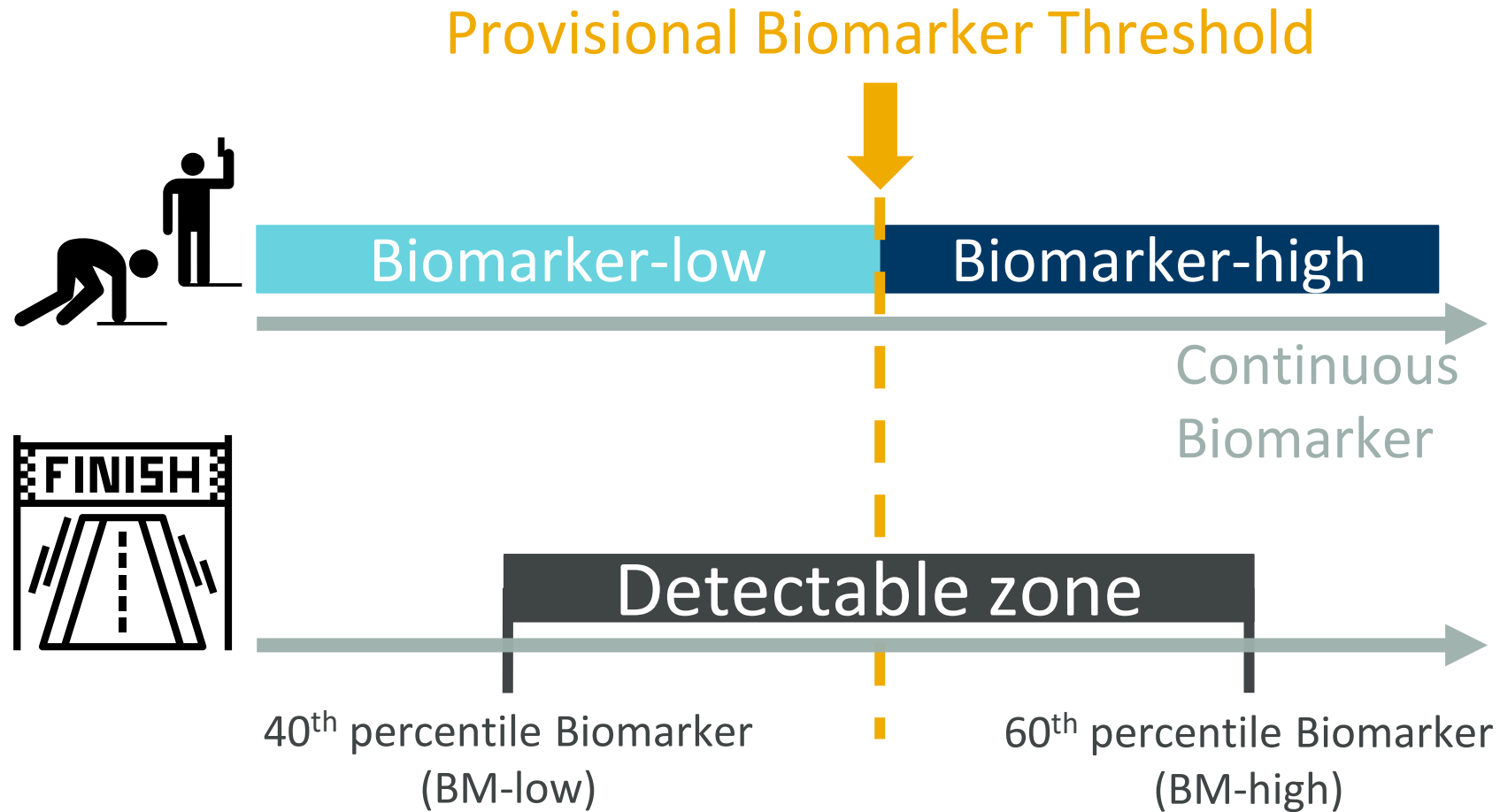


Let's add some biomarker-low patients, but how many?

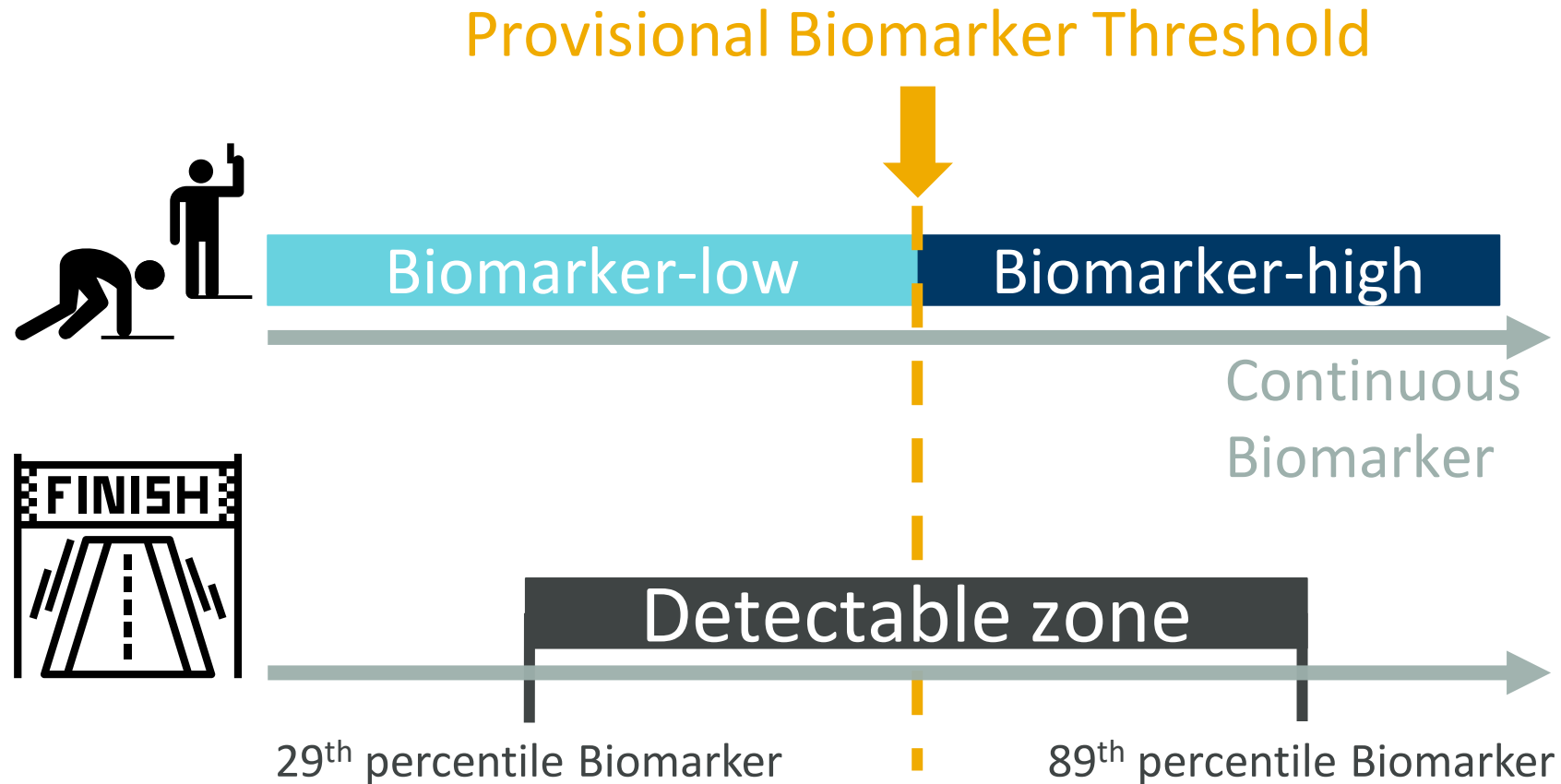
Hazard Ratio BM-high vs. BM-low, taking into account the treatment*biomarker interaction



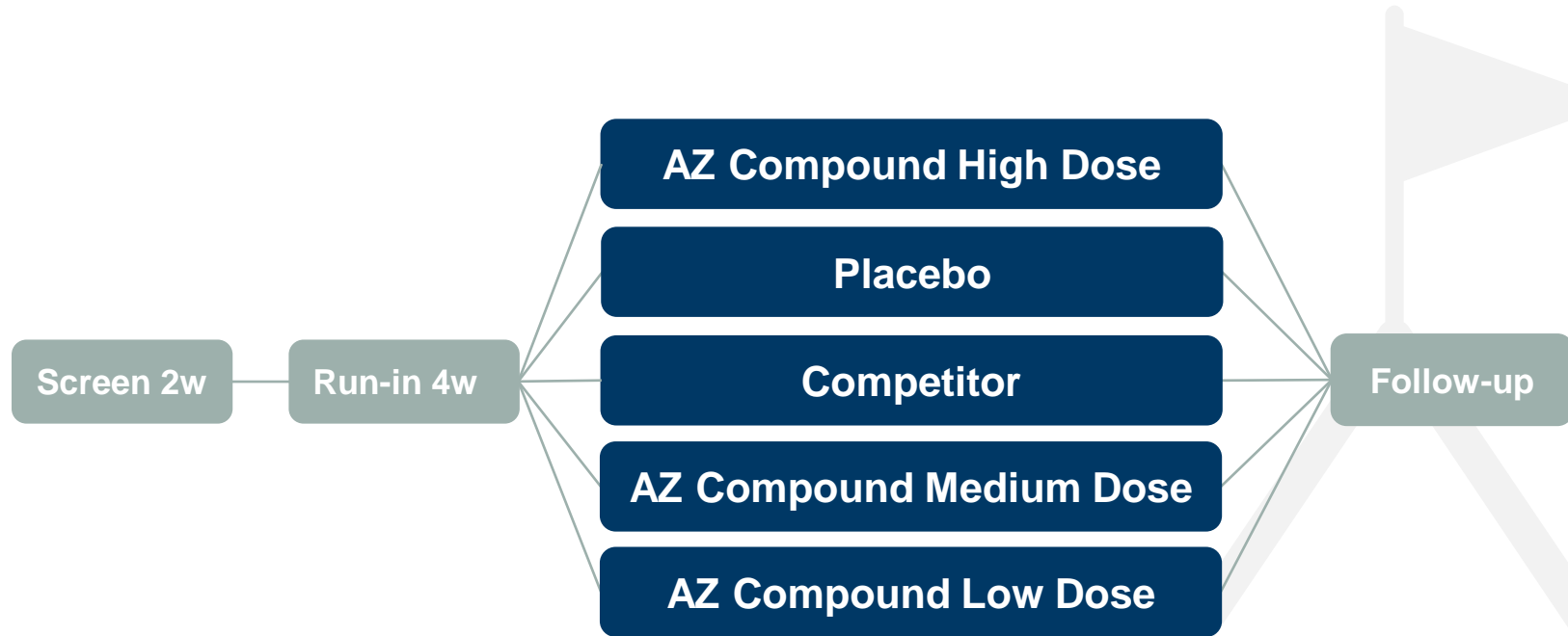
Adding as many BM-low patients as there are BM-high patients to fine-tune the biomarker threshold



Adding as many BM-low patients as there are BM-high patients to fine-tune the biomarker threshold



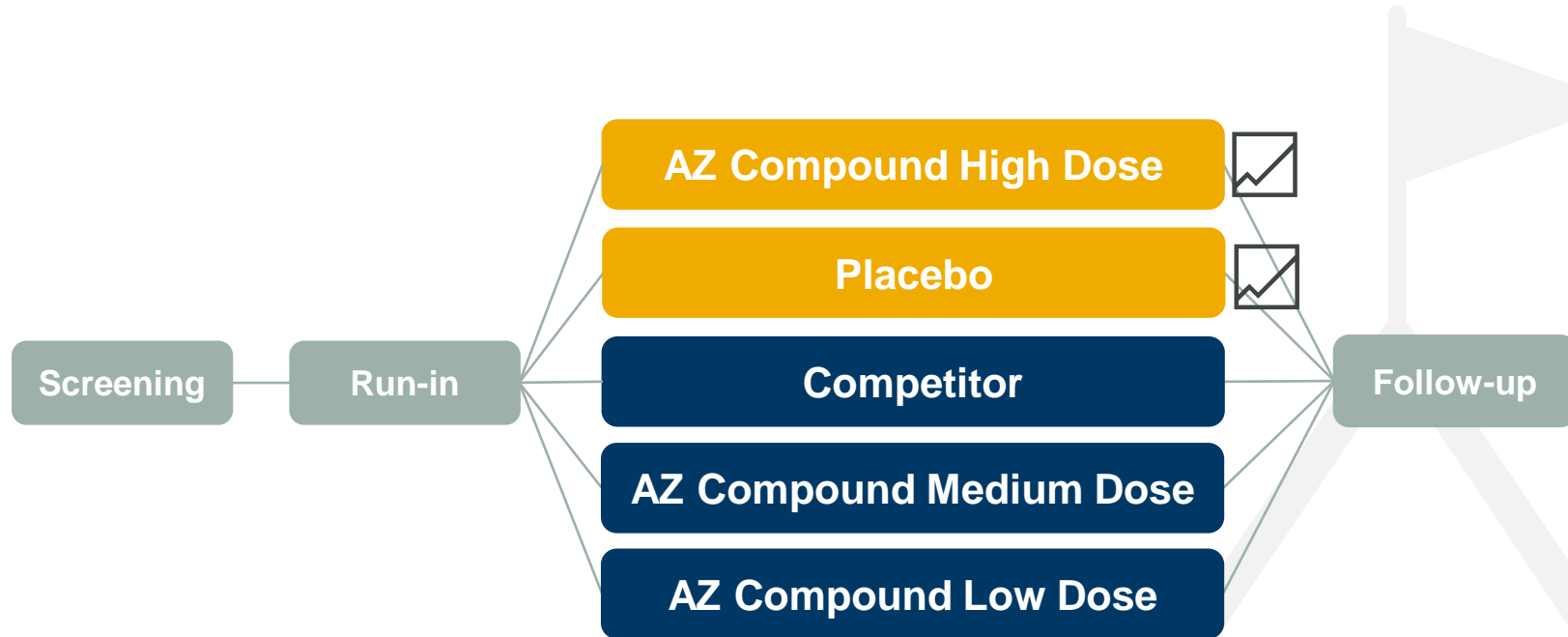
The PhIIb, without the biomarker-low patients



BM-high patients only



With biomarker-low patients, that's a quite large PhIIb!

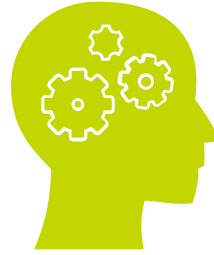


BM-high patients only

BM-high & BM-low patients



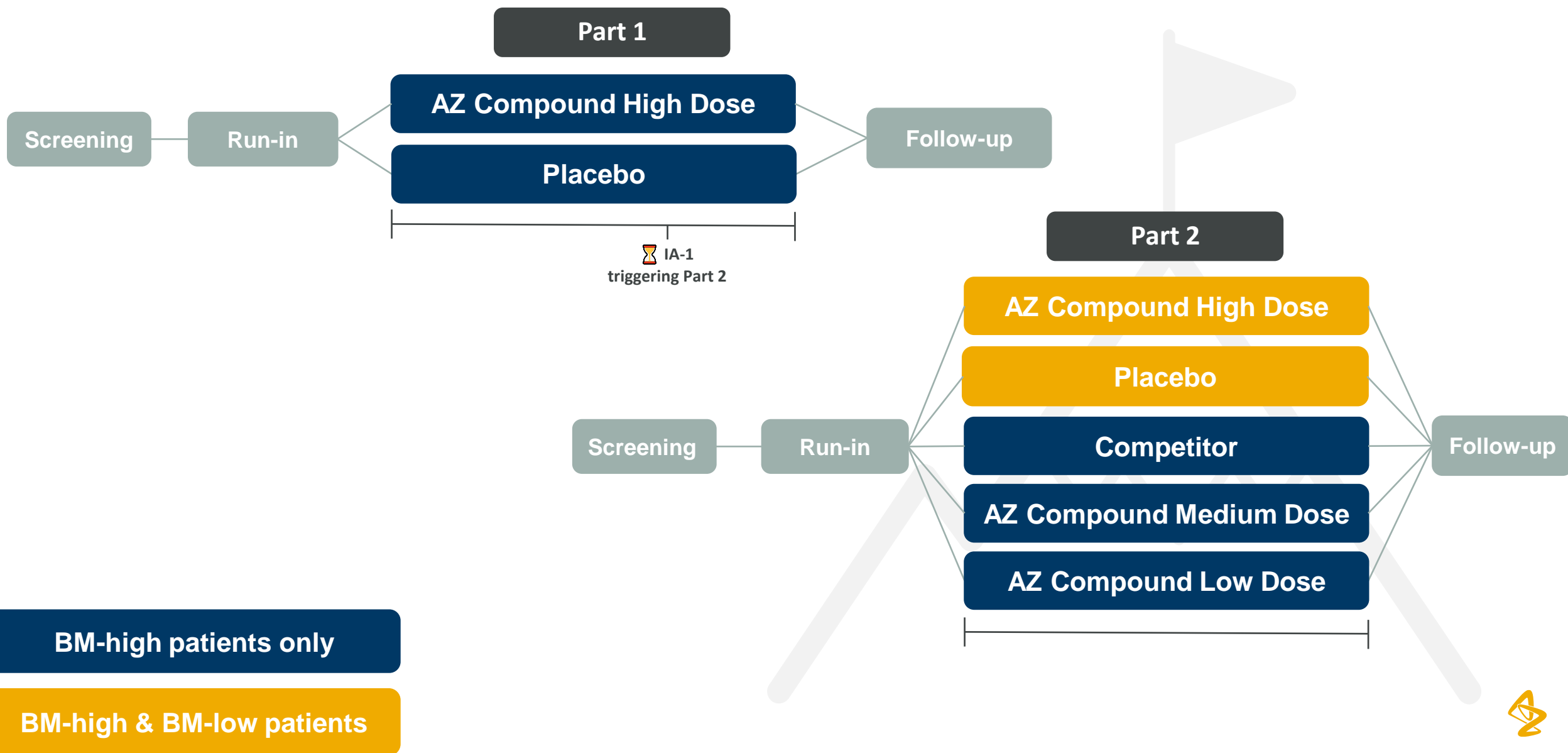
That's a very big upfront investment for a PhII!



You Should Be Entrepreneurial



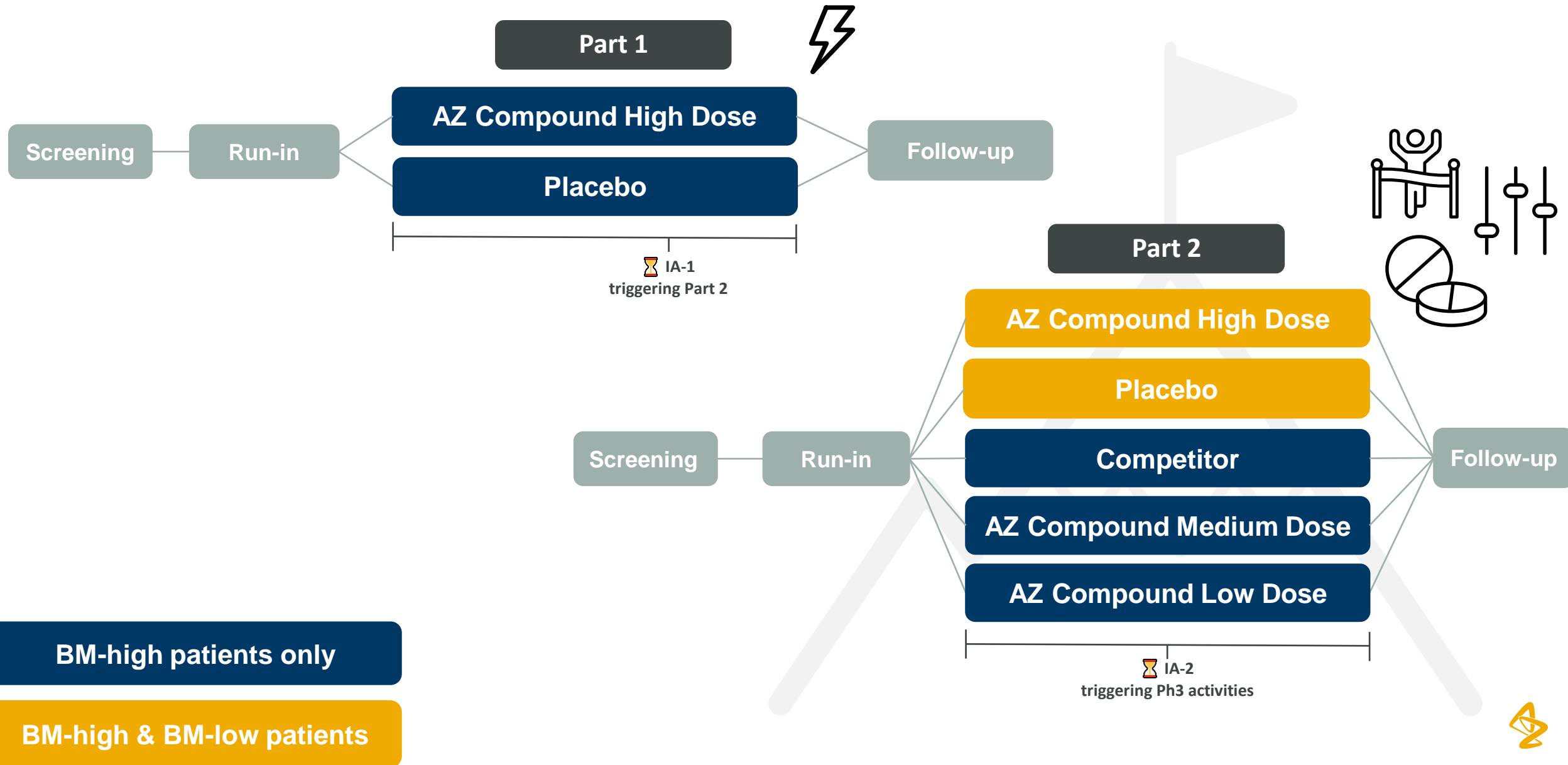
Ok, let's go for a seamless PhII with one interim then!



Can you not be a bit more entrepreneurial? 🤔



Let's go for a seamless PhII with 2 interim analyses!





Let's think about medicines
the same way we think about bikes! 😊





Thank you.





Thank you.





Thank you.





Thank you.





Thank you.





Thank you.





Thank you.





Thank you.



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