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Add-on trials in depression

Case Study 1

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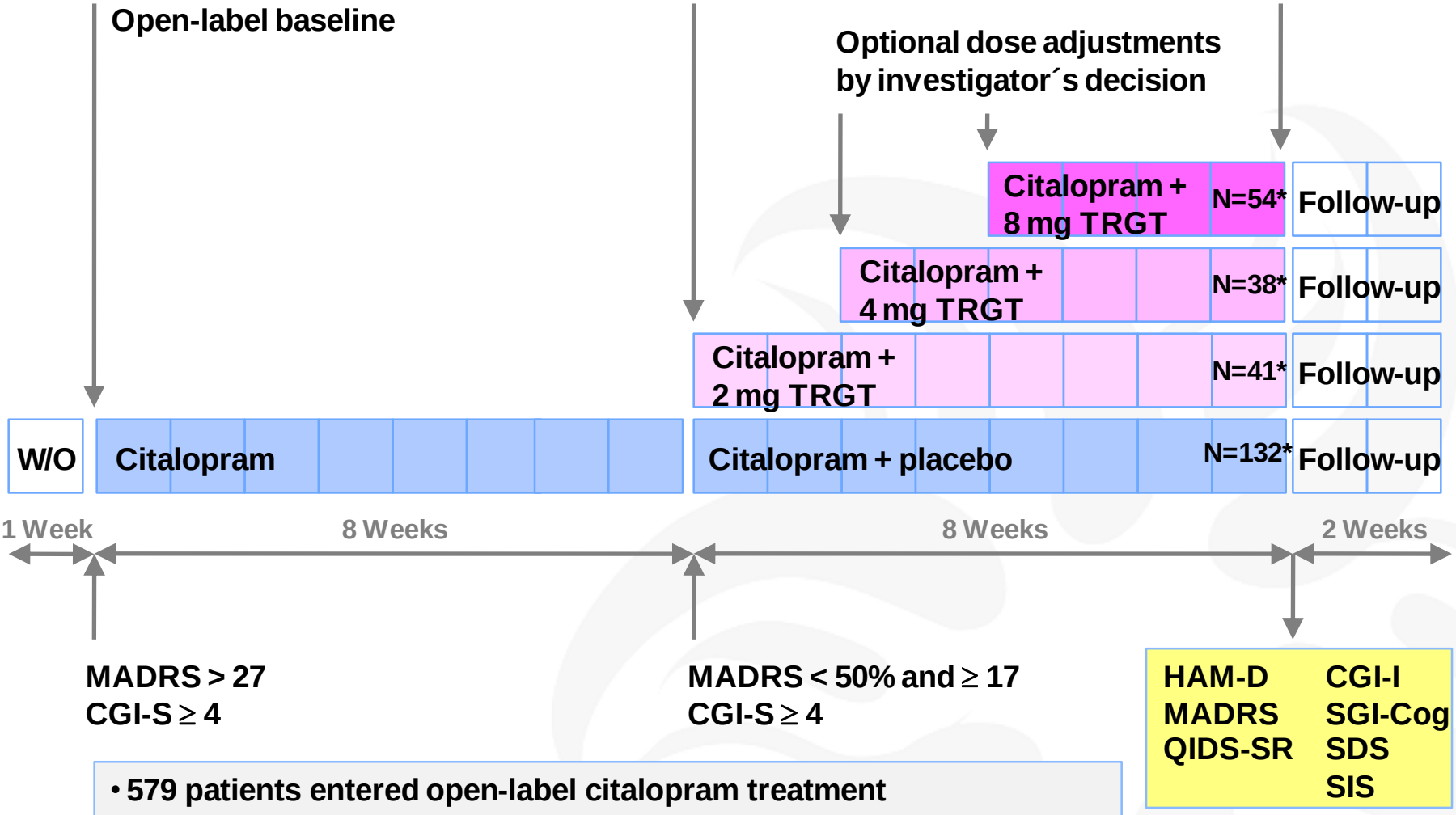
TRGT Phase IIB Study Design



- 579 patients entered open-label citalopram treatment
- 270 patients were randomized to add-on of either placebo or TRGT

*ITT Subjects in Double Blind Phase by End Dose

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Design Considerations

- Prospective identification of inadequate response
- Single SSRI as background ADT
- Physician driven up-titration
- Use of both HAMD (primary) and MADRS
- PRO's to assess depression and cognition
- PRO's to assess functionality and irritability

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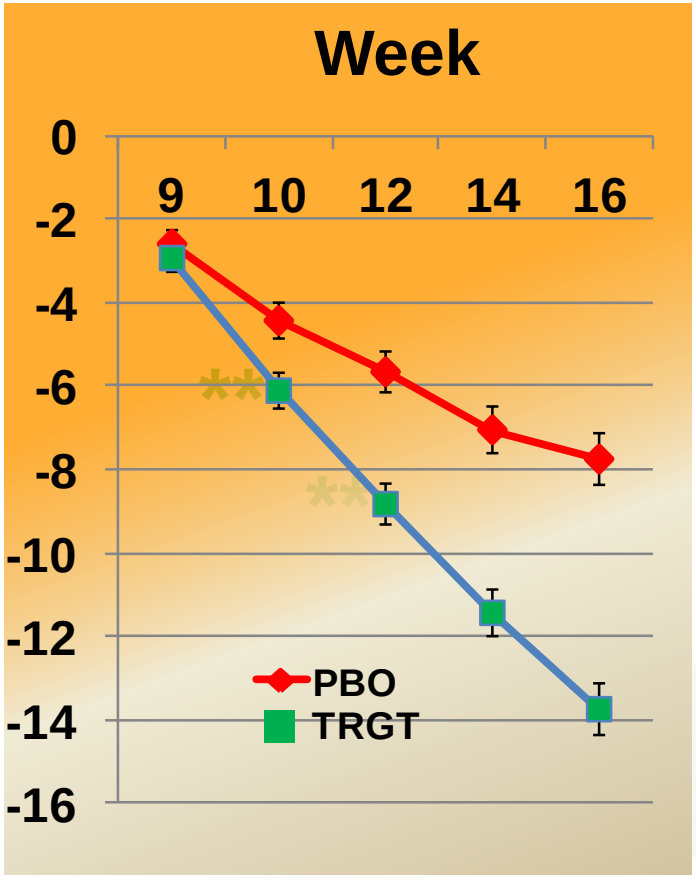
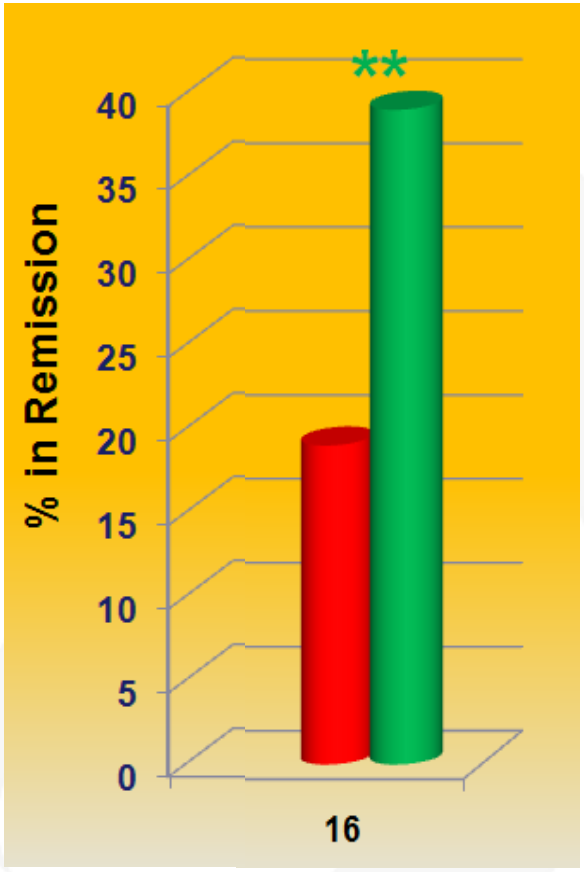
Phase IIB: HAMD-17 Change Score (ITT)

Antidepressant efficacy



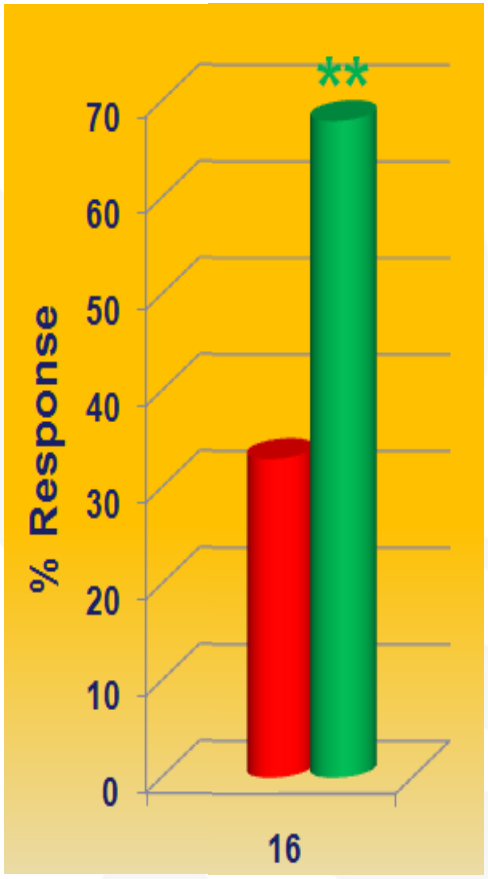
Change in HAM-D Score

Remission



HAMD-17 ≤ 7

Response



HAMD-17 reduced by 50%

All secondary endpoints were statistically significant (P < 0.0001)

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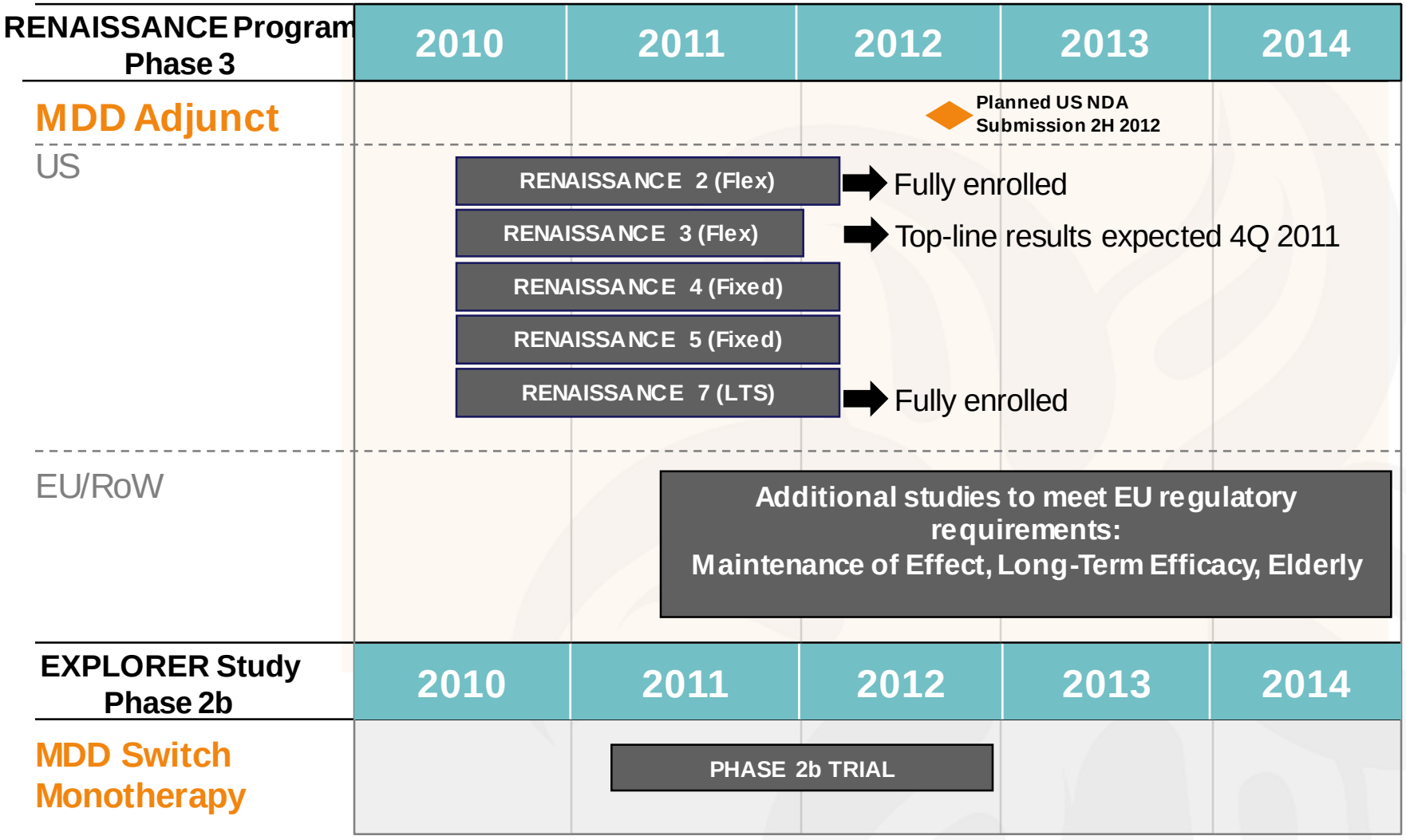
TRGT Clinical Program for Major Depressive Disorder



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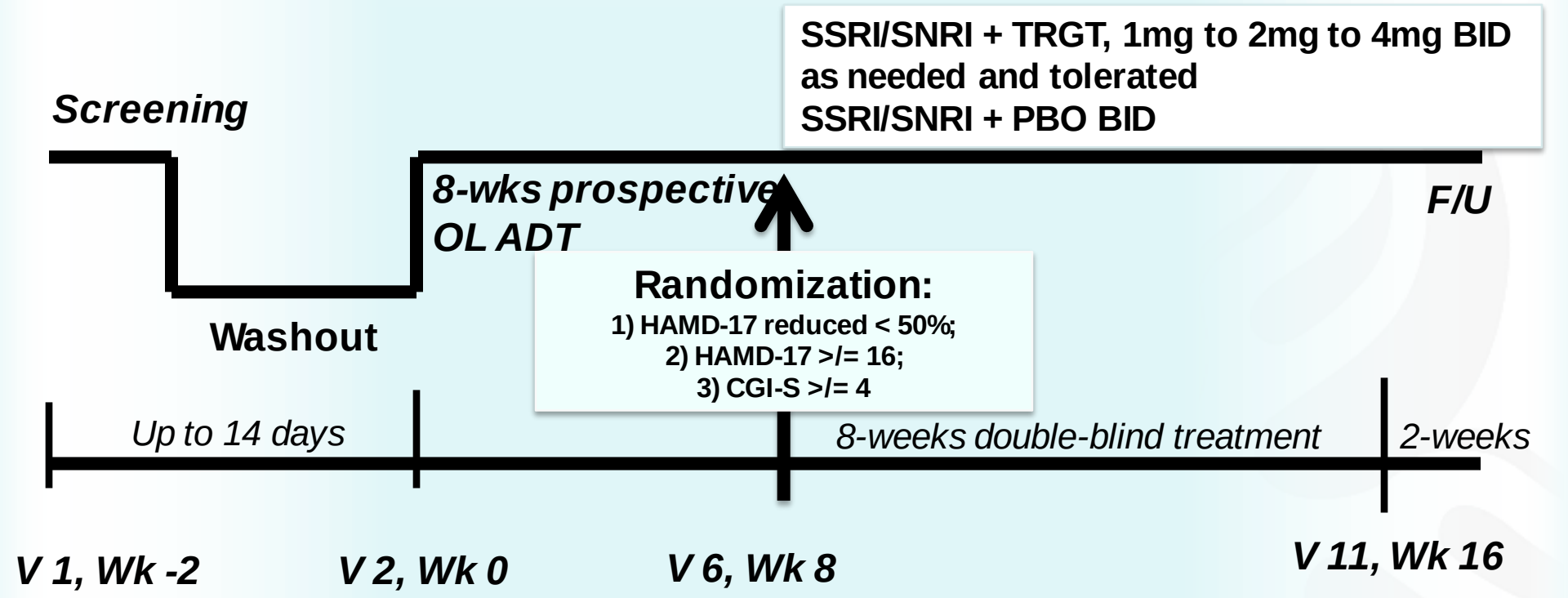
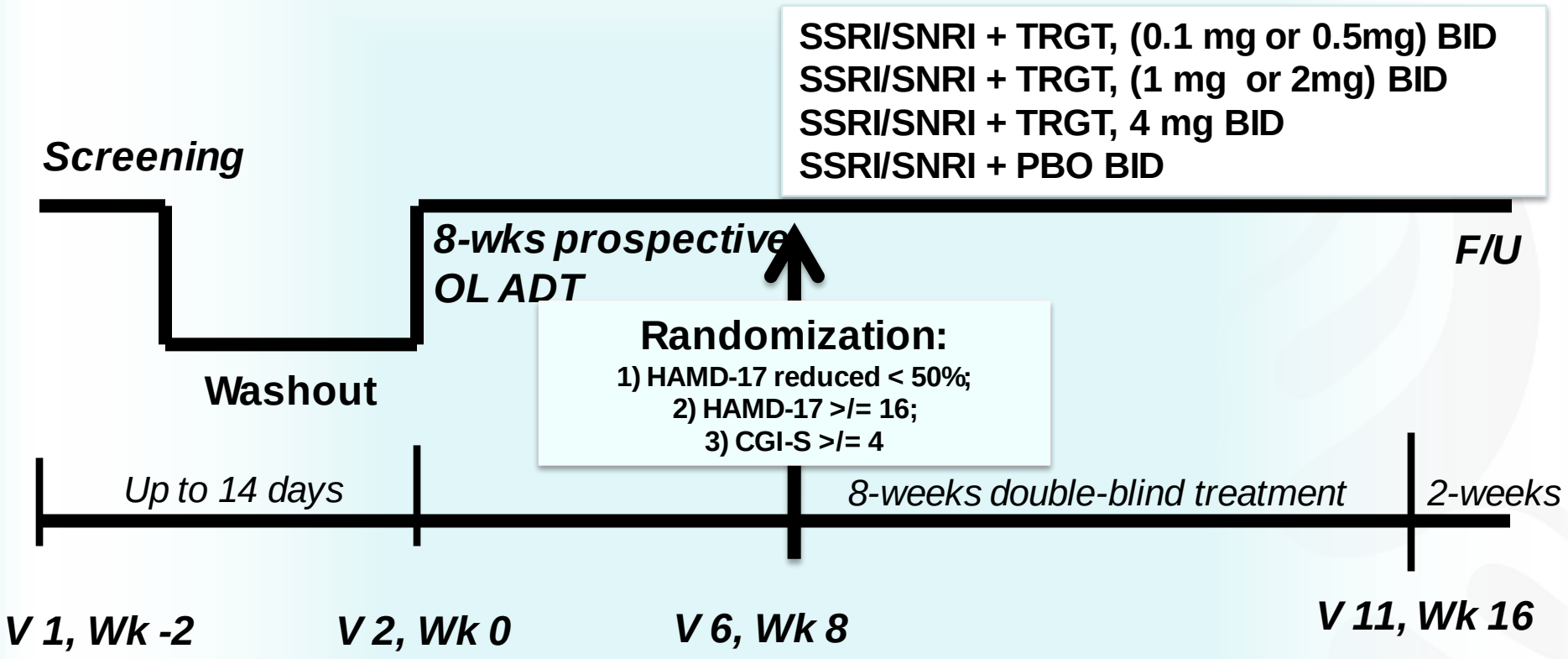
Phase 3 Flex Dose Study Design (2 studies)



- Must not have more than 1 inadequate response to ADT in current episode
- Screening: Ham-D-17 ≥ 20, CGI-S ≥ 4

Phase 3 Fixed Dose Study Design (2 studies)



- Must not have more than 1 inadequate response to ADT in <u>current</u> episode
- Screening: Ham-D-17 ≥ 20, CGI-S ≥ 4

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Protocol changes

- Used both MADRS (primary) and HAMD
- Slightly different inclusion and randomization requirements
- 5 SSRI's and 2SNRI's allowed as background ADT
- Up-titration determined by algorithm not physician
- 2 fixed dose studies included