

**Title:** Supplementary Data 1

SMO in complex with SAG1.3 at a time point of 50 ns of simulation 1

**Title:** Supplementary Data 2

SMO in complex with SAG1.3 at a time point of 200 ns of simulation 1

**Title:** Supplementary Data 3

SMO in complex with SAG1.3 at a time point of 50 ns of simulation 2

**Title:** Supplementary Data 4

SMO in complex with SAG1.3 at a time point of 200 ns of simulation 2

**Title:** Supplementary Data 5

SMO in complex with SAG1.3 at a time point of 50 ns of simulation 3

**Title:** Supplementary Data 6

SMO in complex with SAG1.3 at a time point of 200 ns of simulation 3

**Title:** Supplementary Data 7

Inactive FZD6 model in complex with SAG1.3 at a time point of 50 ns of simulation

**Title:** Supplementary Data 8

Inactive FZD6 model in complex with SAG1.3 at a time point of 250 ns of simulation

**Title:** Supplementary Data 9

Inactive FZD6 model in complex with SAG1.3 at a time point of 450 ns of simulation

**Title:** Supplementary Data 10

Inactive FZD6 model in complex with SAG1.3 at a time point of 650 ns of simulation

**Title:** Supplementary Data 11

Inactive FZD6 model in complex with SAG1.3 at a time point of 850 ns of simulation

**Title:** Supplementary Data 12

Inactive FZD6 model in complex with SAG1.3 at a time point of 1000 ns of simulation

**Title:** Supplementary Data 13

Active-like FZD6 model in complex with SAG1.3 at a time point of 200 ns of simulation 1

**Title:** Supplementary Data 14

Active-like FZD6 model in complex with SAG1.3 at a time point of 400 ns of simulation 1

**Title:** Supplementary Data 15

Active-like FZD6 model in complex with SAG1.3 at a time point of 600 ns of simulation 1

**Title:** Supplementary Data 16

Active-like FZD6 model in complex with SAG1.3 at a time point of 800 ns of simulation 1

**Title:** Supplementary Data 17

Active-like FZD6 model in complex with SAG1.3 at a time point of 1000 ns of simulation 1 **Title: Title:**

**Title:** Supplementary Data 18

Active-like FZD6 model in complex with SAG1.3 at a time point of 200 ns of simulation 2

**Title:** Supplementary Data 19

Active-like FZD6 model in complex with SAG1.3 at a time point of 400 ns of simulation 2

**Title:** Supplementary Data 20

Active-like FZD6 model in complex with SAG1.3 at a time point of 600 ns of simulation 2

**Title:** Supplementary Data 21

Active-like FZD6 model in complex with SAG1.3 at a time point of 800 ns of simulation 2

**Title:** Supplementary Data 22

Active-like FZD6 model in complex with SAG1.3 at a time point of 1000 ns of simulation 2

**Title:** Supplementary Data 23

Active-like FZD6 model in complex with SAG1.3 at a time point of 200 ns of simulation 3

**Title:** Supplementary Data 24

Active-like FZD6 model in complex with SAG1.3 at a time point of 400 ns of simulation 3

**Title:** Supplementary Data 25

Active-like FZD6 model in complex with SAG1.3 at a time point of 600 ns of simulation 3

**Title:** Supplementary Data 26

Active-like FZD6 model in complex with SAG1.3 at a time point of 800 ns of simulation 3

**Title:** Supplementary Data 27

Active-like FZD6 model in complex with SAG1.3 at a time point of 1000 ns of simulation 3

**Title:** Supplementary Data 28

Active-like FZD7 model in complex with SAG1.3 at a time point of 100 ns of simulation

**Title:** Supplementary Data 29

Active-like FZD7 model in complex with SAG1.3 at a time point of 300 ns of simulation

**Title:** Supplementary Data 30

Active-like FZD7 model in complex with SAG1.3 at a time point of 500 ns of simulation

**Title:** Supplementary Data 31

Docking poses of Bodipy-cyclopamine to inactive FZD6 model

**Title:** Supplementary Data 32

mol2 Docking poses of purmorphamine to inactive FZD6 model

**Title:** Supplementary Data 33

Docking poses of purmorphamine to SMO

**Title:** Supplementary Data 34

6OT0 and FZD6 protein sequence alignment