

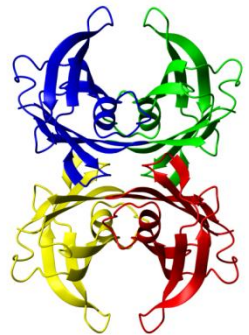
Tafamidis Meglumine

*Potential Disease Modifying
Treatment for TTR Amyloidosis*

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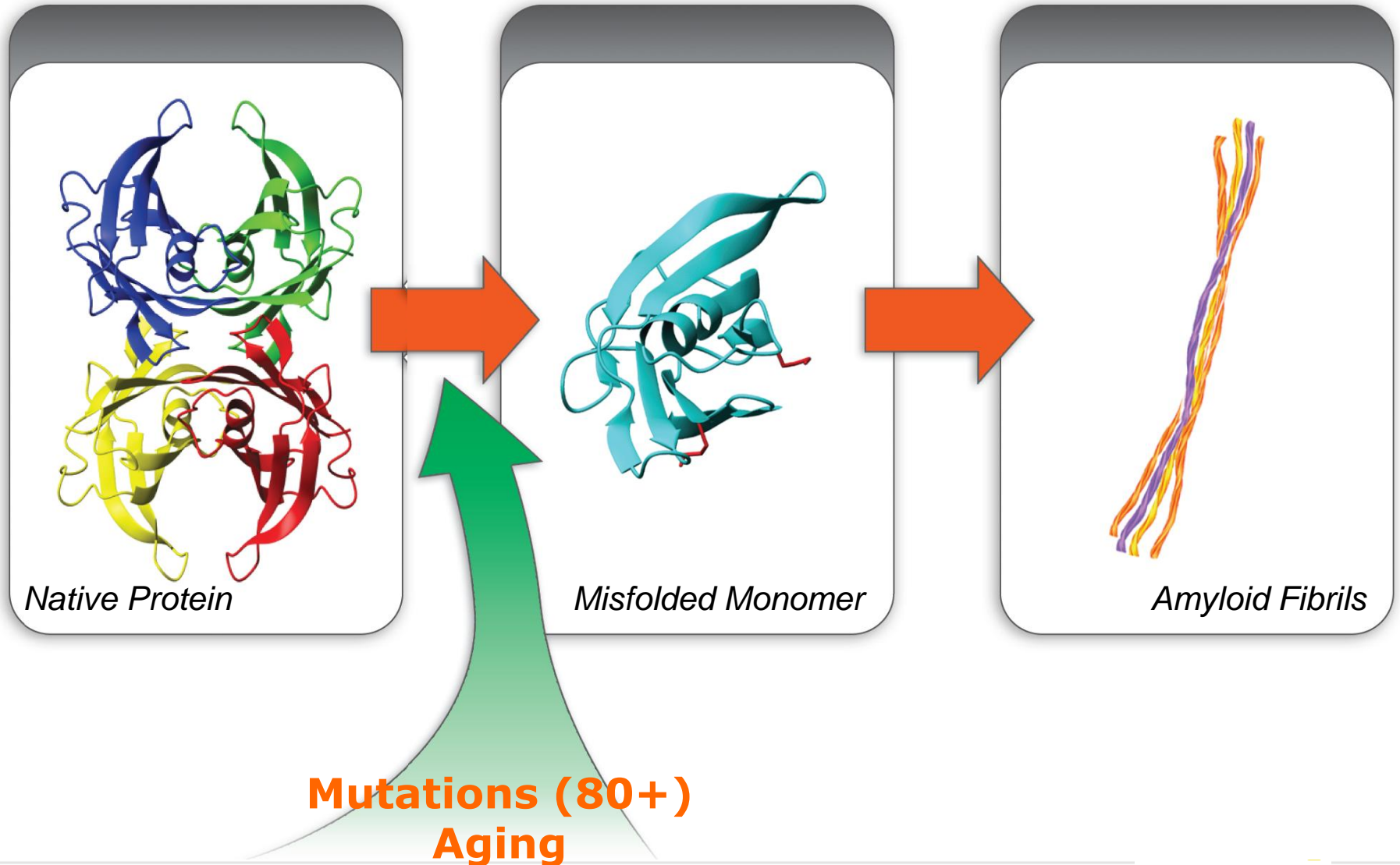
*Amyloidosis Support Group Patient Meeting
October 31 – November 1, 2009
Chicago*



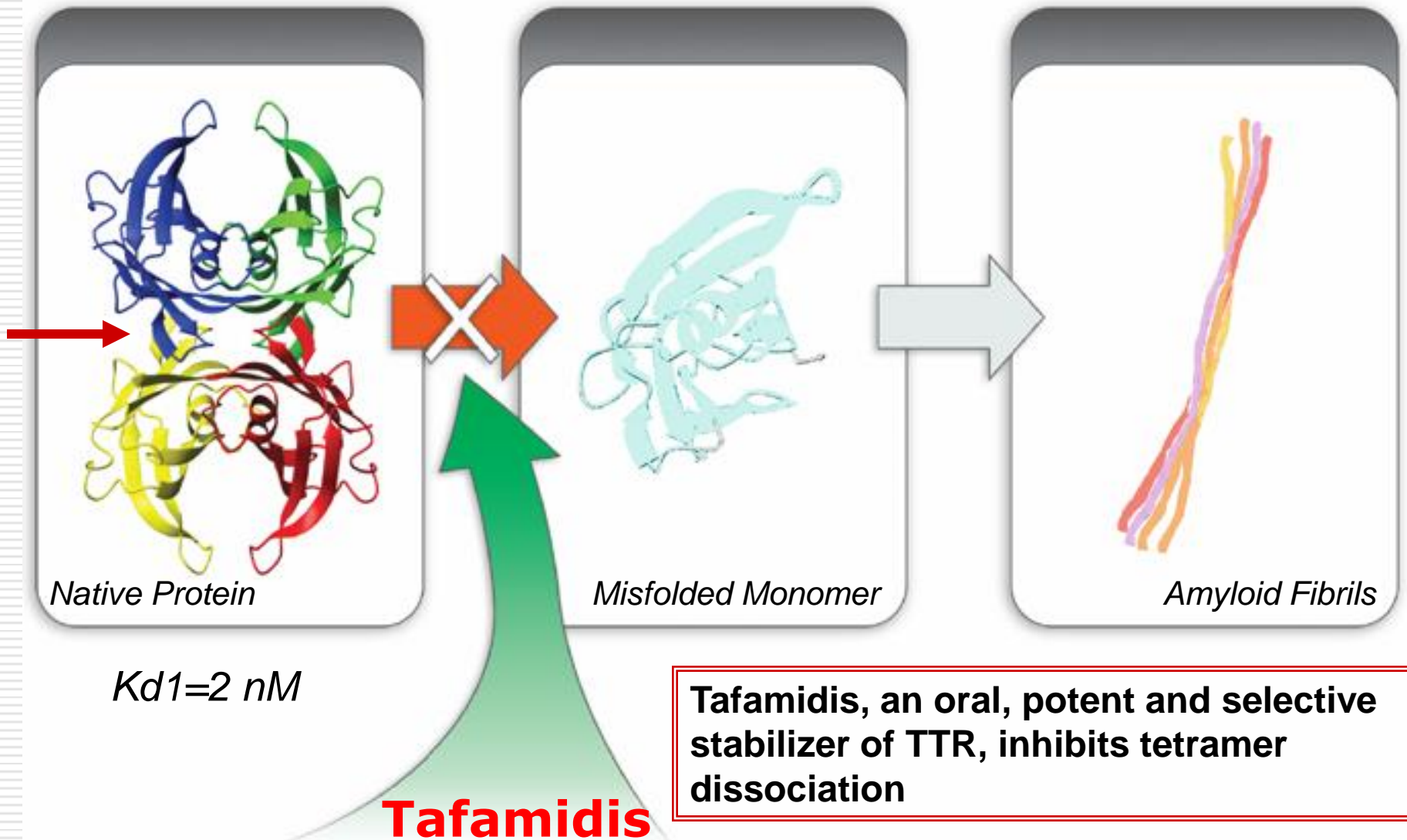
Tafamidis

- ❑ Tafamidis, previously known as Fx-1006A, a selective and potent stabilizer of transthyretin (TTR)
 - Binds to the TTR protein and stabilizes the correctly folded protein
 - Inhibits amyloid formation in the test tube
 - No “off-target” pharmacology (e.g. no NSAID activity)
 - Oral, once daily, first in class compound
- ❑ Being evaluated as a disease modifying treatment for TTR amyloidosis (ATTR)
- ❑ Being developed by FoldRx Pharmaceuticals, Inc., Cambridge MA

Cause of TTR Amyloidosis



Halting TTR Amyloidosis



Tafamidis Development Program

- ❑ Dedicated to understanding of the natural history of TTR amyloidosis
 - Conducted natural history study in patient with TTR amyloid cardiomyopathy (TRACS)
 - ❑ Support the design of subsequent treatment studies
 - Conducted study evaluating appropriateness of clinical endpoints in assessing disease severity in patients with TTR amyloid polyneuropathy
 - ❑ Support the endpoints chosen in the treatment studies
- Supporting a number of academic run research efforts (for example – improving early diagnosis)

Tafamidis Development Program

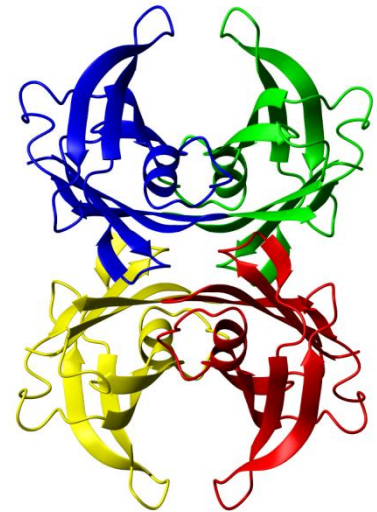
- ❑ Dedicated to understanding of the effects of tafamidis on disease progression in patients with TTR amyloidosis
 - Recently completed Phase II/III trial in patients with V30M TTR amyloidosis
- ❑ Ongoing clinical trials in patients with:
 - ❑ V30M TTR amyloidosis
 - ❑ Non-V30M TTR amyloidosis
 - ❑ V122I or wild-type TTR amyloid cardiomyopathy

Fx-005

Safety and Efficacy of Orally Administered Tafamidis in Patients with Transthyretin Familial Amyloid Polyneuropathy

A Phase II/III, Randomized,
Double-blind, Placebo-
Controlled Study

Key Results



Fx-005 Study Design

- ❑ Randomized, Placebo-controlled, Multi-center Study
 - 8 international sites
- ❑ 128 patients with V30M TTR amyloidosis (1:1 randomization)
 - 20 mg soft gelatin capsule once daily; placebo
- ❑ Key inclusion criteria:
 - V30M mutation
 - Positive amyloid biopsy
 - Documented peripheral and/or autonomic neuropathy (stage 1 and early stage 2)
- ❑ Key exclusion criteria:
 - Prior liver transplant
- ❑ Treatment duration – 18 months

Fx-005 Assessments

Main Assessments

- NIS-LL – Neuropathy Impairment Score – Lower Limb
 - Scores the neurological exam of the legs, according to muscle weakness, sensory abnormalities and loss of reflexes
- Norfolk QOL-DN – Quality of Life
 - Patient questionnaire that assesses the impact of the various aspects of the neurologic disease on his/her quality of life

Other Assessments

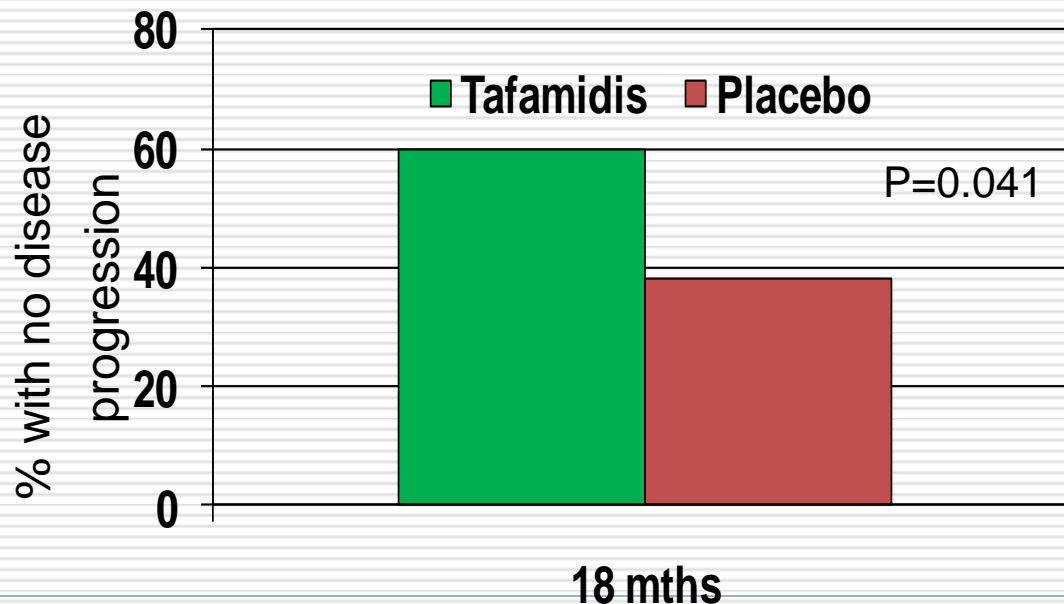
- Objective measures of nerve function, including nerve conduction studies and quantitative sensory testing
- Modified Body Mass Index (mBMI) – a measure of the wasting aspect of this disease

Fx-005 Results

- ❑ Of the 128 patients enrolled, 91 (71%) completed the study
 - Majority of the patients who discontinued from the study (26/37, 70%) did so to undergo liver transplantation - 13 patients in each treatment group
 - Tafamidis was well tolerated – only 3 patients in each treatment group discontinued the study due to a side effect
- ❑ Of the 91 patients completing the study, 86 are participating in the open label extension study (Fx-006)

Fx-005 Results – *NIS-LL Responders*

- Tafamidis maintained neurologic function:
 - 60% of tafamidis patients completing the study per protocol had no disease progression – that is, no worsening of their neurologic function compared with 38% of patients on placebo

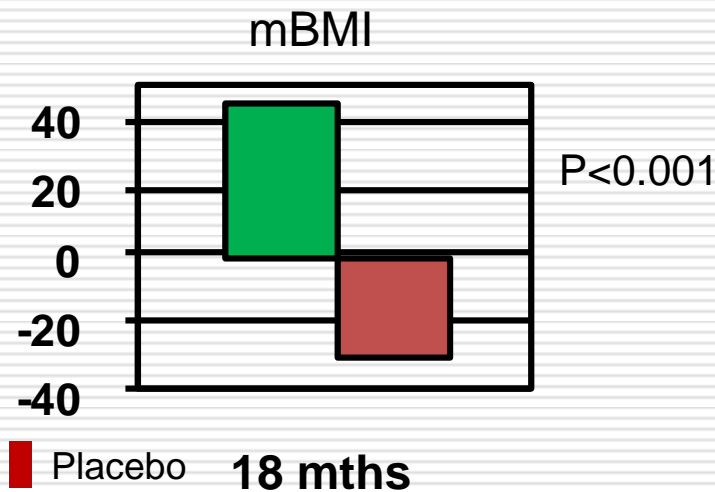
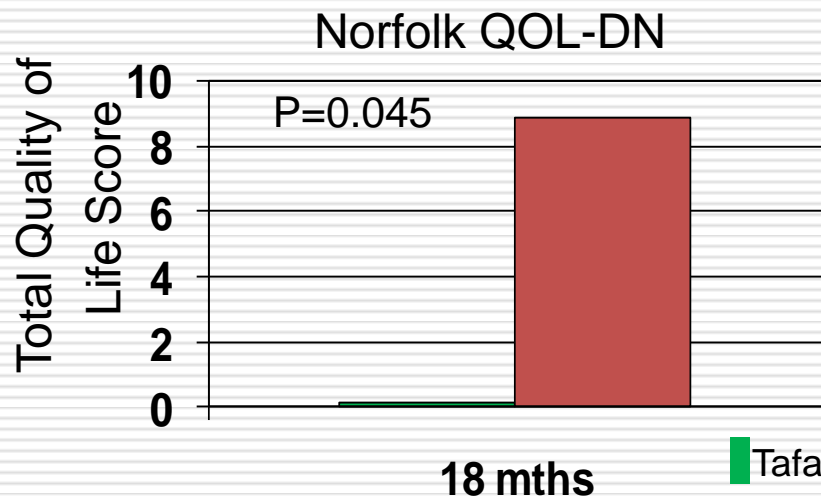


Fx-005 Results

Quality of Life and Nutritional Status

□ Tafamidis reduced burden of disease:

- Those patients receiving tafamidis maintained their quality of life, and experienced an improvement in nutritional status,
- Those patients not on active treatment (placebo) had a worsening of their quality of life, and a deterioration of their nutritional status



Fx-005 Results

- ❑ Other measures of nerve function demonstrated that tafamidis treatment resulted in less deterioration
 - ❑ 50 - 80% less worsening of nerve function
- ❑ The side effects reported in the tafamidis group were similar to those reported in the placebo group

Fx-005

Conclusions and Next Steps

- Patients with V30M TTR amyloidosis who received 18 months treatment with tafamidis experienced
 - Significantly less disease progression
 - Maintained quality of life
 - Side effects similar to placebo
- A US New Drug Application for tafamidis is being planned for second half of 2010

Tafamidis

Additional Treatment Studies

□ Fx1A-201:

- Open label, tafamidis 20 mg once daily, 12 months
- Patients with TTR amyloidosis due to mutations other than V30M
- 21 patients enrolled (enrollment is complete)

□ Fx1B-201:

- Open label, tafamidis 20 mg once daily, 12 months
- Patients with TTR amyloid cardiomyopathy due to V122I or wild-type TTR
- 35 patients enrolled (enrollment complete)

➤ Data Expected first half 2010

Thank You for your Attention

