
**A Rose by Any Other Name -
Our Experience with an RTOR-like Neuroscience Filing**
Carolyn Fisher, Dave Summers & Emma Moore



Agenda

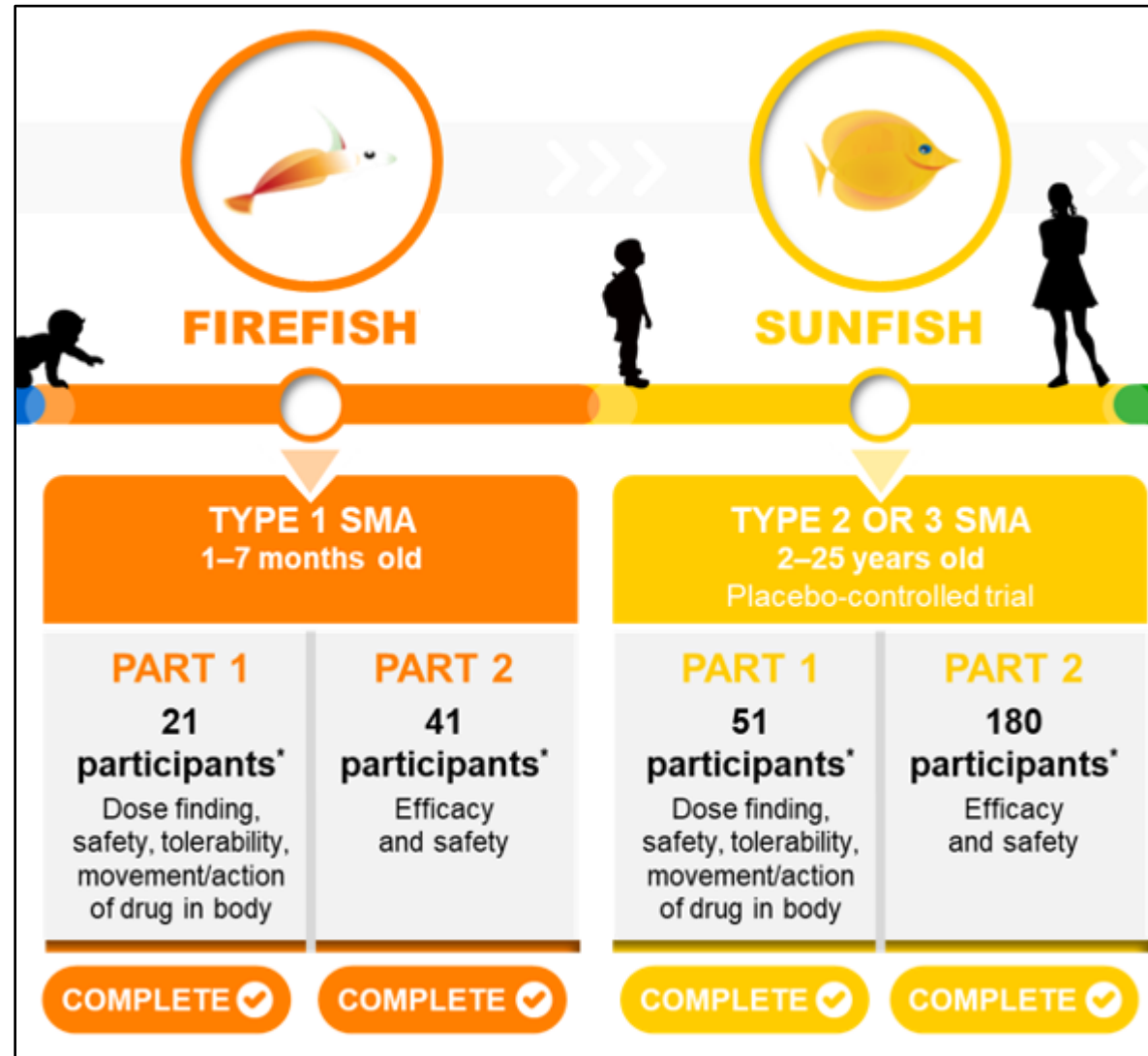
- Our Filing & Roles
 - Why we compare this to an RTOR filing
- General Challenges Faced
- eSub Challenges
- Lessons Learned
- Reflection
 - What we would have done differently
 - How we used our learnings going forward

Our Roles

- Carolyn Fisher
 - Biometrics Submission Team Lead (BSTL)
 - Project Lead for Statistical Programming Team (~15 team members)
- Dave Summers
 - Study Lead for Pivotal study
 - Ophthalmology king & expert at describing analysis to stakeholders
- Emma Moore
 - Study Lead for supporting study
 - Lead on Safety Pooling activities



Overview of Risdiplam and our filing



Numerous Filing Scenarios Considered

Options	Probability
1. Biomarker Data Only (SF & FF) <i>(e.g. US Accelerated Approval)</i>	Low
2. FIREFISH Part 1 Clinical Outcome Data, plus SUNFISH Part1	Medium
3. FIREFISH Part 2 “early file”; Plus SUNFISH Part 1	Medium/High
4. FIREFISH & SUNFISH Part 1; supplement with Part 2 during review	Medium/High
5. Full Package – Part 2 from both studies	High

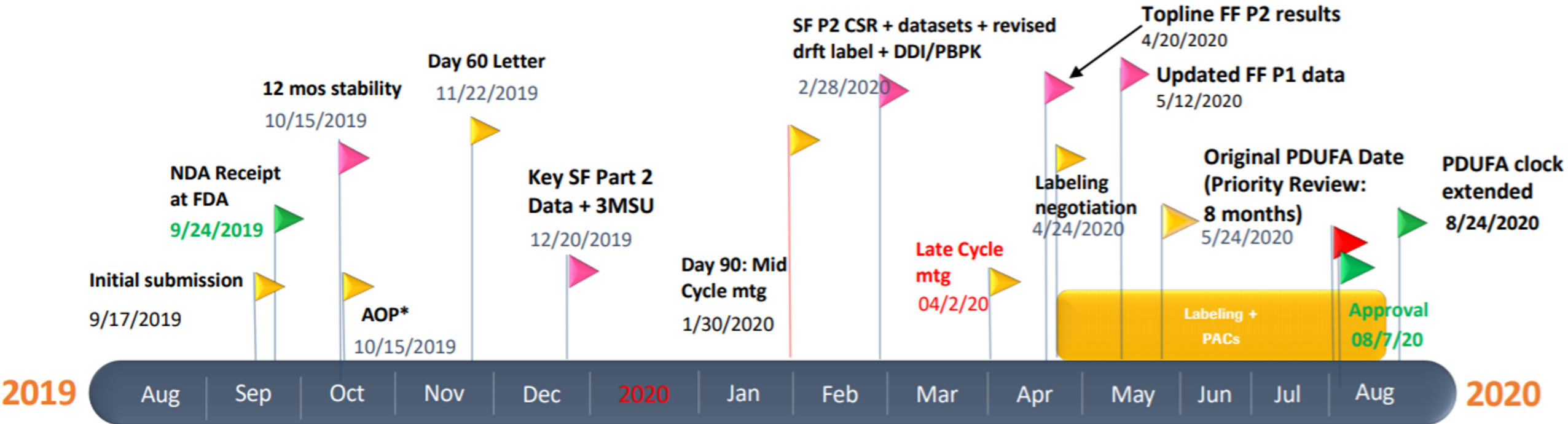
What is an RTOR (Real Time Oncology Review) filing & why have we compared ours to one?

RTOR allows the FDA to review much of the data earlier, before the applicant formally submits the complete application. Unlike rolling review, individual components of a module can be submitted, rather than only fully completed modules.

For our filing:

- Legacy & pooled datasets were requested & sent prior to submission
- Additional data for Sunfish part 2 (not included in the original filing) were requested a week after publishing
 - Only data and outputs shown in the topline results meeting were sent within 4 weeks
 - Rest of study followed in February

Filing Roadmap



'Filing Go' decision made End of January 2019

General Challenges

New data types

Change in entire
clinical science team

Migrated to another
computing environment ~3
months before 'Filing Go'
decision

Intense timelines

Constant change in
requirements

Lots of unplanned
analysis

Completely new
disease area for
Roche

eSub Challenges

Real World Data studies were included

Late addition of efficacy pooling

2.3 Terabytes – VERY large initial NDA submission

Preparation of eSub packages done after reporting

Not much experience within the company using Pinnacle 21

Legacy studies that had closed out needed to be transformed to CDISC standards

One of the first fully CDISC filings for the company

Lessons Learned

**Strong relationships
between departments are the
key to success**

**Don't leave eSub
prep to the last
minute**

**Take time out for
yourself**

**Expect the
unexpected**

**Familiarise yourself
with new systems
ahead of time**

Reflection

What we would have done differently

**Ensured all studies are eSub
ready (or as much as
possible) throughout the
study**

**Conduct team
debriefs whilst
project was ongoing**

**Utilised Interactive
Data Displays (IDDs)
more throughout the
project**

Reflection

How we used our learnings going forward

eSub readiness

**Very clear & firm with
timelines for
additional analysis**

**Team check-ins &
'enforced' downtime**

**Improved stakeholder
relationships**

Robust programs



Please feel free to leave questions in the Q&A box!

***Doing now what patients
need next***