From Benchtop to Approval in Record Time: A Case Study of Ronapreve

Part 2
Partnership between Regeneron and Roche

Roche entered into a collaboration with Regeneron in summer 2020 to increase the global supply of the REGN-COV2 antibodies.
J-NDA Required Documentation for Exceptional Approval Pathway

Exceptional approval pathway was requested early in submission preparation and confirmed by MHLW at approval

- Only five other products have been confirmed exceptional approval by MHLW
  - As of Oct 26: Remdesivir, Comirnaty, Covid-19 Vaccine Moderna, Vaxzevria, Sotrovimab

- Minimum CMC documentation for exceptional approval is the Application Form (M1.2)
  - Information of formulation (composition)
  - Manufacturing sites
  - Manufacturing process description, basal media composition
  - Release test methods, specifications, and reference standard
  - Storage conditions and shelf-life setting

- However in Ronapreve case, PMDA required M1/M2.3/M3, same as normal filing

- To speed preparation, EU M3 was leveraged and submitted to PMDA as is
J-NDA Module 3 Rolling Review Timeline

March 2021
- Molecule general information and characterization
- DS Process, Controls, Validation, and Platform SL Strategy

April 2021
- DP Process, Controls, and Validation

May 2021
- Comparability package for Roche sites
- Stability Updates

July 2021
- Final virus clearance validation data*

*negotiated with PMDA before submission

Close collaboration and communication with the HA made this work!
Ronapreve J-NDA timeline

April 2021

- (3/31) Disclosure of M3 (Mar) to Chugai
- M1 preparation in Chugai
  - M1 English version (DS, Analytical) Preparation & review
- (4/30) Adjudication of Chugai/Roche/Regeneron

May 2021

- (4/28) Disclosure of M3 (Apr) to Chugai
- M1 English version (DP) Preparation & review
- (5/26) Disclosure of M3 (May) to Chugai
- (4/30) Adjudication of Chugai/Roche/Regeneron

June 2021

- (5/10) M3 (Mar & Apr) pre-submission
- (5/28) M1 draft pre-submission

July 2021

- M1 modification
- M2 modification
- (6/29) formal submission
- (7/19) approval

Number of inquiries
(Sub-items are included in brackets)

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PMDA M3 pre-review

- (6/20) inquiry (1st)
- (6/1) inquiry (2nd)
- (6/16) inquiry (3rd)
- (6/18) inquiry (4th)
- (6/30) inquiry (5th)
- (7/2) inquiry (6th)
- (7/6) inquiry (7th)
- (7/9) inquiry (8th)

PMDA review

- Response
- Response
- Response
- Response
- Response
- Response
- Response
- Response
Lessons Learned

Expectation Setting and Pre-negotiation with the HA is key
- PMDA was familiar with timing and content of rolling review
- Allowed for some data to be provided post-approval

Leverage novel ways of working
- Worked to create JM1 and JM2 from EU M3

Utilizing a shared web-based platform between multiple companies speeds rapid response to HA questions

Translation and back translation takes significant time and effort during short turn around Q&A responses
Ronapreve Global Highlights

1.5M
Doses to be delivered to patients by end of 2021

IMA
4 Approvals - JP, UK, AU, and EU approvals received in record time from date of submission

59
EUA & Import Licence Approvals

~70%
reduction in risk of hospitalization or death in non-hospitalized patients

20%
reduction in risk of mechanical ventilation or death in hospitalized patients

775+
Q&A Answered (150 in Japan in 1.5 months)

Module 3 Documents
Multiple updates to sections as a result of rolling review submission

800+

Indications Approved Globally
- Pre-exposure prophylaxis
- Post-exposure prophylaxis
- Hospitalized
- Non-hospitalized

4 Approvals - JP, UK, AU, and EU approvals received in record time from date of submission