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

Part 2

RONAPREVE®
casirivimab and imdevimab

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

	Regeneron (REGN)		Roche/Genentech
Technical Responsibilities	Manufacture of Product	Studies supporting Tech Transfer, Method Val & Testing	Manufacture of Product
	Development Studies & Control System		Site-dependent Studies
Regulatory Responsibilities	US Emergency Use Authorization & Biological License Application	EU/UK Market Authorization Application	All other Emergency Use Authorization & Market Authorization Applications

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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!

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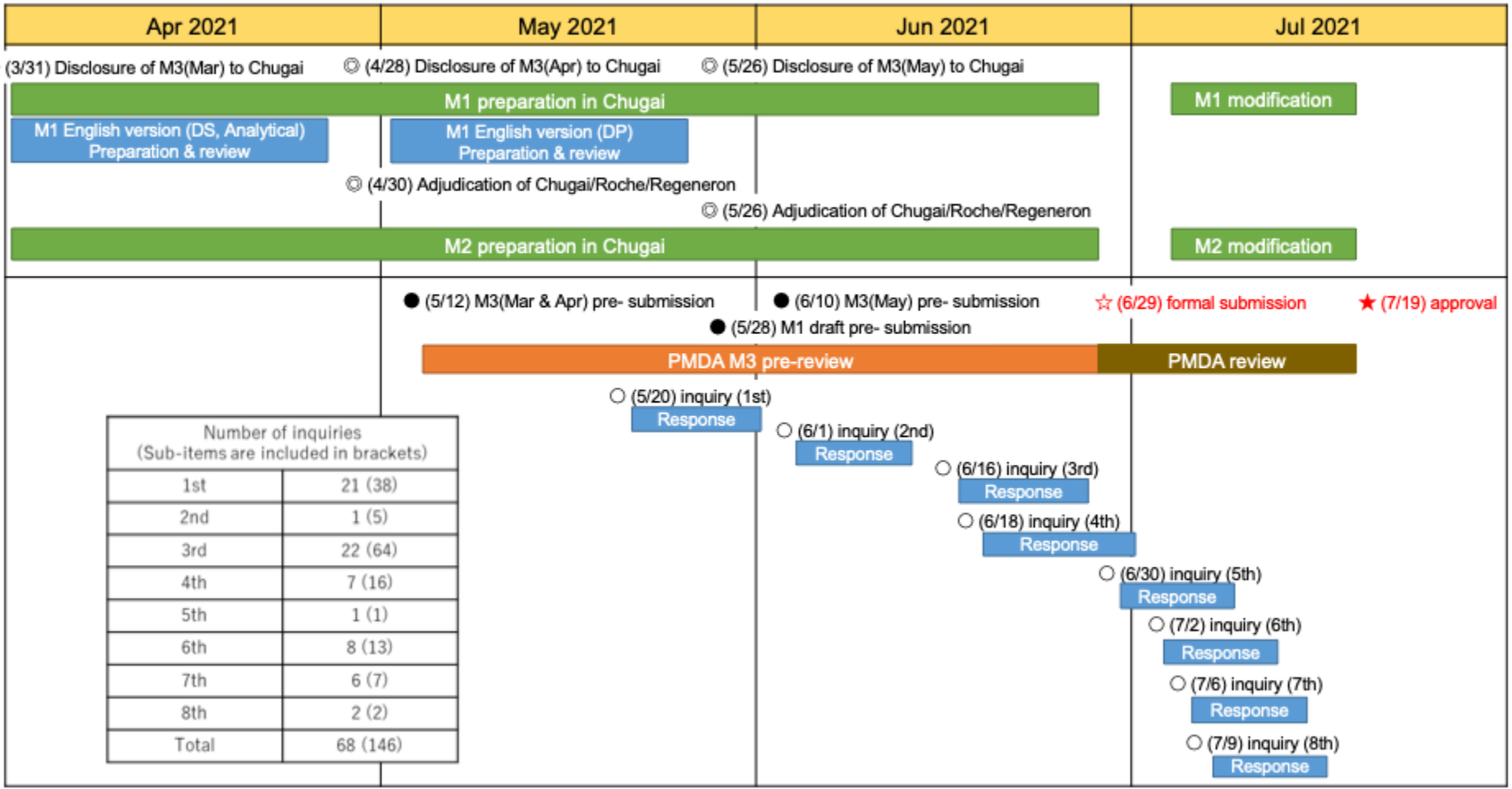
Ronapreve J-NDA timeline

Chugai/Roche/Regeneron collaboration !!



Number of inquiries (Sub-items are included in brackets)	
1st	21 (38)
2nd	1 (5)
3rd	22 (64)
4th	7 (16)
5th	1 (1)
6th	8 (13)
7th	6 (7)
8th	2 (2)
Total	68 (146)

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

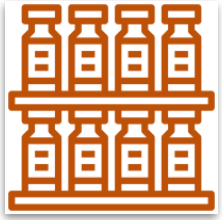
Utilizing a shared web-based platform between multiple companies speeds rapid response to HA questions

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)

800+

Module 3 Documents

Multiple updates to sections as a result of **rolling review submission**

Indications Approved Globally

4

- Pre-exposure prophylaxis
- Post-exposure prophylaxis
- Hospitalized
- Non-hospitalized

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