Opening Remarks

BLA 761088

CT-P10, a proposed biosimilar to US-Rituxan

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CT-P10 Regulatory History

351(k) Pathway	
April 28, 2017	BLA 761088 Submitted
February 28, 2018	Complete Response
May 28, 2018	BLA 761088 Resubmitted

CT-P10 Proposed Indications

The Applicant is seeking licensure of CT-P10 for the following indications for which US Rituxan is currently licensed:

- Non-Hodgkin's Lymphoma (NHL)
  - Relapsed or refractory, low grade or follicular, CD20-positive B-cell NHL as a single agent
  - Previously untreated follicular, CD20-positive, B-cell NHL in combination with first line chemotherapy and, in patients achieving a complete or partial response to Rituxan in combination with chemotherapy, as single-agent maintenance therapy
  - Non-progressing (including stable disease), low-grade, CD20-positive, B-cell NHL as a single agent after first-line cyclophosphamide, vincristine, and prednisone (CVP) chemotherapy

Regulatory Background

- The **Biologics Price Competition and Innovation Act of 2009 (BPCI Act)** was signed into law on March 23, 2010.
- BPCI Act creates an ***abbreviated licensure pathway for biological products shown to be biosimilar to or interchangeable with*** an FDA-licensed reference product.
  - A biological product that is demonstrated to be "***highly similar***" to an FDA-licensed biological product (the reference product) may rely for licensure on, among other things, publicly-available information regarding FDA's previous determination that the reference product is safe, pure and potent.
  - This licensure pathway permits a biosimilar biological product to be licensed under 351(k) of the Public Health Service Act (PHS Act) based on **less than a full complement of product-specific preclinical and clinical data** → **abbreviated** licensure pathway**.**

Biosimilarity

Biosimilar or **Biosimilarity** means:

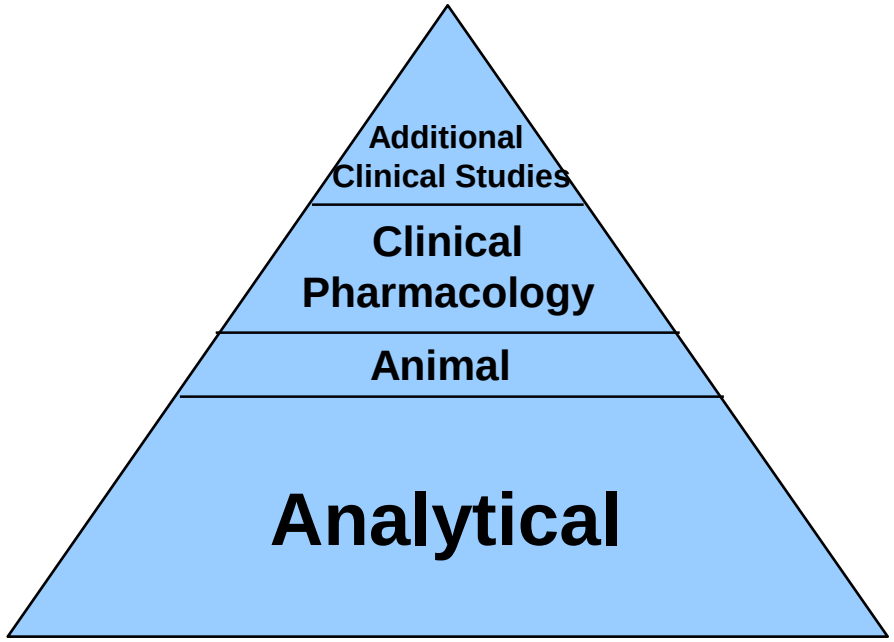
- That the biological product is **highly similar** to the reference product notwithstanding minor differences in clinically inactive components; and

- There are **no clinically meaningful differences** between the biological product and the reference product in terms of the safety, purity, and potency of the product.

Goals of "Stand-alone" and Biosimilar Development are Different

"Stand-alone" Development Program, 351(a)
Goal: To establish safety and efficacy of a new product

"Abbreviated" Development Program, 351(k)
Goal: To demonstrate biosimilarity (or interchangeability) to a reference product



What does this difference mean from a development perspective?

Biosimilar Development Key Concepts

- **Analytical similarity data** is the foundation of biosimilar development.

- Understanding the relationship between quality attributes and the clinical safety & efficacy profile aids ability to determine **residual uncertainty** about biosimilarity and to predict expected “clinical similarity” from the quality data.

Biosimilar Development Key Concepts

- The nature and scope of clinical studies will depend on the extent of residual uncertainty about the biosimilarity of the two products **after** conducting an extensive analytical similarity assessment.
- Comparative clinical study(ies) will be necessary to support a demonstration of biosimilarity if there are **residual uncertainties** about whether there are clinically meaningful differences between the proposed biosimilar and reference product.
- Scientific justification must be provided to support extrapolation to other conditions of use.
- The content of a biosimilar development program is based on stepwise development and approvability is based on the totality of the evidence submitted by the sponsor.

Evidence Supporting CT-P10

Data	Source
Analytical similarity	➢ Pairwise comparisons between US-licensed Rituxan and CT-P10 lots.
Nonclinical pharmacology and toxicology	➢ Comparative 8-week repeat-dose toxicity study in cynomolgus monkeys ➢ Tissue cross-reactivity study (human tissues)
Immunogenicity	➢ **CT-P10 3.2**: Randomized, double-blind, active-controlled, parallel group study in patients with rheumatoid arthritis
Clinical Pharmacology	➢ **CT-P10 3.2**: Randomized, double-blind, active-controlled, parallel group study in patients with rheumatoid arthritis ➢ **CT-P10 3.3**: Randomized, double-blind, active-controlled, parallel group study in patients with advanced follicular lymphoma ➢ **CT-P10 3.4**: Randomized, double-blind, active-controlled, parallel-group study in patients with low tumor burden follicular lymphoma
Clinical Safety and Efficacy	➢ **CT-P10 3.3**: Randomized, double-blind, active-controlled, parallel group study in patients with advanced follicular lymphoma ➢ **CT-P10 3.4**: Randomized, double-blind, active-controlled, parallel-group study in patients with low tumor burden follicular lymphoma

Key Topics to Consider

- Topic 1: Discuss whether the evidence supports a demonstration that CT-P10 is highly similar to US-licensed Rituxan, notwithstanding minor differences in clinically inactive components.
- Topic 2: Discuss whether the evidence supports a demonstration that there are no clinically meaningful differences between CT-P10 and US-licensed Rituxan.
- Topic 3: Discuss whether there is adequate justification to support licensure for the proposed indications sought by the Applicant.

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Voting Question

Does the totality of the evidence presented support licensure of CT-P10 as a biosimilar to US-licensed Rituxan for the following indications?

Treatment of adult patients with Non-Hodgkin's Lymphoma (NHL)

- Relapsed or refractory, low grade or follicular, CD20-positive B-cell NHL as a single agent
- Previously untreated follicular, CD20-positive, B-cell NHL in combination with first line chemotherapy and, in patients achieving a complete or partial response to a rituximab product in combination with chemotherapy, as single-agent maintenance therapy
- Non-progressing (including stable disease), low-grade, CD20-positive, B-cell NHL as a single agent after first-line cyclophosphamide, vincristine, and prednisone (CVP) chemotherapy