

27th Annual Fordham IP Conference

# Reasonable protection of antibody patents

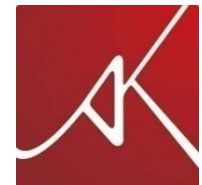
- The right balance between patentees and competitors -

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# Market of antibody drugs

Top 10 drugs by 2018 sales (\$bn)

Source: EvaluatePharma\* 15 November 2017



<http://info.evaluategroup.com/rs/607-YGS-364/images/EPV18Prev.pdf>

# Characteristics of dispute over antibody patents

- Party
  - Originator vs. Originator
  - Originator vs. follow-on manufacturers (biosimilar companies)

- Cost for development of the alleged products

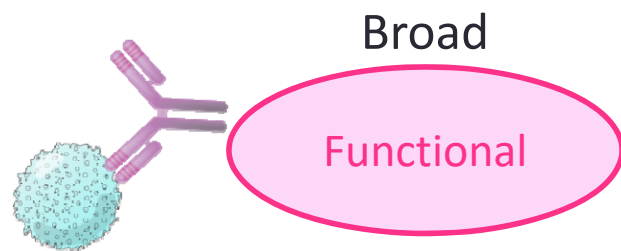
Very high, even for biosimilars, because more evaluation of quality characteristics both by the clinical and non-clinical tests are necessary.

(FYI, between \$100 million and \$250 million, biosimilars in general)

Erwin A. Blackstone, PhD et al, “The Economics of Biosimilars”, Am Health Drug Benefits. 2013 Sep-Oct; 6(8): 469–478.

# Issues on antibody patents

- Protection –Claim drafting



Pro: Class of antibodies can be covered.  
Con: Risk of lack of written description requirements, patentability

Limited



Pro: Strong as to written description requirements  
Con: Antibodies having slightly different SEQs may not be covered by the claim

- Scope of patent- Claim construction  
How should a functionally claim be reasonably construed ?

# Alirocumab (PCSK 9 antibody) cases

## *Amgen vs. Sanofi*

- **Patent infringement case**

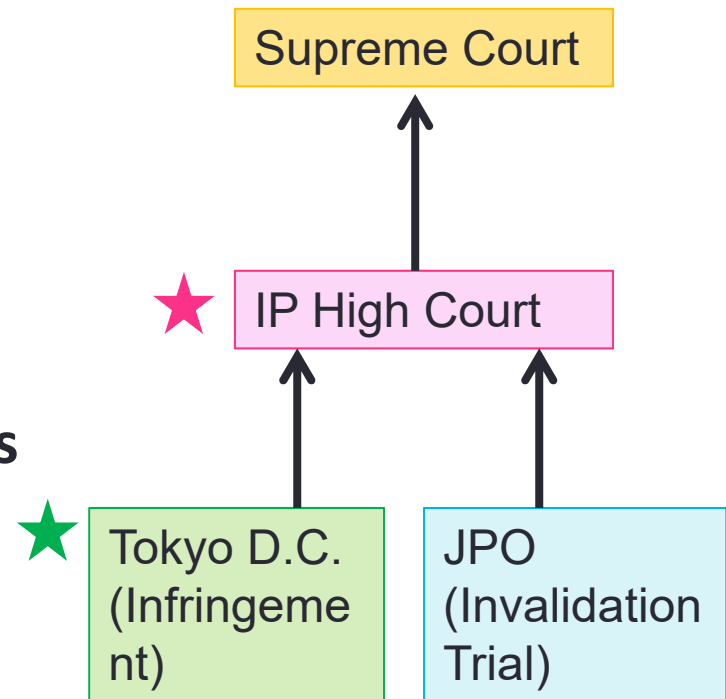
Tokyo District Court decision on January 17, 2019 (2017(Wa)16468)

Issue: **Claim construction, validity**

- **Validity cases (Appeal against decisions by the JPO)**

IP High Court decision on December 27, 2018 (2017(Gyo-ke) 10225 and 10226)

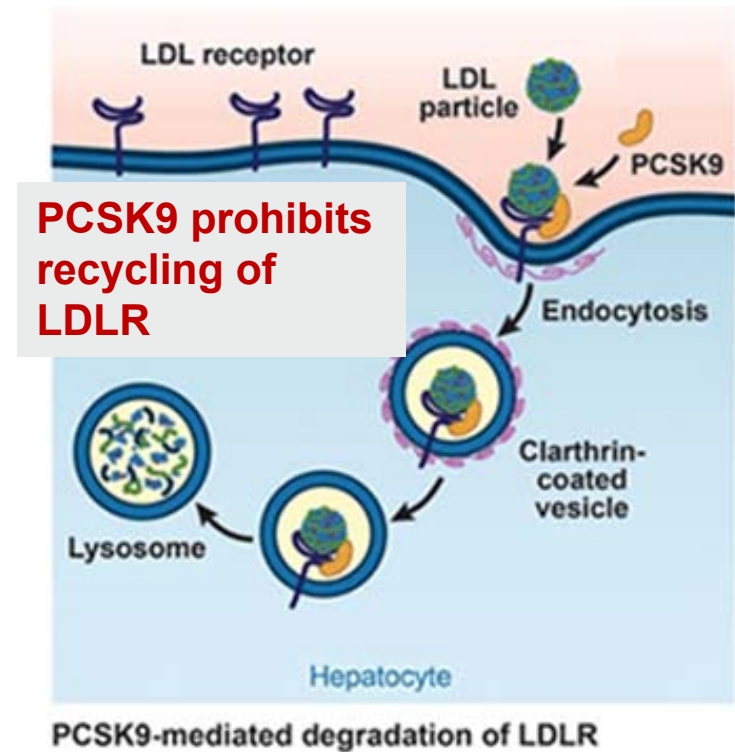
Issues: **Inventive step, support requirement, enablement**



# Facts

- Technical field:  
PCSK9 inhibitors to treat high cholesterol.
- Patentee (Amgen)'s Product:  
Repatha™ (evolocumab)
- Sanofi's Product:  
Praluent™ (alirocumab)  
Alirocumab is not described in the specification of the Present Patents.

## PCSK9 Mechanism of Action



Lambert G, et al. *J. Lipid Res.* 2012;53:2515-2524.<sup>[6]</sup>

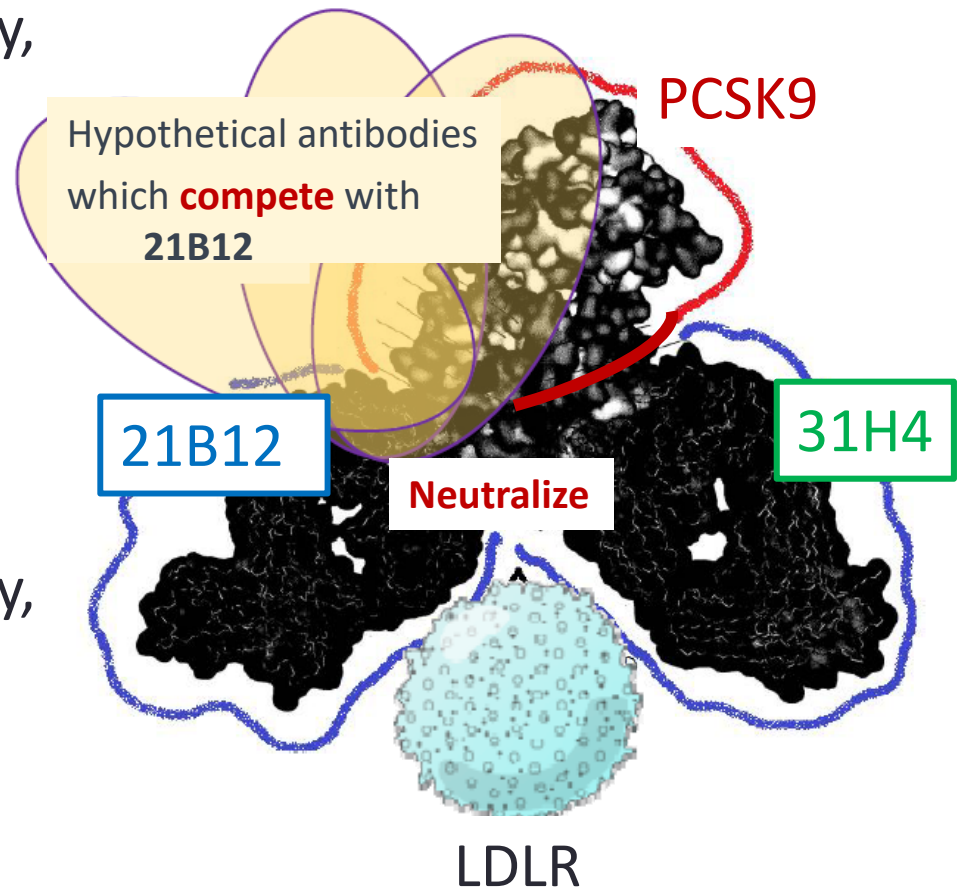
## Patents at Issue (JP5705288, JP590633)

- Invention 1:(Simplified)

A: An isolated monoclonal antibody,  
B : which is capable of **neutralizing** binding of PCSK9 to LDLR,  
C: wherein the antibody **competes** with **21B12 antibody**.

- Invention 2:(Simplified)

A: An isolated monoclonal antibody,  
B : which is capable of **neutralizing** binding of PCSK9 to LDLR,  
C: wherein the antibody **competes** with **31H4 antibody**.



**Neutralize:** Bind to a ligand and prohibit or reduce biological effects of the ligand

# Infringement- Claim Construction (Tokyo D.C.)

- Construction by Sanofi:

The claim should be limitedly construed to antibodies obtained by substituting one or a few amino acids of the antibodies described in the specification.

- Finding by the Court:

The claim is not limitedly construed as Sanofi argues.

(Reason)

**Taking description of the specification regarding how to screen and produce competing antibodies with 21B12 and 31H4 into account,** a POSA would have understood that antibodies which satisfy enablement are not limited to the antibodies obtained by substituting one or a few amino acids of the antibodies described in the specification.

➡ Sanofi's antibody falls into the scope of the claim.

Number of antibodies described in the specification: **32**

	Competition
With 21B12 not 31H4	16
Both	2
With 31H4 not 21B12	7
None	1

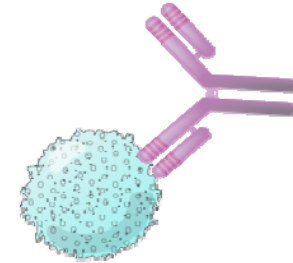
Number of antibodies having **neutralizing** effect: **20**



# Validity- Inventive step (1) (IP High Court)

## Prior Art

D1: J. Clin. Invest., vol 116(11), pp. 2995-3005(2006)



Followings are described:

- Experiments resulting PCSK9 reduces LDLR protein level in liver by binding with LDLR.
- Anti human polyclonal antibodies against PCSK9 obtained by injecting PCSK9 to a rabbit.

But followings are **not** described:

- The antibodies are capable of **neutralizing** binding of PCSK9 to LDLR.
- The antibodies **compete** with **21B12 antibody** or **31H4 antibody**

# Validity- Inventive step (2) (IP High Court)

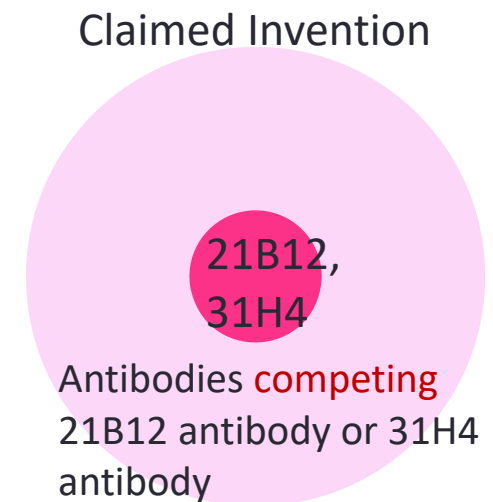
Finding by the IP High Court (Summary): **Inventive**

- A POSA who reads D1 would have motivated to obtain neutralizing antibodies and, based on the common technical knowledge, it would have been possible to obtain **some kind of** monoclonal antibodies.

However, it is common technical knowledge that **difference in the process (e.g. process of obtaining immunized mouse) of producing antibodies leads difference in reaction against antigen of the antibodies.** Taking this into account, optimizing the process for obtaining **21B12 antibody or 31H4 antibody** needs **excessive burden of trial and error** even for a POSA with the knowledge of D1.

- **The antibodies competing with 21B12 antibody or 31H4 antibody** would not have been easily conceived by a POSA based on the same reason.

The Tokyo district court found inventive step based on almost the same reason.



# Discussion (1)

## 1. Impact of the decision

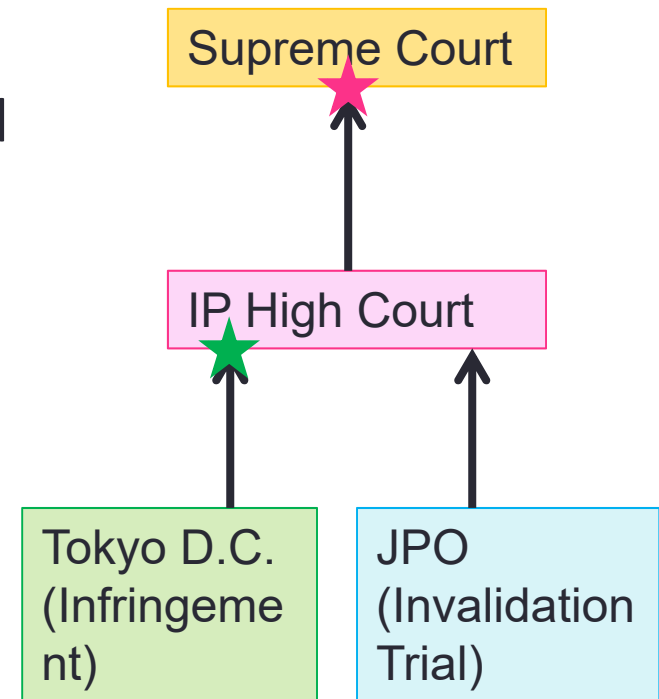
The infringement court broadly construed the functionally defined antibody claim and found infringement .

- Rather big reaction by pharma industry.

## 2. What happens next?

Sanofi appealed against all decisions.

It seems that the main issue would be whether the IP High Court will change the decision on infringement.



## Discussion (2)

### 3. Personal view on the decisions

The IP high Court found that also the antibodies **competing** 21B12 antibody or 31H4 antibody would not have been conceived by a POSA, because the process to obtain those antibodies are different from the process of common technical knowledge.

If the process to obtain claimed antibodies is essential for the present patents, is it still open to challenge of non-infringement of Sanofi's products ?

Thank you !



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