

Therapeutic Anti- IL- 20 mAb for Rheumatoid Arthritis

Institute of Biopharmaceuticals
Development Center for Biotechnology

Development Center for Biotechnology (DCB)

400+ 

RD/BD professionals serving as the innovation hub for early drug development.

36 

Founded in 1984, non-profit RD institution subsidized by the Ministry of Economic Affairs of Taiwan.

1200+ 

The premium drug development entity and connected with 1200+ biotech of TW.

25 

20+ out licensed assets and 5 Spin offs under **out-licensing** and **co-development** model.

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Primary Team



Project Team

Unmet Need

Technology

Opportunity

IP/Dev Status

Summary/Contact

T

Primary Investigator
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E

Project Leader
Chia-Cheng Wu, PhD.



Development Center
for Biotechnology

A

M

- DCB introduced **Murine anti-IL-20 monoclonal antibody (7E)** lead drug for **Rheumatoid Arthritis** drug development from **Cheng-Gong University** and **Chi-Mei Hospital**.
- DCB carried out several pre-clinical activities for IND enabling, including Pharmacology, Toxicology, MCB characterization and Formulation.
- IL-20 belongs to IL-10 family and has been shown to transduce its signal through STAT3 in keratinocytes. IL-20 is correlated with proinflammatory diseases like **Rheumatoid Arthritis (RA)**, **Psoriasis**, **Psoriatic Arthritis**, and **Acute Renal Failure**.

Introduction

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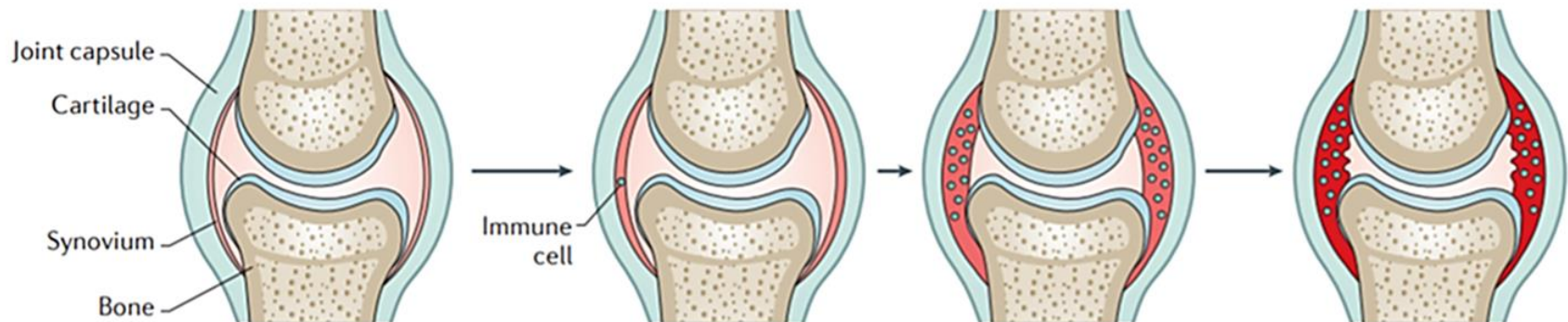
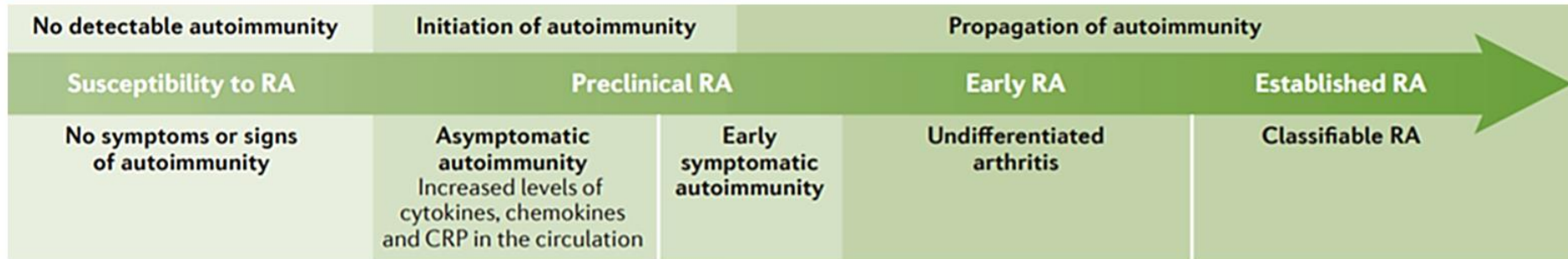
IP/Dev Status

Summary/Contact

Therapeutic IL- 20 Antagonist for Rheumatoid Arthritis

治療性抗介白素-20單株抗體於
類風濕性關節炎之藥物開發

Development and Progression of RA

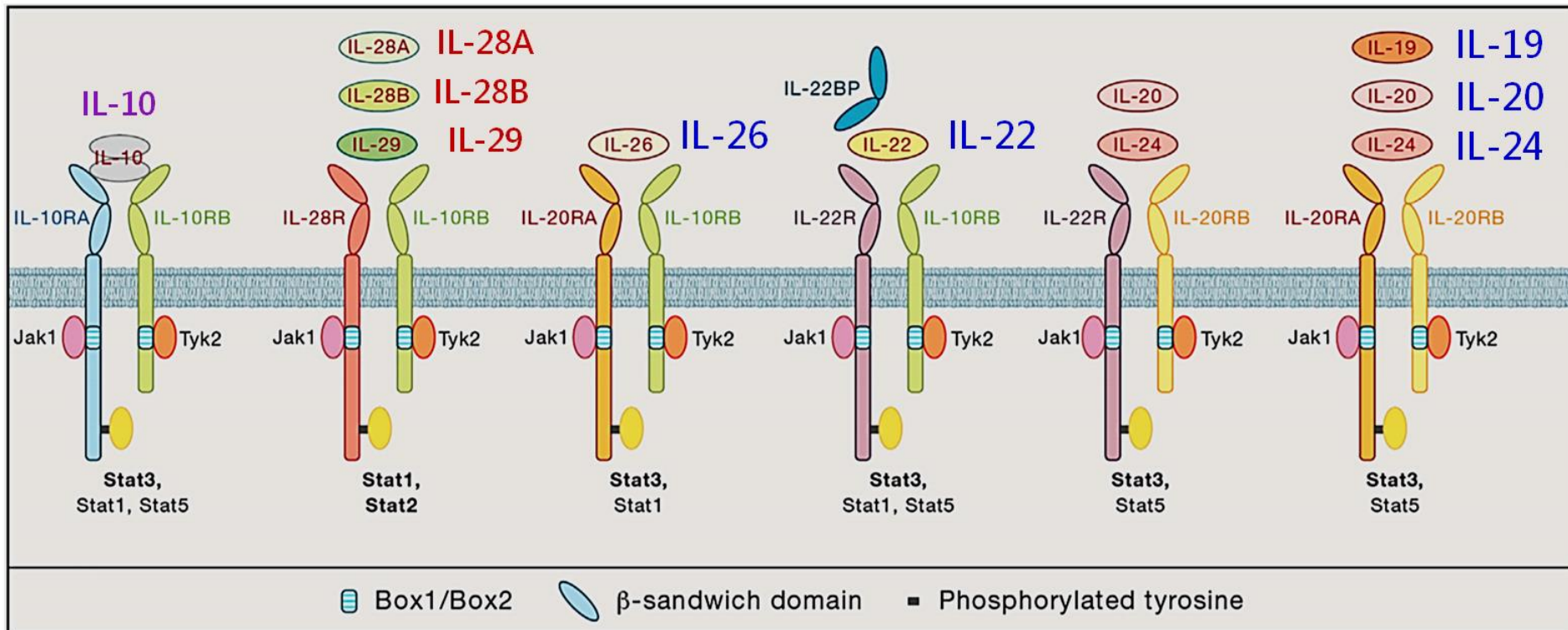


Nat Rev Disease Primers (2018) 4, 1-23.

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- | | |
|-----------------------------|---|
| Therapeutic Drugs
for RA | <p>Steroids</p> <p>Non-Steroid Anti-Inflammation Drugs (NSAIDs)</p> <p>Disease-Modifying Anti-Rheumatic drugs (DMARDs)</p> <p>Biologics</p> |
|-----------------------------|---|
-

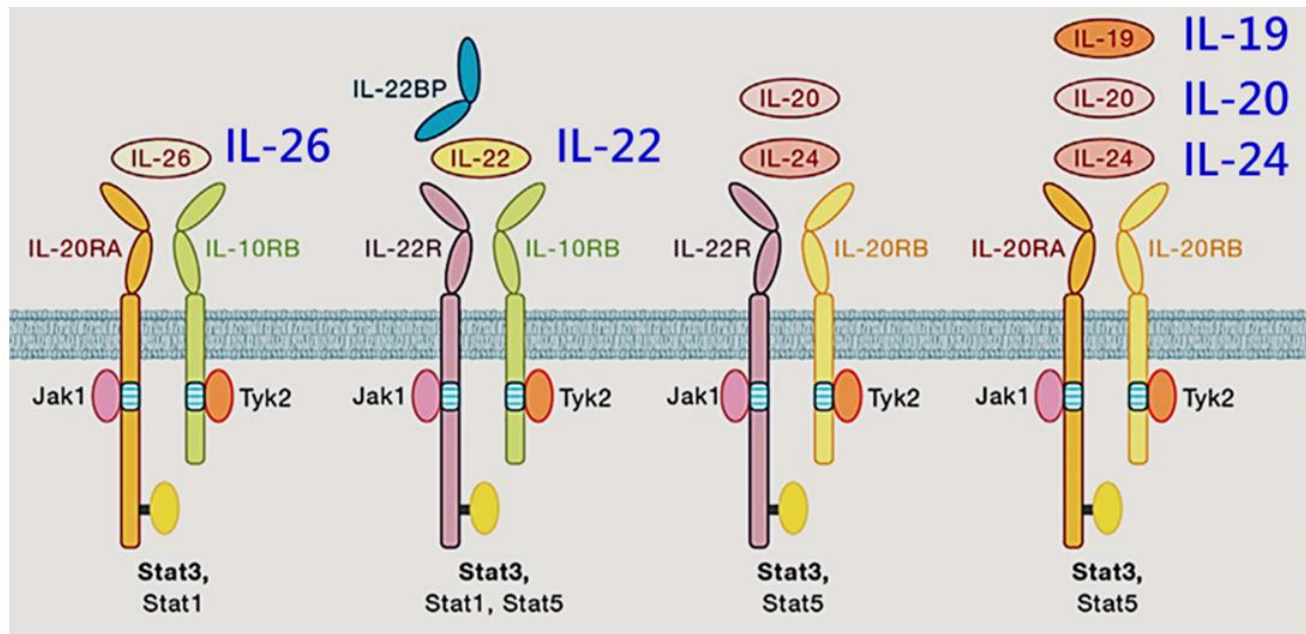
IL-20 Belongs to IL-10 Family which is Comprised of nine Members

- ◆ IL-10;
- ◆ IL-20 subfamily members IL-19, IL-20, IL-22, IL-24 & IL-26;
- ◆ IL-28A, IL-28B & IL-29, same as type III IFNs, IFN- λ 2, IFN- λ 3 & IFN- λ 1.



The Biological roles of IL-20 Family

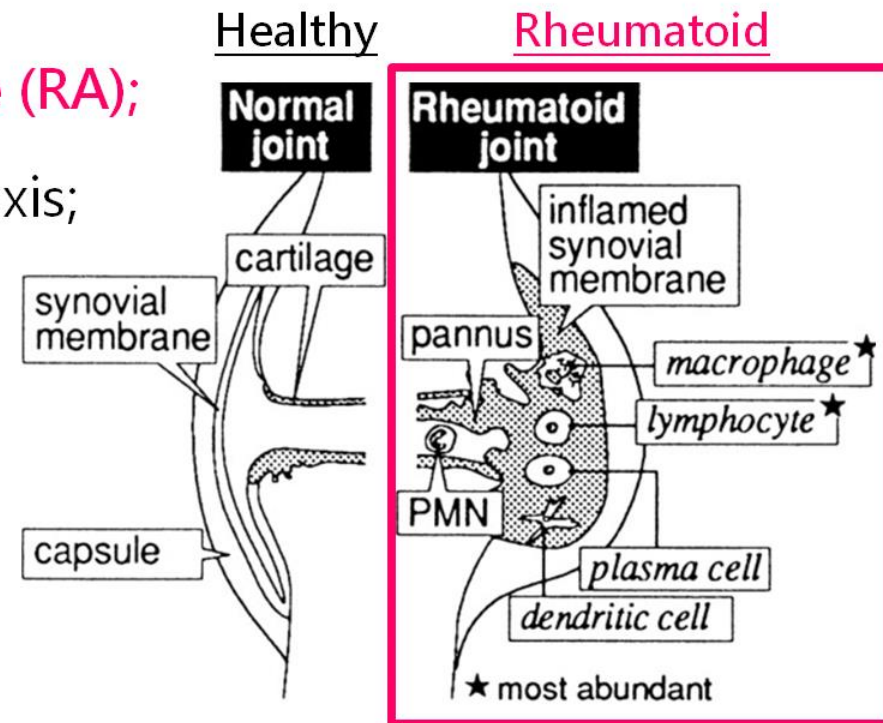
IL-20 family primarily acts on **tissue epithelial cells & stroma cells** to induce innate host defense, and also protects barrier integrity & tissue homeostasis through the promotion of proliferation, remodeling, and repair of various tissues and organs.



Pathogenesis role of IL-20

IL-20 is correlated with the pathogenesis of RA, Osteoporosis, and Cancer-induced Osteolysis through five possible pathways:

- (1) Proinflammatory in Synovial tissue (RA);
- (2) Immune-cell Infiltration & Chemotaxis;
- (3) Osteoclast differentiation;
- (4) Osteoclastogenesis;
- (5) Tumor colonization in bone.



Immunity(2019) 50, 871–891.

Rheumatoid Arthritis(1996) 85, 307-310.

Competitors Analysis for RA & IL-20



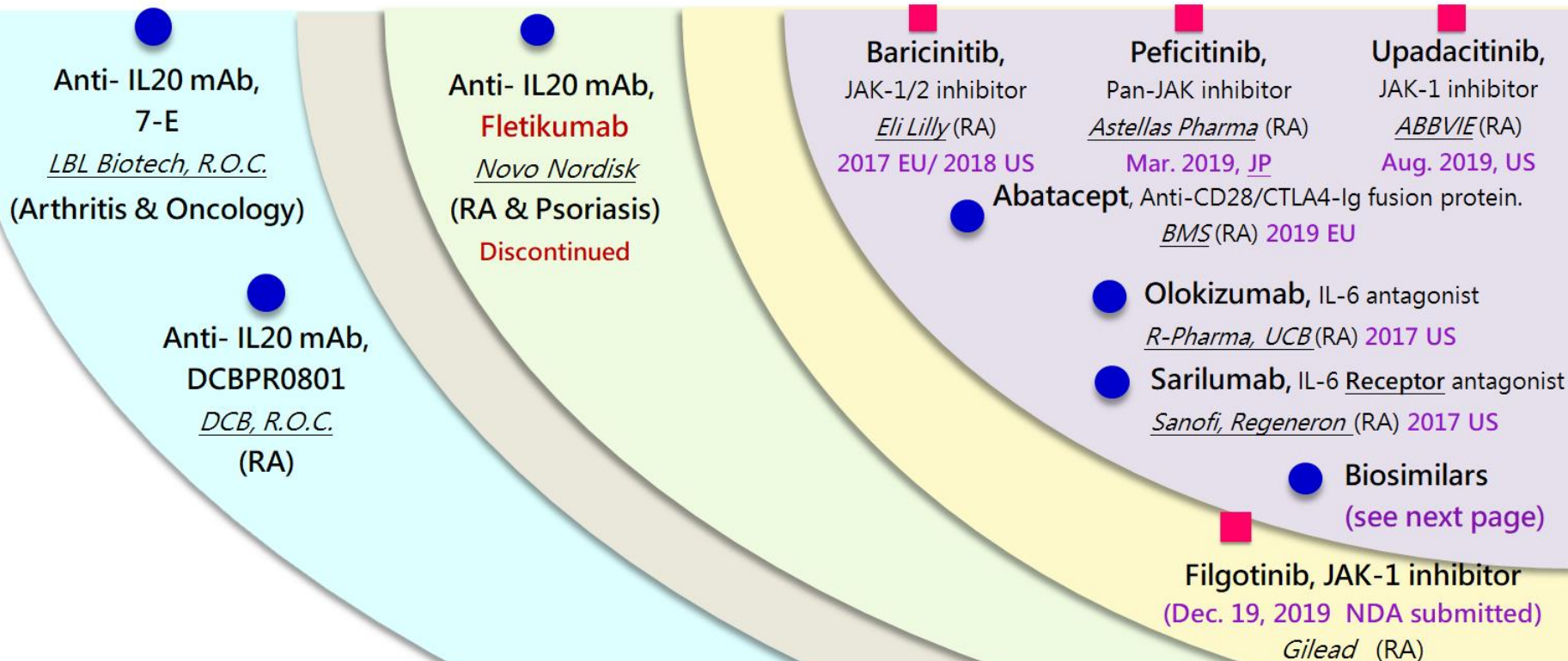
Preclinical

I

II

III

Launch



■ Small Molecular

● Biologics

(In Red: Discontinued due to lack of efficacy)

Source: Medtrack & Integrity & Globo data, Apr. 2019 IEC.
[\(2020.04.10 UPDATED, Sally\)](#)

Biosimilar Competitors for RA

Launch

<p>Baricitinib, JAK-1/2 inhibitor <i>Eli Lilly</i> (RA) 2017 EU/ 2018 US</p>	<p>Peficitinib, Pan-JAK inhibitor <i>Astellas Pharma</i> (RA) Mar. 2019, JP</p>	<p>Upadacitinib, JAK-1 inhibitor <i>ABBVIE</i> (RA) Aug. 2019, US</p>
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- **Olokizumab**, IL-6 antagonist
R-Pharma, UCB (RA) 2017 US
- **Sarilumab**, IL-6 R antagonist
Sanofi, Regeneron (RA) 2017 US

● **Biosimilars** →

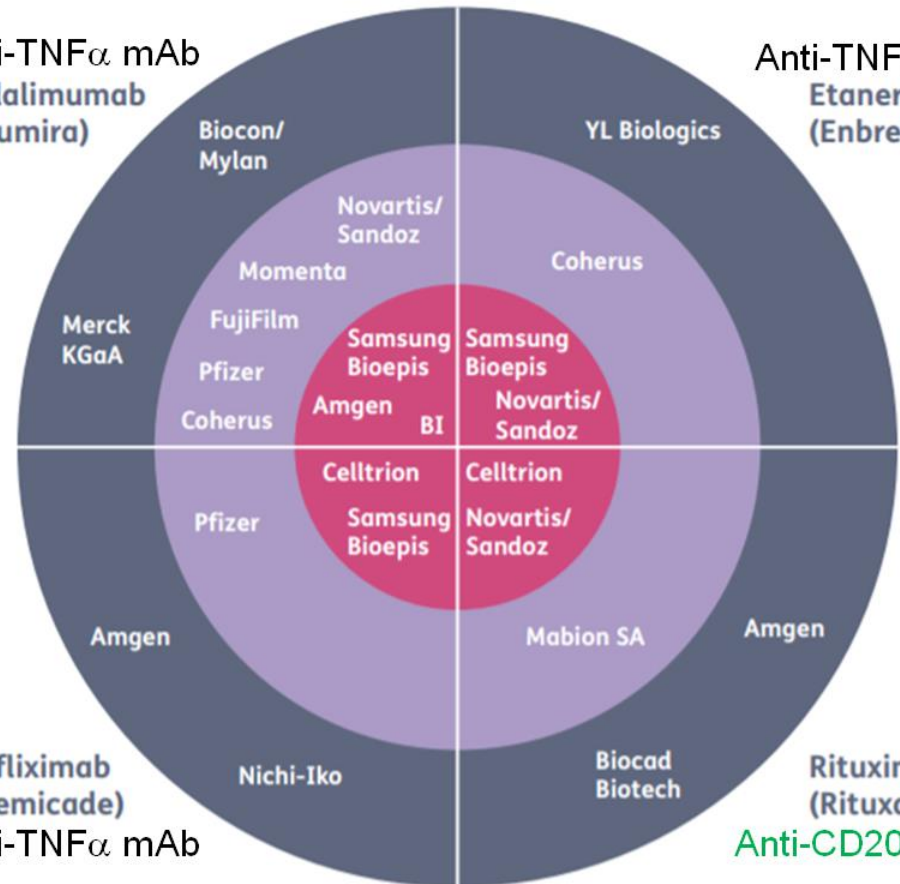
- Small Molecular
- Biologics

Anti-TNF α mAb
Adalimumab (Humira)

Anti-TNF α mAb
Etanercept (Enbrel)

Infliximab (Remicade)
Anti-TNF α mAb

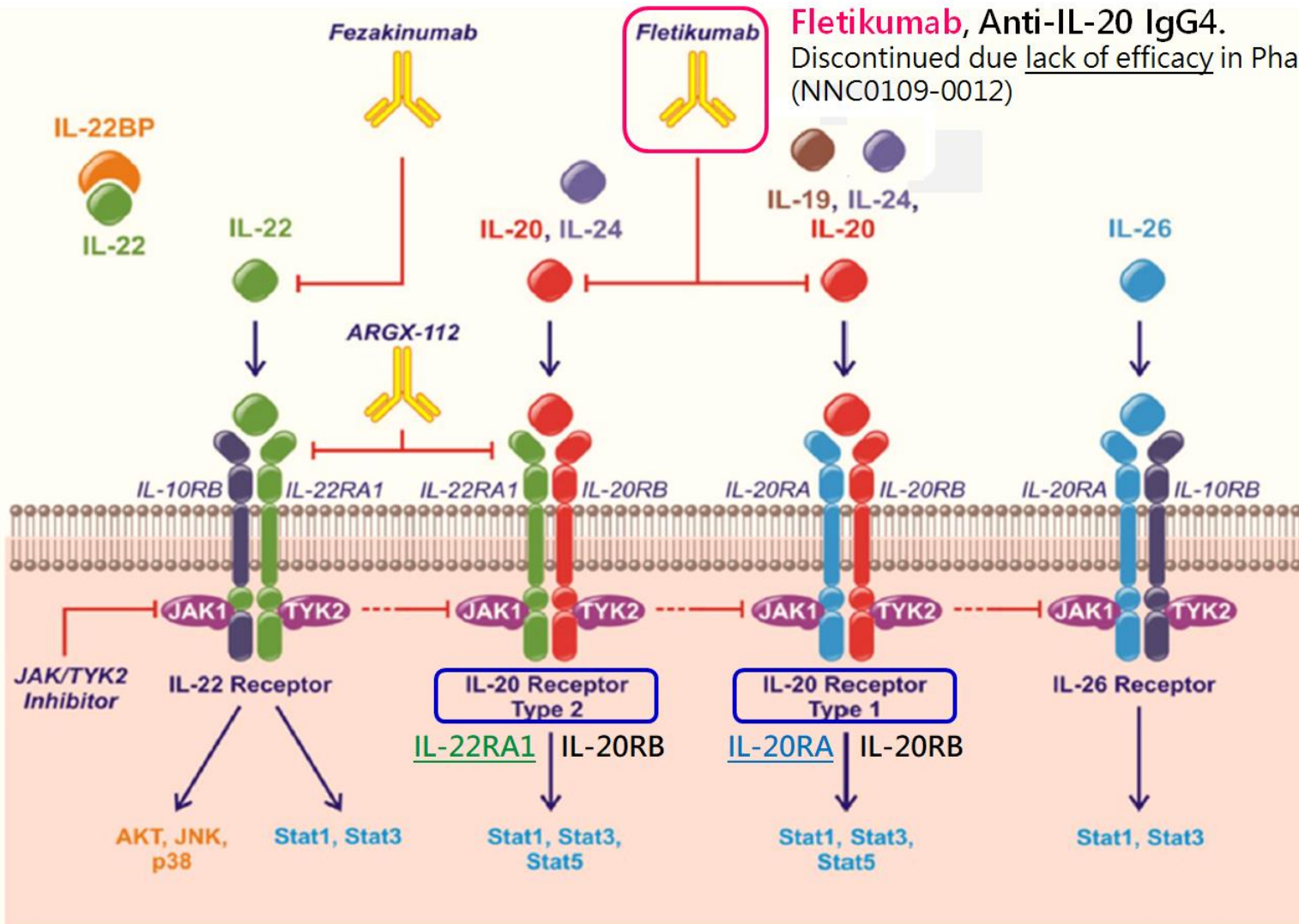
Rituximab (Rituxan)
Anti-CD20 mAb



- Approved/Launched
- Completed
- Open/Closed

Pharma intelligence _RA (2018)

Immunotherapeutic Targets of Cytokine and Cytokine Receptors



Fletikumab, Anti-IL-20 IgG4.
Discontinued due to lack of efficacy in Phase II trial.
(NNC0109-0012)

FDA Approved Immunotherapeutic for Treatment of Rheumatoid Arthritis (RA)



No.	Brand	Biologics	Route	Mechanism	Side Effects	Company (Approval year)
1	Rituxan	Rituximab	IV	Anti-CD20 mAb	Skin Rashes	Genentech (1997)
2	Enbrel	Etanercept	SC	TNF inhibitors	Serious infections including tuberculosis, upper urinary tract infection (UTI)	Immunex Corp. (1998)
3	Kineret	Anakinra	IV	IL-1 receptor antagonist	Diarrhea, stomach pain, Headache	Amgen (2001)
4	Remicade	Infliximab	IV	TNF inhibitors	Chest pain, sore throat, dizziness, fatigue	Centocor Ortho Biotech (2002)
5	Humira	Adalimumab	SC	TNF inhibitors	Bruising at the injection site, nausea, upper respiratory infection	Abbott Lab. (2002)
6	Orencia	Abatacept	SC	Anti-CD28/CTLA4-Ig fusion protein	Increase risk of serious infections, itching rashes, swelling and pain	Bristol-Myers Squibb (2005)
7	Simponi	Golimumab	SC	TNF inhibitors	Increase the risk of serious infections including tuberculosis	Centocor Ortho Biotech (2009)
8	Cimzia	Certolizumab pegol	SC	TNF inhibitors	Tuberculosis, UTI, headache	UCB (2009)
9	Ilaris	Canakinumab	IV	Anti-IL-1 β receptor mAb	Bronchitis, Diarrhoea, Gastroenteritis, vertigo, weight increase	Novartis (2009)
10	Stelara	Ustekinumab	SC	Human IgG1k mAb	Nasopharyngitis, diarrhea, upper UTI, nausea	Janssen Biotech (2009)
11	Actemra	Tocilizumab	IV infusion	Anti-IL-6 receptor antibody	Serious infections, elevated liver enzymes neutropenia, decreased platelet counts	Genentech (2010)
12	Xeljanz	Tofacitinib	PO	Janus Kinase inhibitor	Upper respiratory tract infection, Diarrhoea, Nasopharyngitis	Pfizer (2012)
13	Otezla	apremilast	PO	PDE4 inhibitor	Diarrhoea, nausea, headache	Celgene (2014)
14	Taltz	Ixekizumab	SC	Anti IL- 17A receptor mAb	Injection site reactions, tinea infection, nausea	Eli Lilly (2016)
15	Kevzara	sarilumab	SC	IL- 6 receptor antagonist	Neutropenia, increased ALT, injection site erythema, UTI	Sanofi (2017)

Rheumatoid Arthritis Market (Biologics)



Type	Targets	Status	Drug/ Company	Sale (2011)
Cytokines	TNF- α	Launched	Etanercept/ Amgen Infliximab/ Centocor Ortho Adalimumab/ AstraZeneca Golimumab/ Centocor Ortho Certolizumab pegol/ Celltech	7.3 Billion/ Amgen 6.8 Billion/ Centocor Ortho 7.9 Billion/ AstraZeneca 0.4 Billion/ Centocor Ortho 0.4 Billion/ UCB
	IL-1	Launched	Anakinra/Amgen	0.05 Billion
	IL-6R	Launched	Tocilizumab/Roche Ltd.	0.6 Billion
B cell	CD20	Launched	Rituximab/Roche Ltd.	6.0 Billion (all indications)
T cell	CD28	Launched	Abatacept/BMS	0.92 Billion

in vitro Binding Assay of DCBPR0801



Neutralization of rhIL-20-Induced Luciferase Activity by DCBPR0801

Project Team

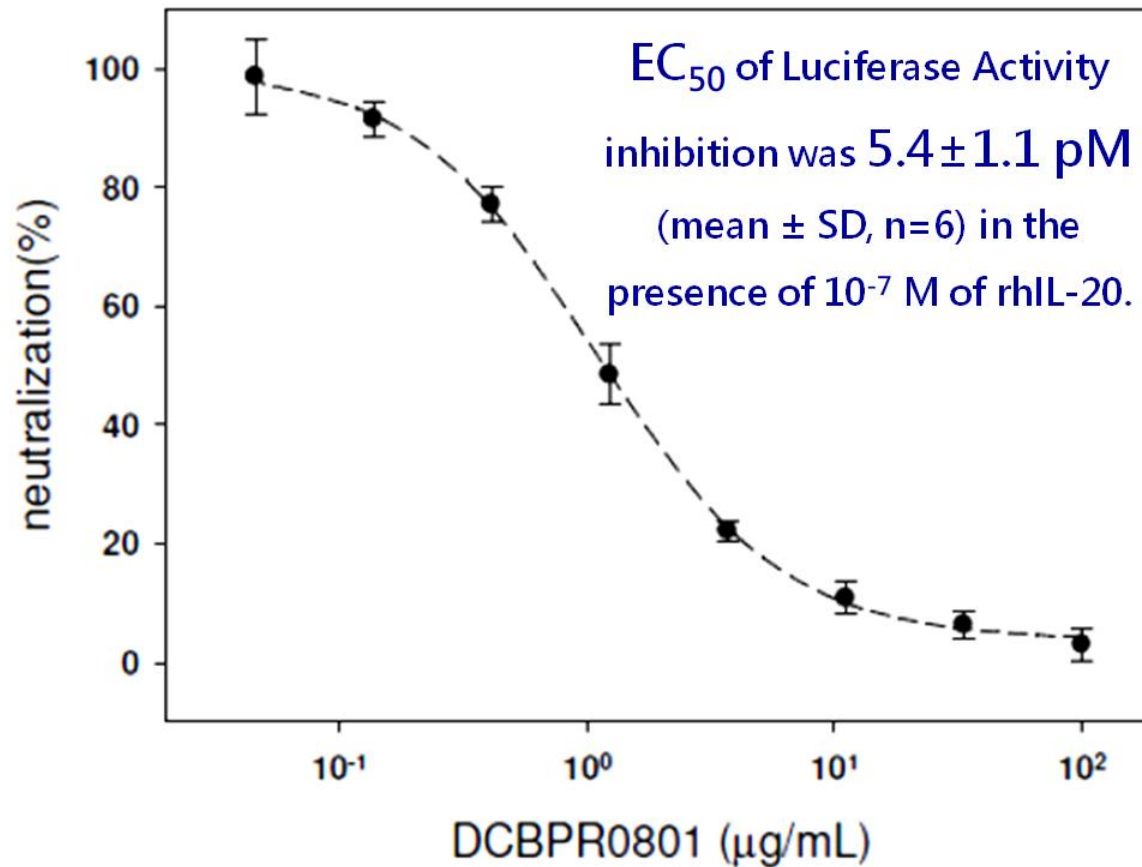
Unmet Need

Technology

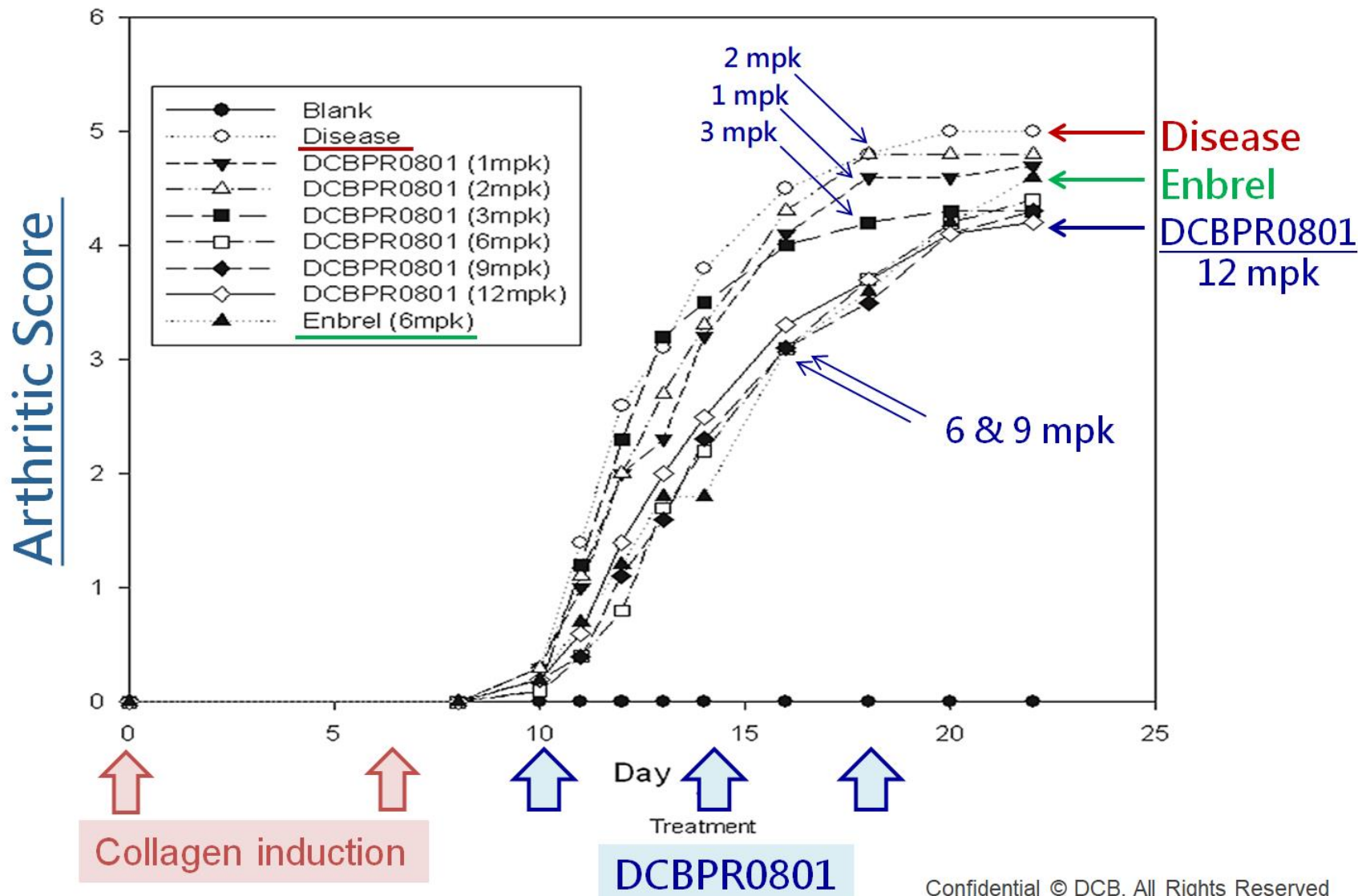
Opportunity

IP/Dev Status

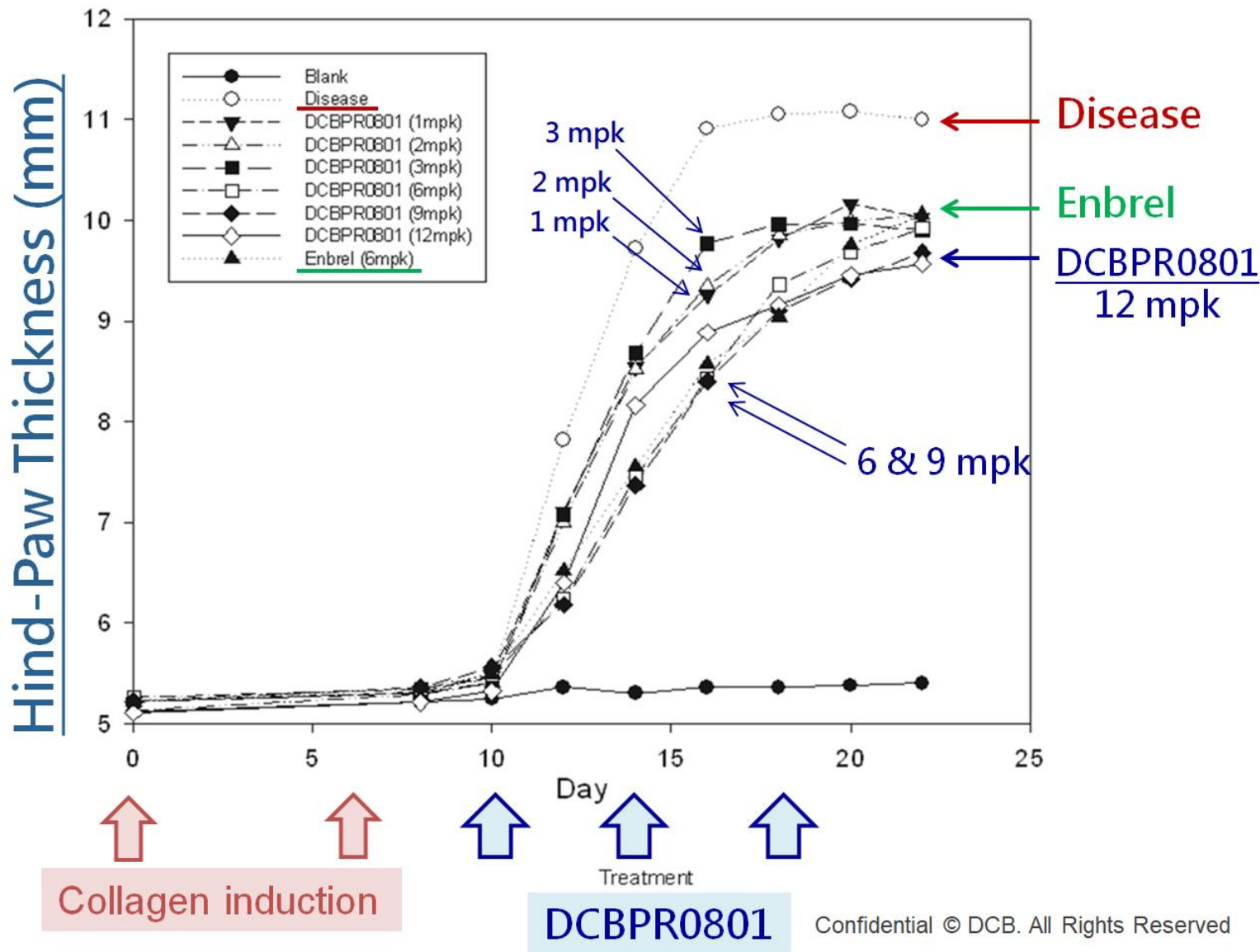
Summary/Contact



DCBPR0801 Reduces the Arthritic Score in Collagen-induced Arthritis (CIA) Rats

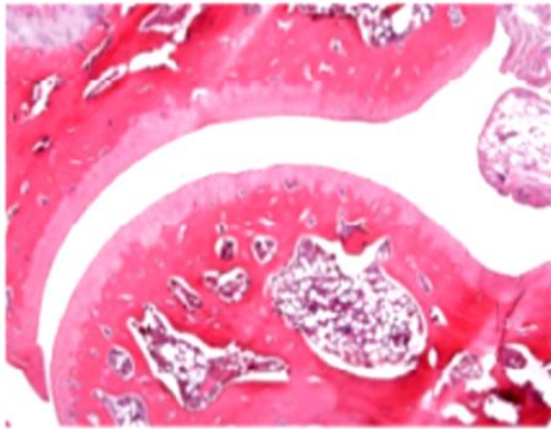


DCBPR0801 Reduces Hind-Paw Swelling in Collagen-induced Arthritis (CIA) Rats

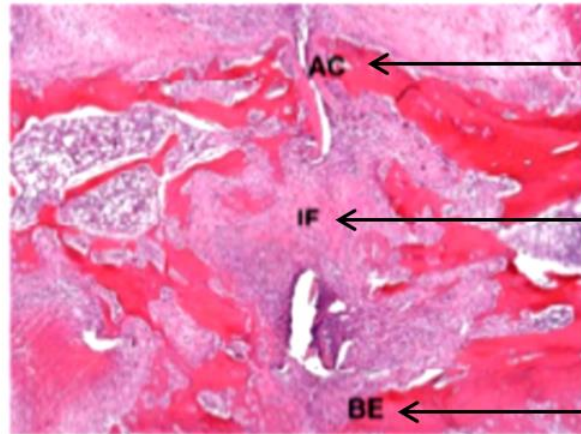


Histopathology of Arthritic Joint Tissues in Collagen-induced Arthritis (CIA) Rats

Normal



Disease

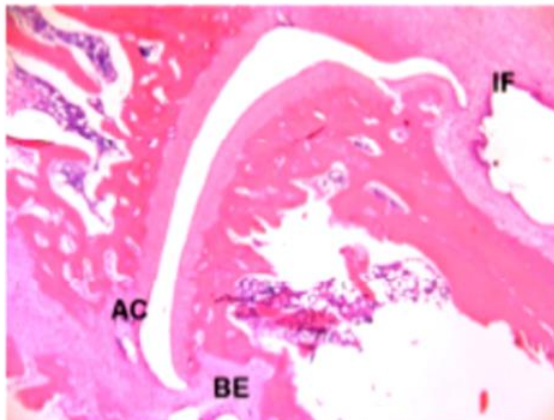


← Articular Cartilage Erosions

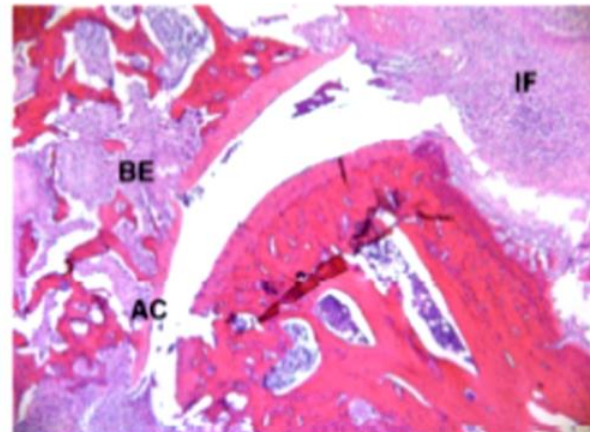
← Inflammatory

← Bone Erosions

DCBPR0801 (6 mpk)



Enbrel (6 mpk)



IF: Inflammatory
AC: Articular cartilage erosions
BE: Bone erosions

Development status of DCBPR0801



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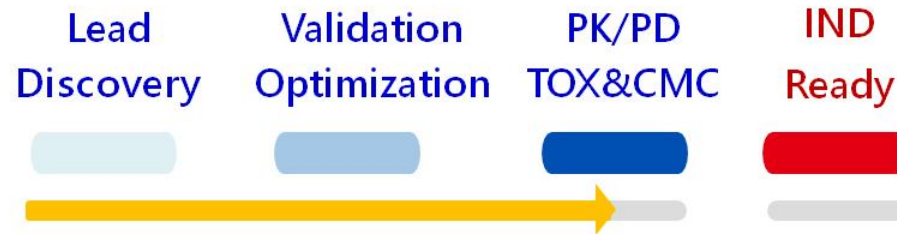
IP/Dev Status

Summary/Contact

Partnership

Exclusive Licensing

Development Status



Expect in the Future

- ❑ GMP- manufacturing & Viral Clearance
- ❑ DS/DP Preparing & Stability
- ❑ IND-Filing

IP Status of DCBPR0801

Name	Country	PCT	Publication No. (Date)	Patent No. (Date)	Expiry Date
HUMANIZED ANTIBODY AGAINST INTERLEUKIN-20 AND TREATMENT FOR INFLAMMATORY DISEASES 對抗介白素-20之 人類化抗體 及發炎性疾病之治療	ROC		201506040 (2015/2/16)	發明第 I572618號 (2017/3/1)	2034/ 04/17
	US	PCT	US 2016-0068595 A1 (2016/3/10)		
	EU	PCT	EP2986640 (2016/2/21)		
	JP	PCT	2016-521272 (2016/7/21)	6358763 (2018/6/29)	2034/ 04/18

Summary/Contact information



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Pre-Clinical Activities have been done:

- ✓ Pharmacology
- ✓ Toxicology in Rats & Cynomolgus monkeys
- ✓ Formulation
- ✓ Process Development

Contact

Innovation & Entrepreneur Core

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Thank you for your attention