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Patent and regulatory issues in Biotech

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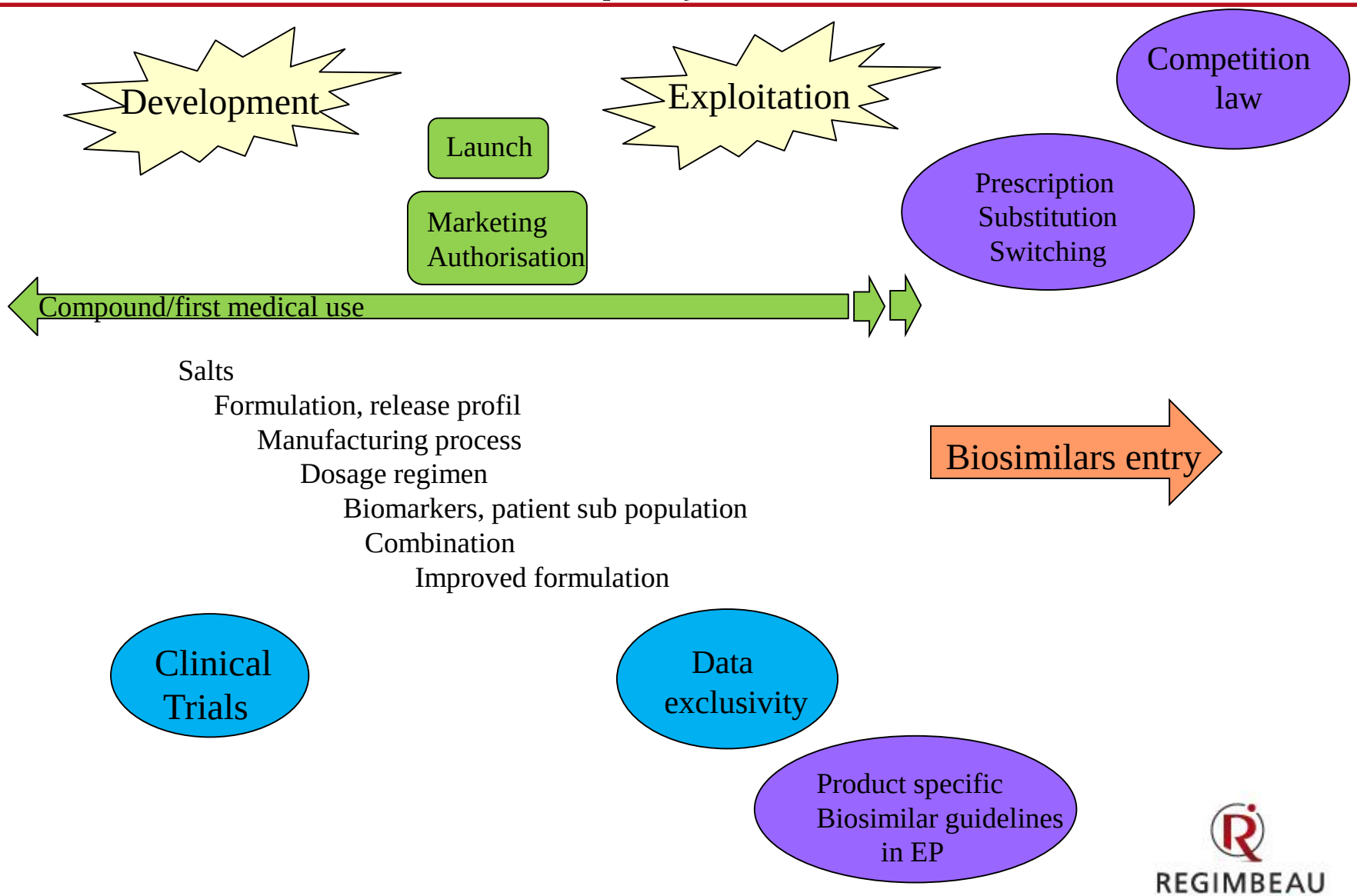
Patent and regulatory issues in biotech
Different levels of interplay



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Patent and regulatory issues in biotech Biosimilars

	Chemical or biological medicament	GENERICS	BIOSIMILARS
Manufacturing process	chemical or biologic	chemical	biologic
Molecule size		Small	Big to Very Big
Development duration	~ 8-12 years	~ 2-3 years	**~ 6-8 years**
Development cost	~ 600-800 M € 500-1000 patients	~ 1-3M € 20-50 patients	**~ 200-300 M € 100-500 patients**
Price decrease	****	~ 70 %	10-35% in EP ~ 20% in France
Substitution	****	Authorised and encouraged by Health Authorities	Substitution / Switching ?

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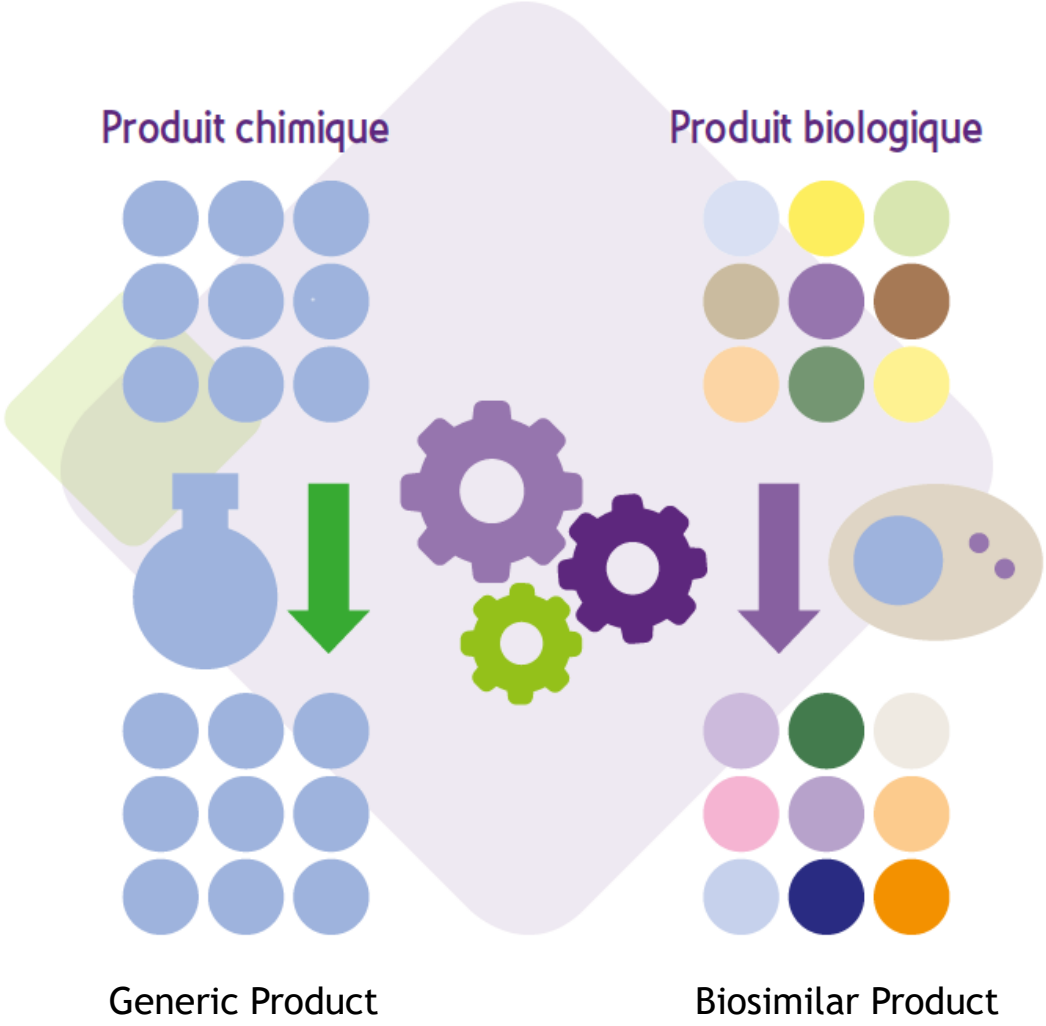
Patent and regulatory issues in biotech Biosimilars



Source : ANSM

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Patent and regulatory issues in biotech
Exemption of infringement in EP

« BOLAR » EXEMPTION	
COUNTRIES	Would be applicable to clinical trials for reference products (in addition to clinical trials for generics and biosimilars)
France, Germany, Poland, Spain, Italy, Great Britain, Denmark, Hungary, Romania	YES
Belgium, Sweden	NO

- Transposition of Directive 2004/27/EC
- Rare Case law

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Patent and regulatory issues in biotech
Product-specific biosimilar guidelines in EP

PRODUCT-SPECIFIC BIOSIMILAR GUIDELINES IN EP		
BIOLOGICALS	**FIRST GUIDELINES**	**REVISION / DATE FOR COMING INTO EFFECT**
Somatropin	01.06.2006	***
Recombinant G-CSF	01.06.2006	*Under revision*
Recombinant human insulin and insulin analogues	01.06.2006	01.09.2015
Recombinant EPO	01.07.2006	01.12.2012
INF-α	Reflection paper 23.04.2009	*Under revision*
LMW Heparin	01.10.2009	**01.06.2017**
Monoclonal Antibodies	01.12.2012	***
Recombinant Follicle-stimulating Hormone	01.09.2013	***
INF-β	01.09.2013	***

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Patent and regulatory issues in biotech
Biosimilars authorised in EP

Médicament de référence	Médicament biosimilaire	Substance active	Laboratoire	Date autorisation
Genotropin	Omnitrope	somatropine	Sandoz GmBH	12/04/2006
Eprex	Binocrit	epoetin alfa	Sandoz GmbH	28/08/2007
	Epoetin Alfa Hexal	epoetin alfa	Hexal AG	28/08/2007
	Abseamed	epoetin alfa	Medice Arzneimittel Pütter GmbH	28/08/2007
	Retacrit	epoetin zeta	Hospira UK Limited	18/12/2007
	Silapo	epoetin zeta	Stada Arzneimittel AG	18/12/2007
Neupogen	Biograstim	filgrastim	AbZ-Pharma GmbH	15/09/2008
	Tevagrastim	filgrastim	Teva GmbH	15/09/2008
	Ratiograstim	filgrastim	Ratiopharm GmbH	15/09/2008
	Filgrastim Hexal	filgrastim	Hexal AG	06/02/2009
	Zarzio	filgrastim	Sandoz GmbH	06/02/2009
	Nivestim	filgrastim	Hospira UK Limited	08/06/2010
	Grastofil	filgrastim	Apotex Europe BV	18/10/2013
	Accofil	filgrastim	Accord Healthcare Ltd	18/09/2014
Remicade	Remsima	infliximab	Celltrion Healthcare Hungary Kft.	10/09/2013
	Inflectra	infliximab	Hospira UK Limited	10/09/2013
	Flixabi[1]	infliximab	Samsung Bioepis UK Limited	01/04/2016[1]
GONAL-f	Ovaleap	follitropin alfa	Teva Pharma B.V.	27/09/2013
	Bemfola	follitropin alfa	Finox Biotech AG	27/03/2014
Lantus	Abasaglar	insulin glargine	Eli Lilly Regional Operations	09/09/2014
Enbrel	Benepali	etanercept	Samsung Bioepis UK Limited	19/11/2015 [1]

1. Recommandation du comité des spécialités pharmaceutiques (CHMP, EMA)

Clexane	Thorinane	enoxaparin sodium	Pharmaten SA	15/09/2016
Clexane	Inhixa	enoxaparin sodium	Techdow Europa AB	15/09/2016
Lantus	Lusduna	insulin glargine	MSD Limited	04/01/2017

Sources : ANSM, EMA

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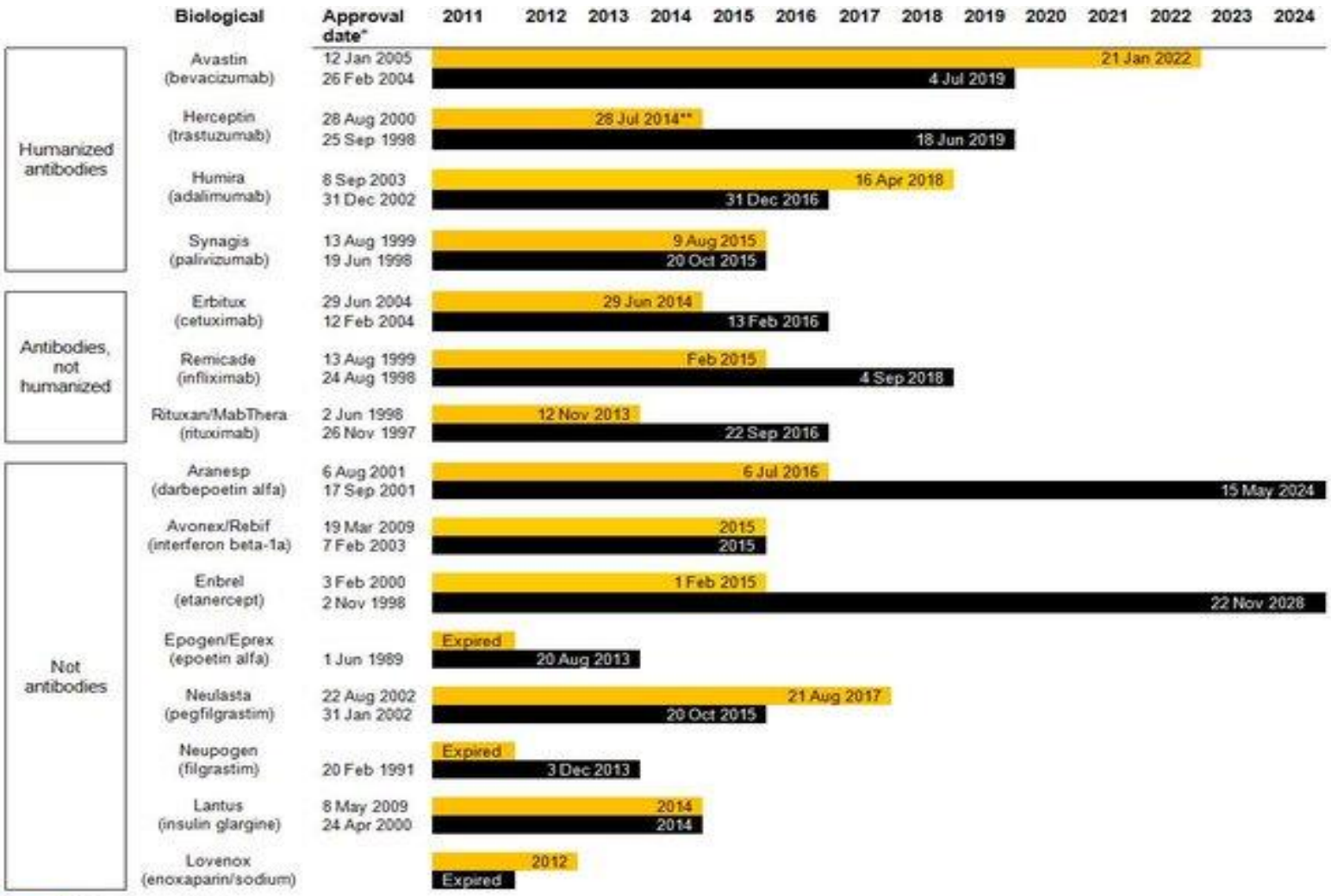
Patent and regulatory issues in biotech

Expiration dates of major patents for best selling biologicals



Source : GaBi online

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Patent and regulatory issues in biotech
Biosimilars forecast

- Poor penetration rate but rapidly increasing
- 1/3 of the medical products in development
- End of important patents in the coming years
- Ever growing market
  - Global market :
    - USD 1.7 billion in 2014
    - USD 3.39 billion in 2016
    - USD 11-35 billion by 2021…
  - With
    - Regulatory uncertainty
    - Important variation between countries and therapy areas

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Patent and regulatory issues in biotech Prescription/Substitution/Switching

- Pressure from governments for saving public money
- Decision of the physician or of the pharmacist
- National level

- In France :
  - Possible substitution for new treatment
  - Article L.5125-23-2 of the Public Health Code recently changed
  - Substitution is now possible during the treatment
  - Under the control of the physician
  - who has to inform the patient
  - And to organise the clinical survey

  - 30 M€ economy expected in 2017

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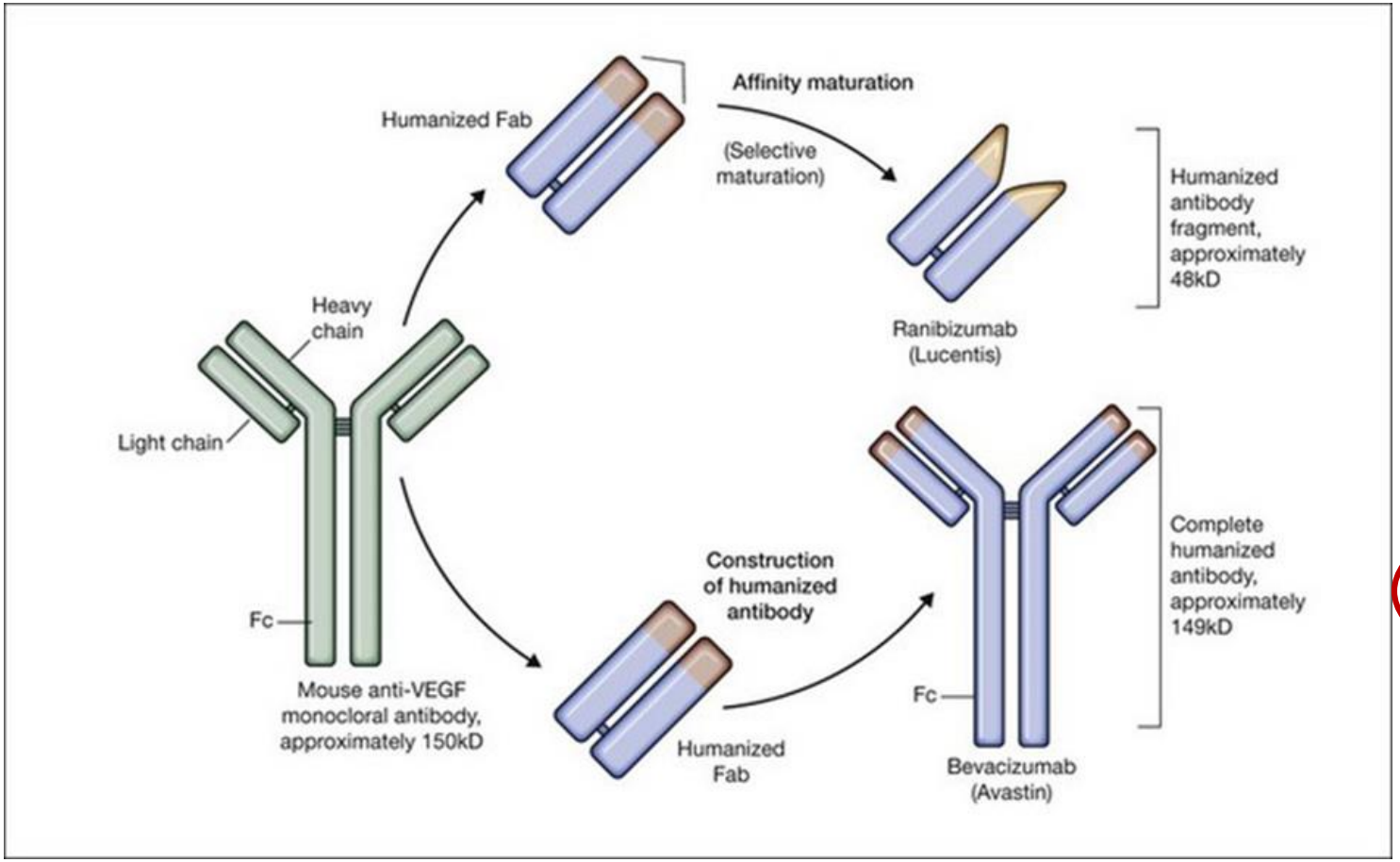
Patent and regulatory issues in biotech
Competition law : Lucentis / Avastin case

Genentech



Novartis

Roche

Source : NEJM, 2006

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Patent and regulatory issues in biotech
Competition law : Lucentis / Avastin case

GENENTECH

ROCHE

EP 451 216 and EP 1 325 932
SPCs Bevacizumab
AVASTIN

Complete humanized antibody

MA : Antitumoral

MA 2004

Off-label : AMD
Price in France 50 euros

NOVARTIS

EP 451 216 and SPC
Ranibizumab
LUCENTIS

Fragment of humanized antibody

MA : AMD

MA 2007

On-label : AMD
Price in France 800 euros

Same therapeutic activities: Vascular Endothélial Growth Factor (VEGF) Inhibition
Differences : structures, administration route, dosage and side effects

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Patent and regulatory issues in biotech
Competition law : Lucentis / Avastin case

In Italy:

- February 27, 2014, the Italian Competition Authority fines Roche and Novartis
  - ROCHE € 96.6 Millions
  - NOVARTIS € 92 Millions

- Decision confirmed in Appeal

- Referral to the CJEU (pending)

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Patent and regulatory issues in biotech
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In France:

- March 19, 2015, the French Commission benefits/risks of the French National Health Authority (ANSM) gave a favorable opinion for a Temporary Recommendation of Use (RTU)

- June 24, 2015, ANSM issued a RTU for Avastin in the treatment of Age-related Macular Degeneration (AMD) without the Roche's consent

- Roche appealed before the Council of State (Conseil d'Etat) :
  - September 21, 2015, no injunction
  - Case on the merits pending

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Thank you for your attention

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