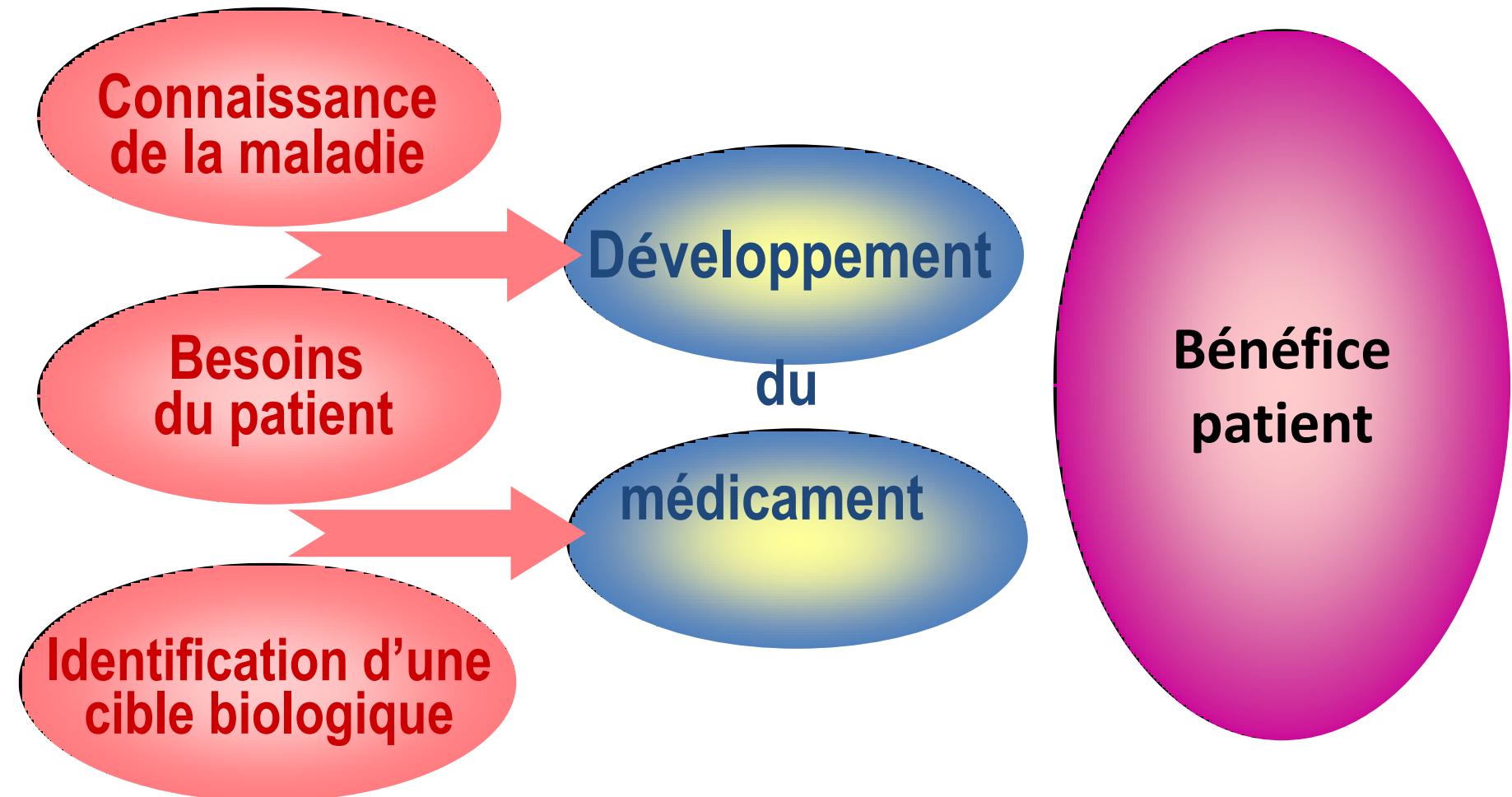


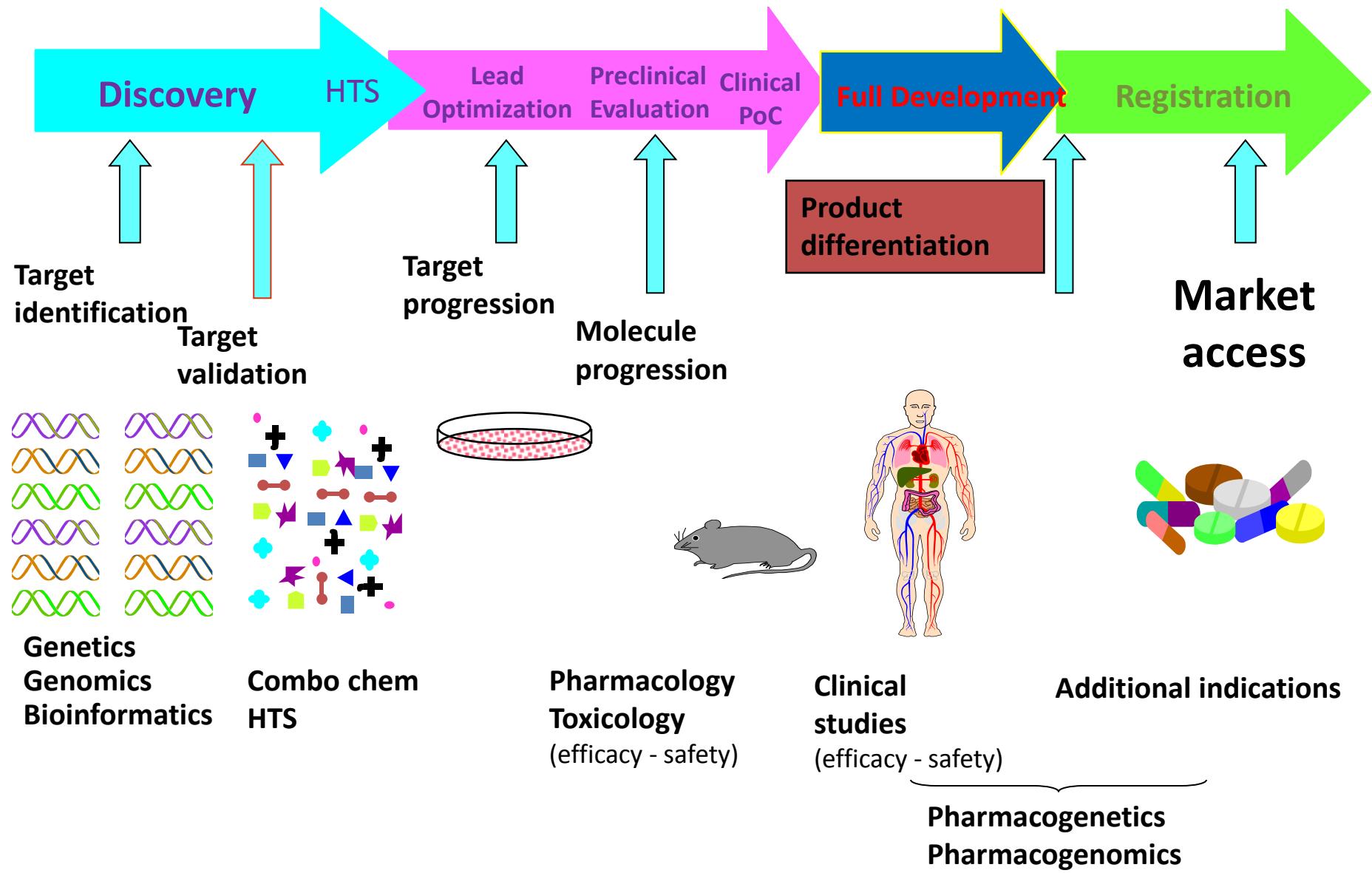
# **Accès à l' Innovation Thérapeutique En Gastro-Entérologie**

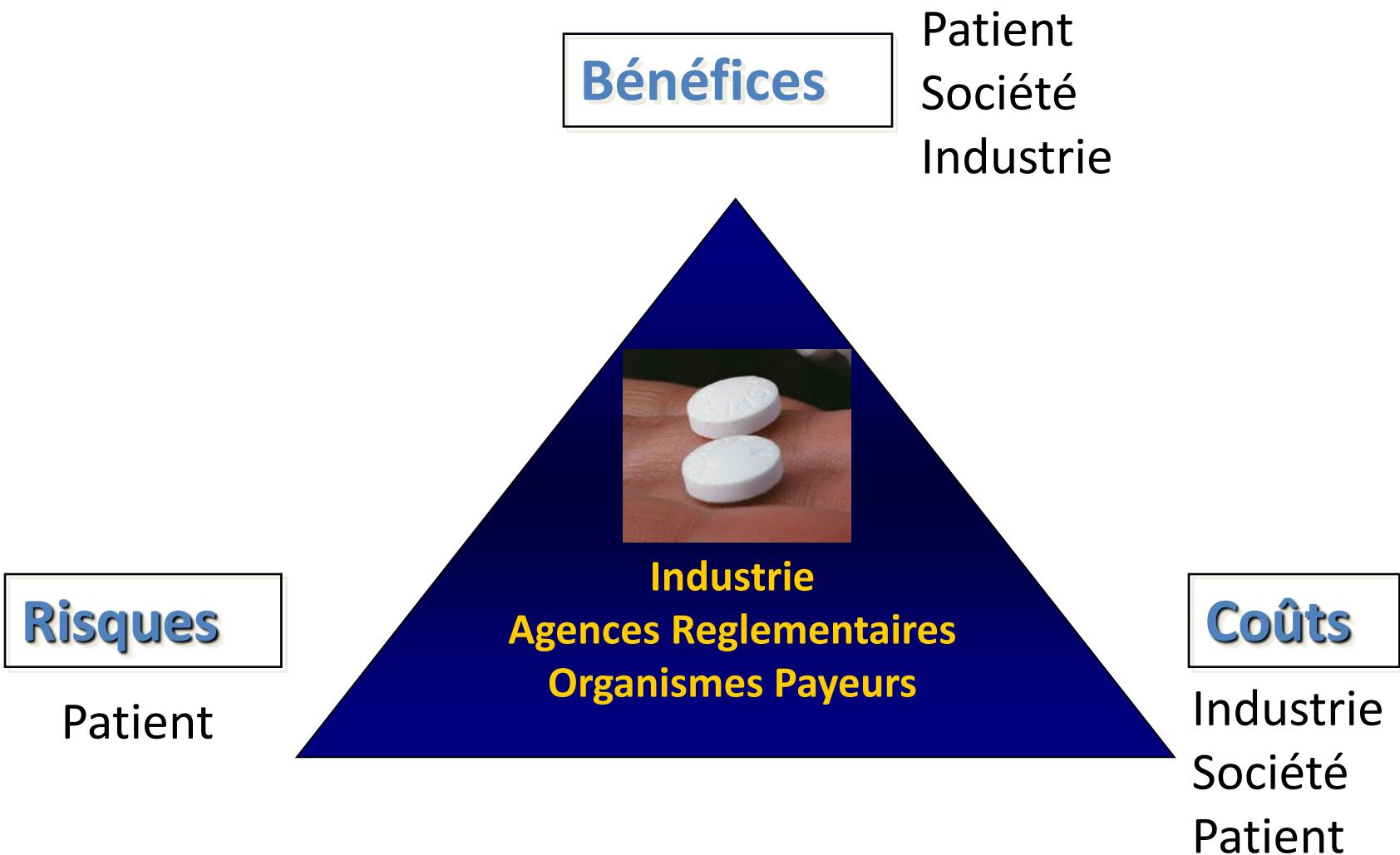
**Dr Bernard AVOUAC**  
Rhumatologue  
Ancien président de la  
Commission de la Transparence

# LE DÉVELOPPEMENT DU MÉDICAMENT

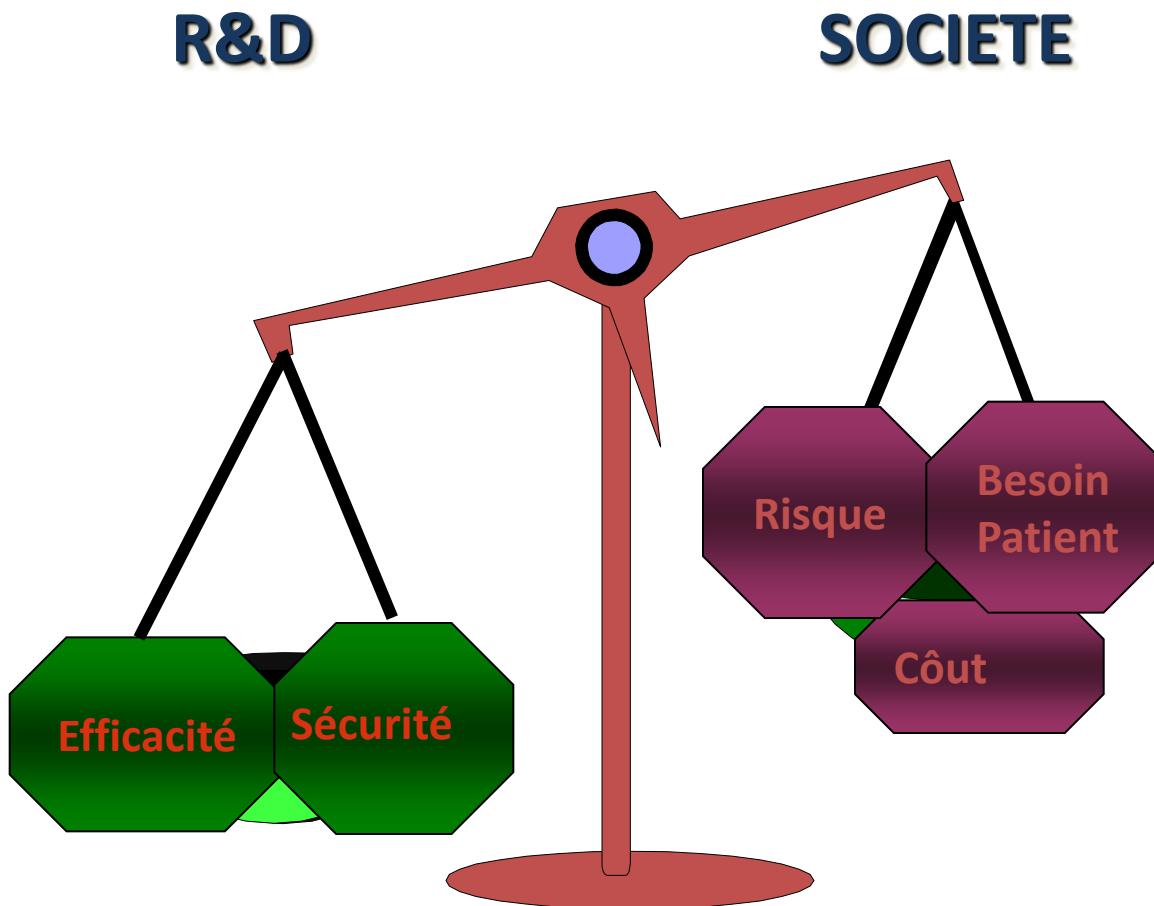


# Découverte et Développement du Medicament





# Où est la juste balance?



# EMA : procédures accélérées

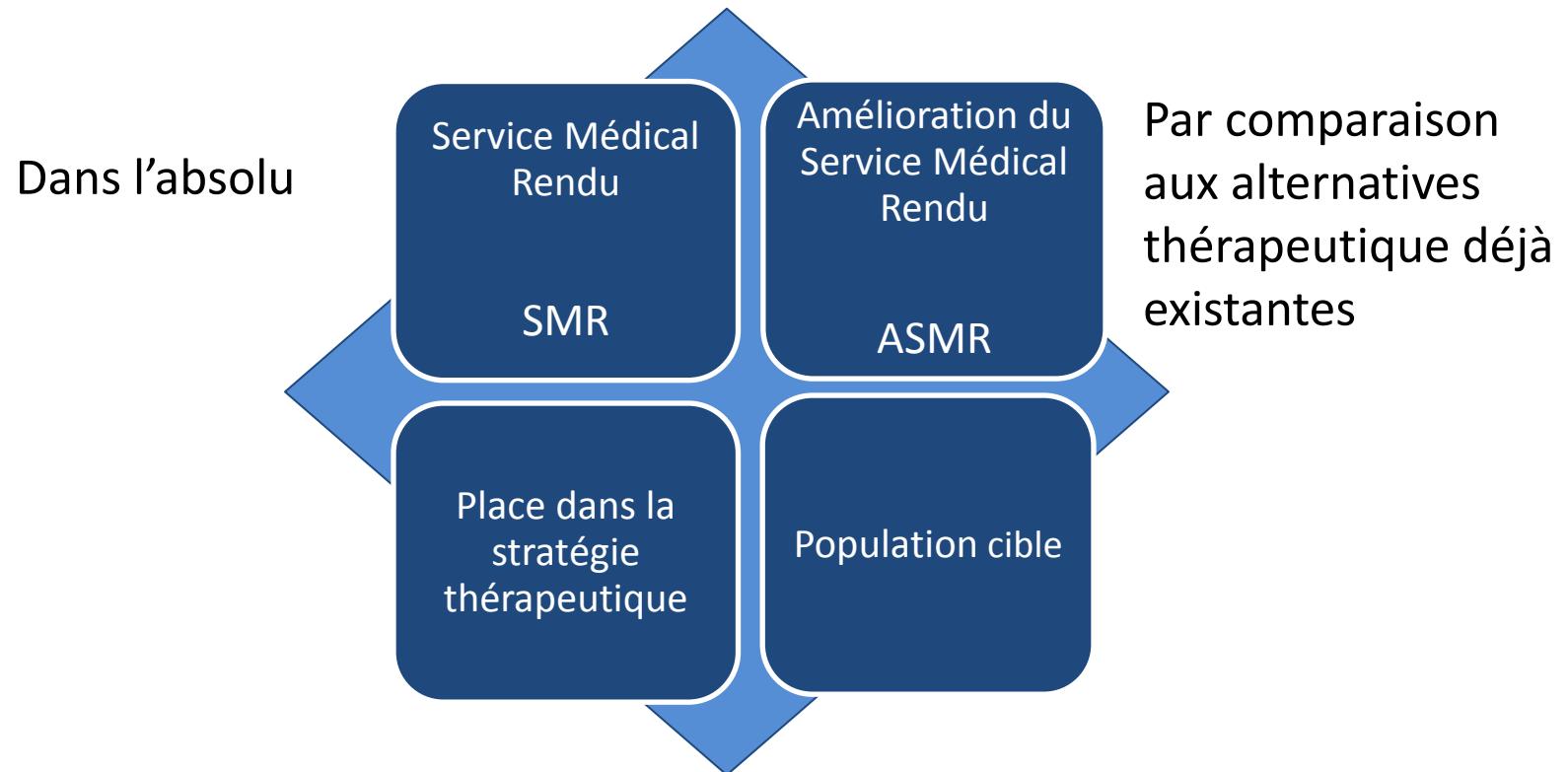
- **L'AMM conditionnelle** : valide seulement 1 an au lieu de 5 et nécessite de compléter l'évaluation
- **L'AMM pour circonstances exceptionnelles** : lorsque le dossier d'évaluation du médicament n'est pas complet et qu'il existe un besoin thérapeutique
- **L'AMM accélérée** : 150 jours au lieu de 210 jours en cas d'intérêt majeur du point de vue de la santé publique
- **L'Adaptive Pathways** : procédure de mise à disposition précoce en cas de besoin non satisfait dans une sous-population avec poursuite du développement clinique

# Mise à disposition avant AMM en France

- **Les ATU dites nominatives**
  - Demandées par le médecin prescripteur au bénéfice d'un patient nommément désigné
  - Elles sont accordées si l'efficacité et la sécurité des médicaments sont présumées favorables en l'état des connaissances scientifiques
- **Les ATU dites de cohorte**
  - Sollicitées par le laboratoire
  - Elles sont accordées à des médicaments dont l'efficacité et la sécurité sont fortement présumées par les résultats d'essais cliniques en vue d'une demande d'AMM
  - La demande d'AMM doit avoir été déposée ou l'entreprise doit s'engager à la déposer dans un délai déterminé

# LA COMMISSION DE LA TRANSPARENCE (CT)

- ❖ La CT évalue les médicaments et émet un avis sur leur prise en charge par la Sécurité sociale et/ou leur utilisation à l'hôpital
- ❖ Jugement sur l'intérêt thérapeutique du produit, par indication thérapeutique :



# LE SMR ET L'ASMR

**SMR**  
= valeur intrinsèque du produit



**ASMR**  
= progrès thérapeutique apporté

- Par indication ou dans une sous-population relevant de l'AMM
- Par rapport à un comparateur ou dans le cadre d'une stratégie thérapeutique



Critères d'évaluation :

- Efficacité et effets indésirables;
- Place dans la stratégie thérapeutique
- Gravité de la pathologie
- Caractère préventif, curatif ou symptomatique
- Intérêt de santé publique

4 niveaux de SMR :

Important, modéré, faible, insuffisant

Critères d'évaluation :

- Niveau de preuve apporté
- Pertinence des critères retenus
- Quantité d'effet observée

Echelle graduée de 1 à 5 :

I : Progrès thérapeutique majeur.

II : Amélioration importante

III : Amélioration modeste

IV : Amélioration mineure

V : Absence d'amélioration avec avis favorable à l'inscription

# Inflammatory Bowel Disease

## Disease Background and Treatment Paradigm

### Background

**Inflammatory Bowel Disease** is an umbrella term for disorders causing chronic inflammation of the intestinal tract and includes Crohn's disease and ulcerative colitis.

#### Crohn's Disease

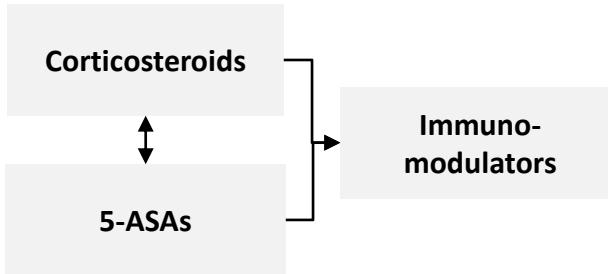
- Inflammation of the lining of the digestive tract (may affect any part of the GI tract)
- ~780,000 individuals affected in the US
- ~1.1 million individuals affected in the EU

#### Ulcerative Colitis

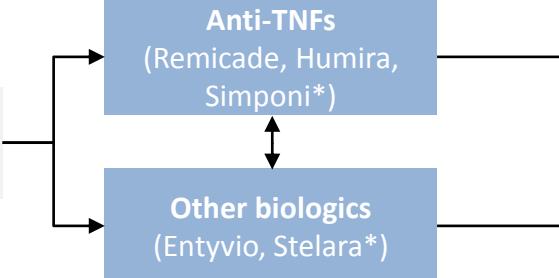
- Inflammation and sores in the colon (large intestine) and rectum
- ~900,000 individuals affected in the US
- ~1.5 million individuals affected in the EU

### Treatment Paradigm

#### First Line



#### Second Line

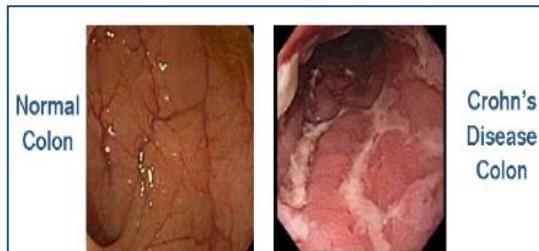


#### Third Line

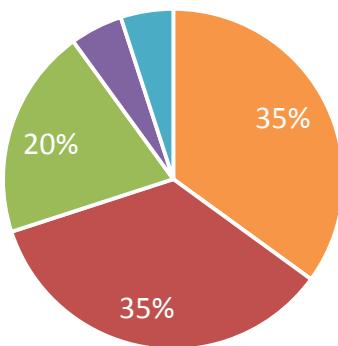


# MALADIE DE CROHN

## Normal Colon vs. Crohn's Disease Colon



Anatomic Location



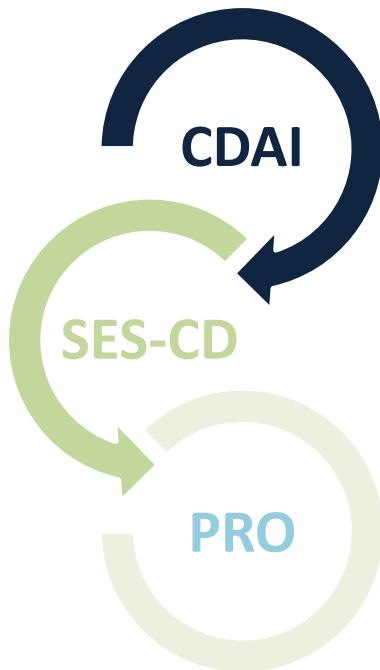
- Ileocolitis
- Ileitis
- Granulomatous colitis

- Crohn's Disease (CD) is a relapsing and remitting autoimmune disorder where disease exacerbations are followed by periods of remission
- CD is characterized by its location within the GI tract – most commonly it affects the ileum, colon or both
- The disease is characterized by a range of symptoms, most commonly including abdominal pain, diarrhea, vomiting, fever and weight loss
- The exact cause of CD is unknown, although it is thought to be due to a set of genetic, microbial and environmental factors
- There is no cure for CD, most patients (~70-80%) will require surgery – and ~45% will require multiple surgeries – to correct issues such as strictures and fistulae

# Traditional endpoint requirements for CD are evolving and changing measures need to be acknowledged in new clinical trials

- Developed over 40 years ago, the CD Activity Index (CDAI) historically is the “gold” standard requirement for measuring disease activity in clinical trials
- However, mostly due to its complexity, the CDAI is seldom used in clinical practice. It has also been recognized in recent years that the CDAI has a number of limitations
- The reliability and validity of the index have been questioned because of:
  - Inconsistency (physicians do not always follow formal scoring protocols in reporting symptoms) and some physician evaluations are subjective
  - Short-term perspective (only captures patient condition over recent days)

*As a result..*



- Regulatory bodies are considering replacing CDAI with a combination of patient-reported outcomes and endoscopy measurements

Mild	Moderate	Severe	Fistulizing
<ul style="list-style-type: none"> <li>• CDAI of 150-220</li> <li>• Patients are ambulatory, eating and drinking, without dehydration; may have tenderness, mass, obstruction, or less than 10% weight loss</li> <li>• 34% of diagnosed patients*</li> </ul>	<ul style="list-style-type: none"> <li>• CDAI of 220-450</li> <li>• Patients have failed treatment for mild disease</li> <li>• Prominent symptoms – fever, weight loss, abdominal pain and tenderness, intermittent nausea or vomiting, or anemia.</li> <li>• C-reactive protein (CRP) elevated above the upper limit of normal</li> <li>• 34% of diagnosed patients*</li> </ul>	<ul style="list-style-type: none"> <li>• CDAI &gt; 450</li> <li>• Persistent symptoms despite intensive treatment</li> <li>• Cachexia (BMI &lt; 18 kg m<sup>-2</sup>), or evidence of obstruction or abscess</li> <li>• CRP increased</li> <li>• 32% of diagnosed patients*</li> </ul>	<ul style="list-style-type: none"> <li>• Presence of perianal or non-perianal fistulae</li> <li>• Considered to be a sign of active disease</li> <li>• Medical treatment of underlying active disease is typically consistent with treatment for severe CD</li> </ul>



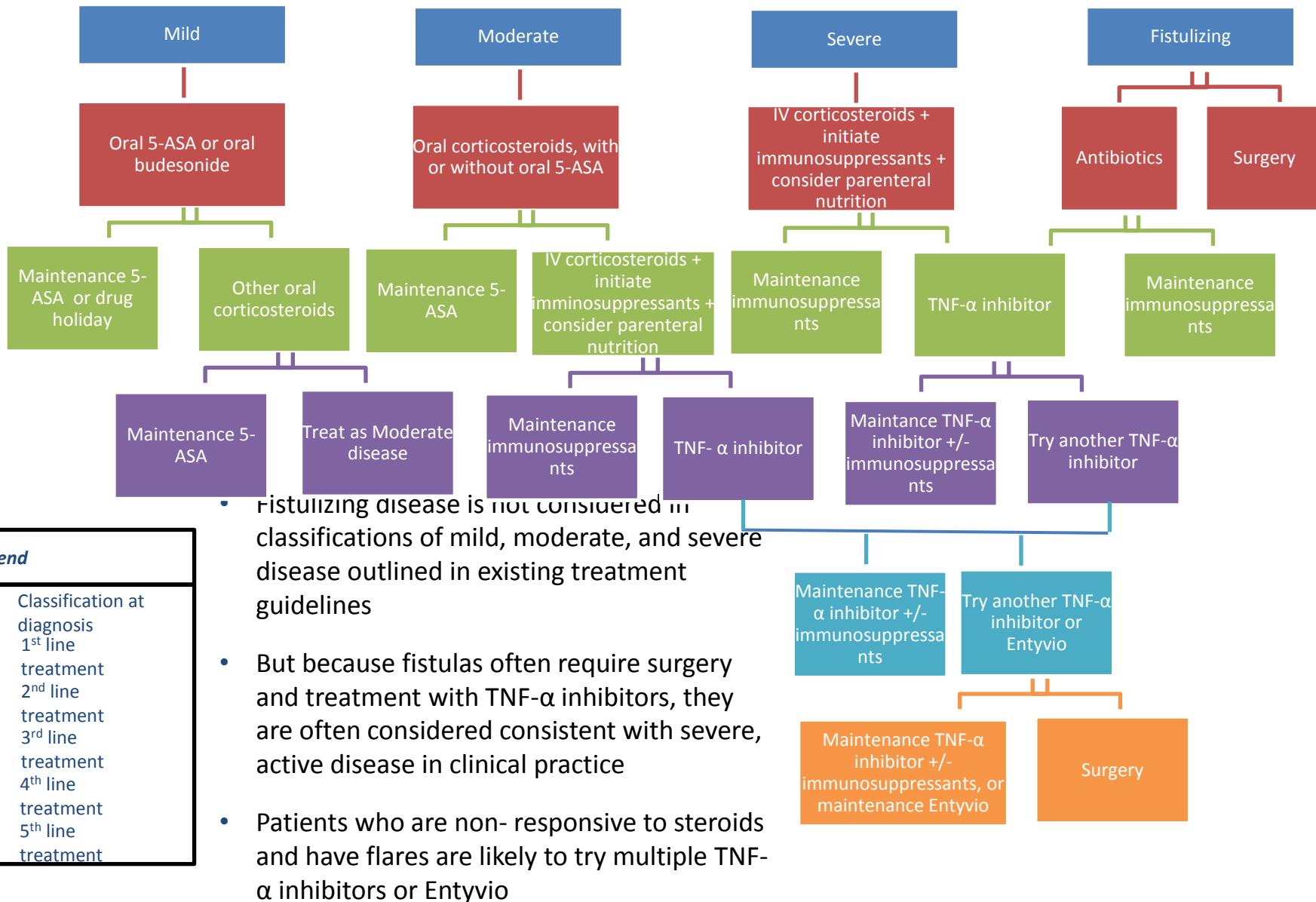
Goal

### Remission

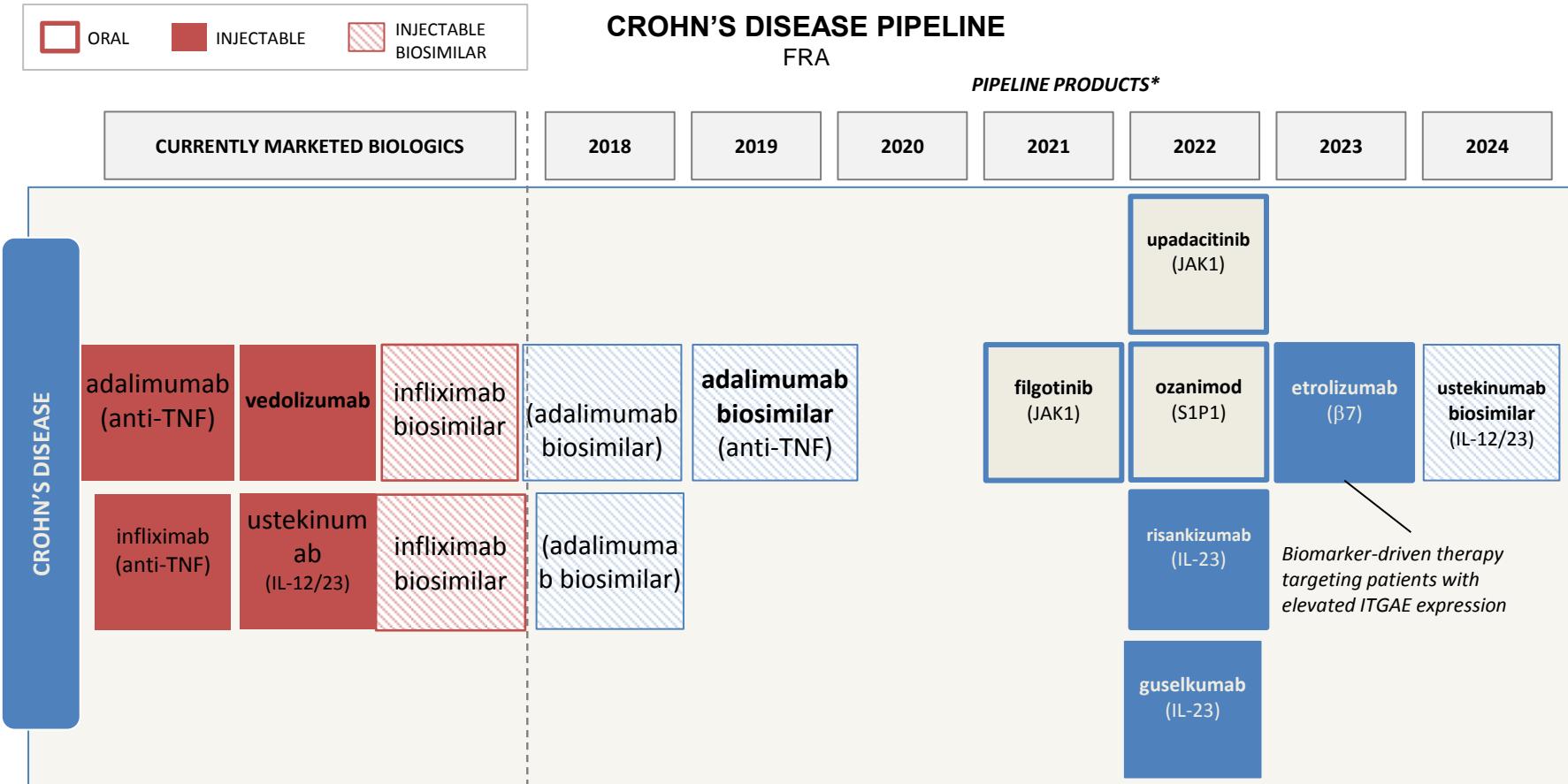
- CDAI (approximate) of <150
- Patients who are spontaneously asymptomatic or asymptomatic with nonsteroidal treatment (patients who require steroids to maintain remission are considered steroid-dependent)

- CD severity is determined at diagnosis based on the physician's assessment of patient's symptoms
- Most patients have active disease at diagnosis
- As CD is a relapsing and remitting disease, patients can transition from one severity category to another depending on treatment and individual fluctuations in the disease

# TREATMENT PATHWAY



# Competitive Landscape: Pipeline



- **HUMIRA (adalimumab) biosimilars are expected to launch in 2018** in FRA; **REMICADE (infliximab) biosimilars (INFLECTRA, REMSIMA)** have already launched and represent 40% of biologic market share across indications
- **Etrolizumab** is a biomarker-driven biologic, which is **expected to launch from 2023**
- **STELARA (ustekinumab) biosimilars are expected in 2024**

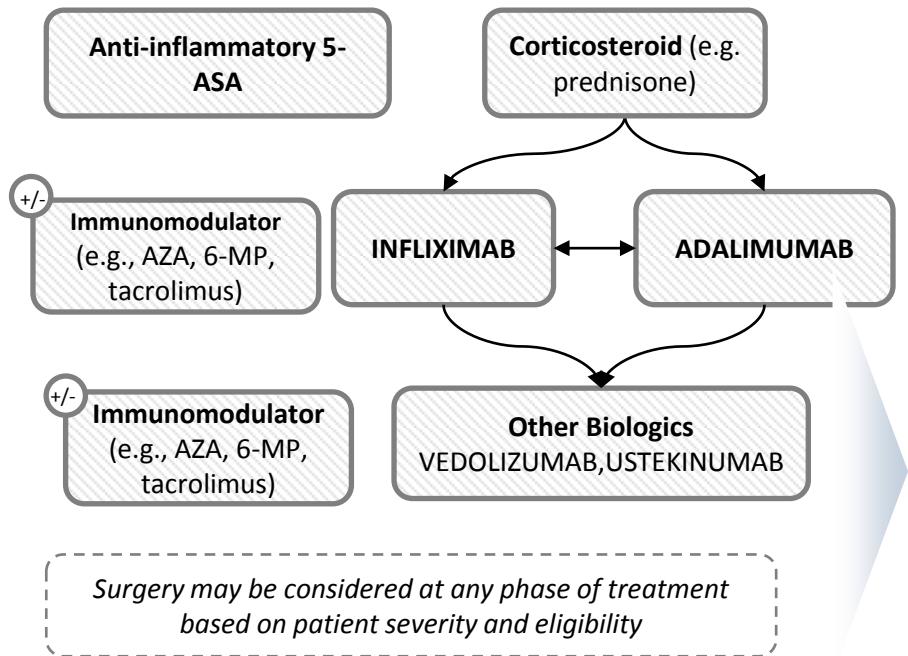
\* NOTE: Estimated based on projected launch dates from secondary research. BI: Boehringer Ingelheim; IL: interleukin; ITGAE: integrin  $\alpha$ E gene; JAK: Janus kinase; PDE: phosphodiesterase; S1P1: sphingosine-1-phosphate receptor 1; TNF: tumor necrosis factor.

Source: CBP secondary research

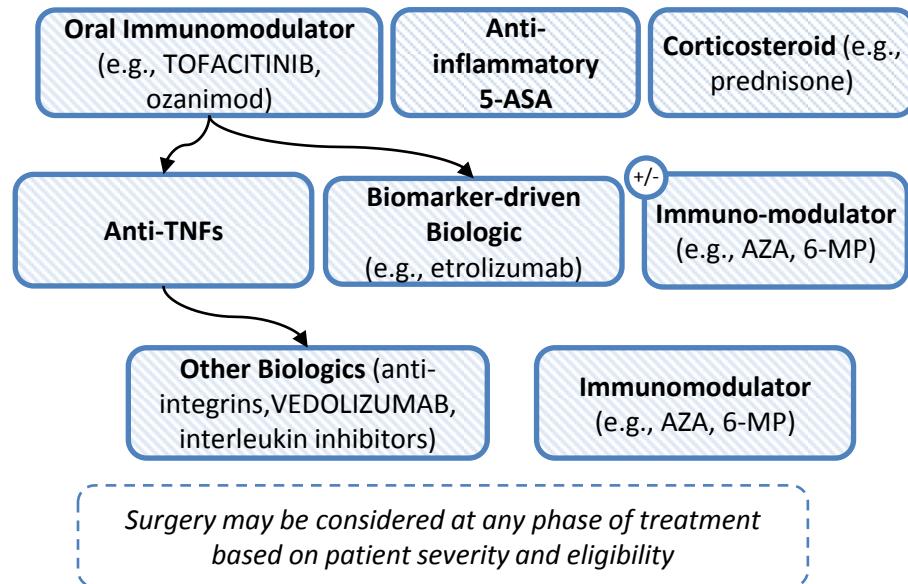
# FRA Competitive Landscape Stimulus: Treatment Algorithm

## TREATMENT ALGORITHM CROHN'S DISEASE

### CURRENT ALGORITHM



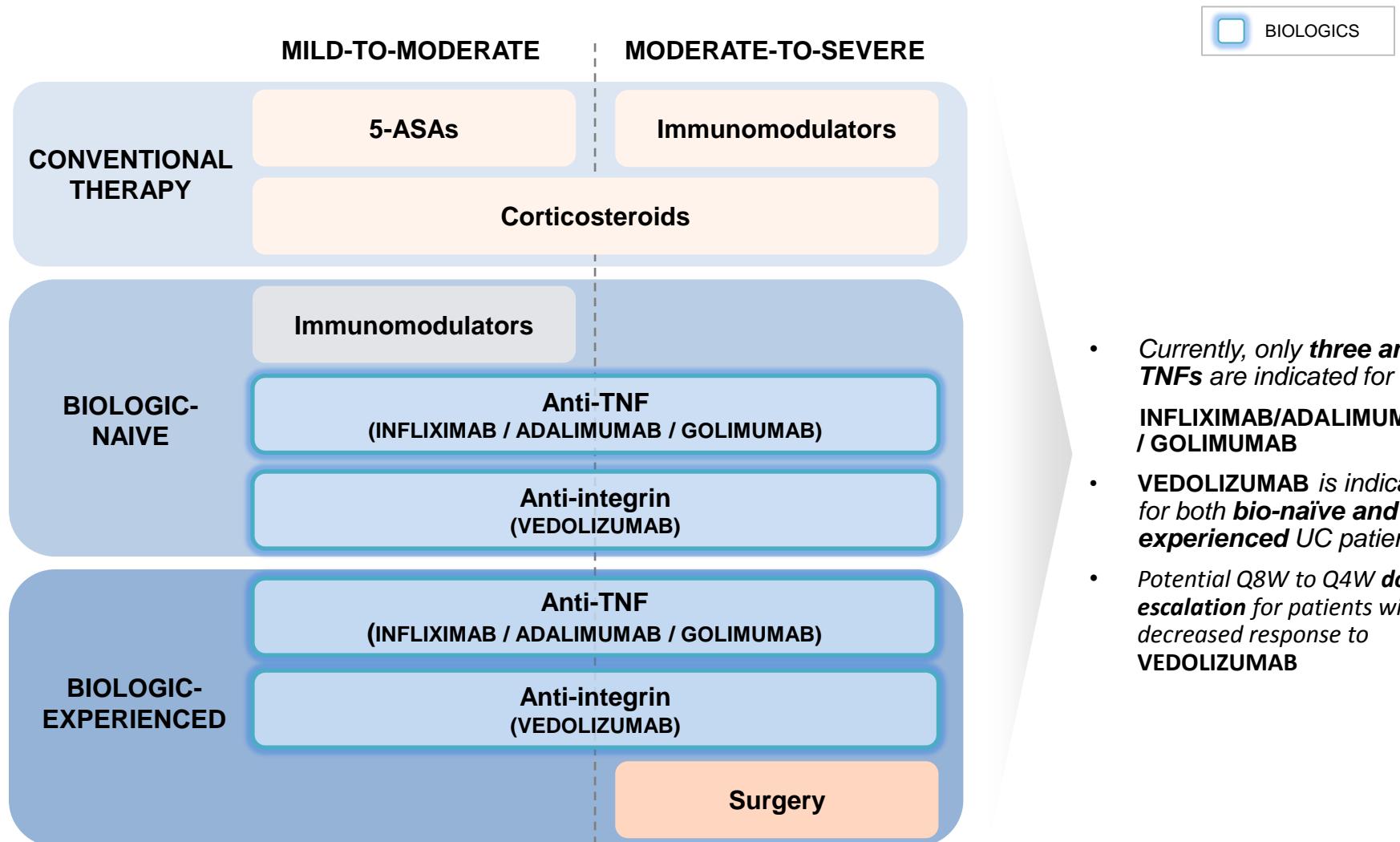
### ALGORITHM IN 2027



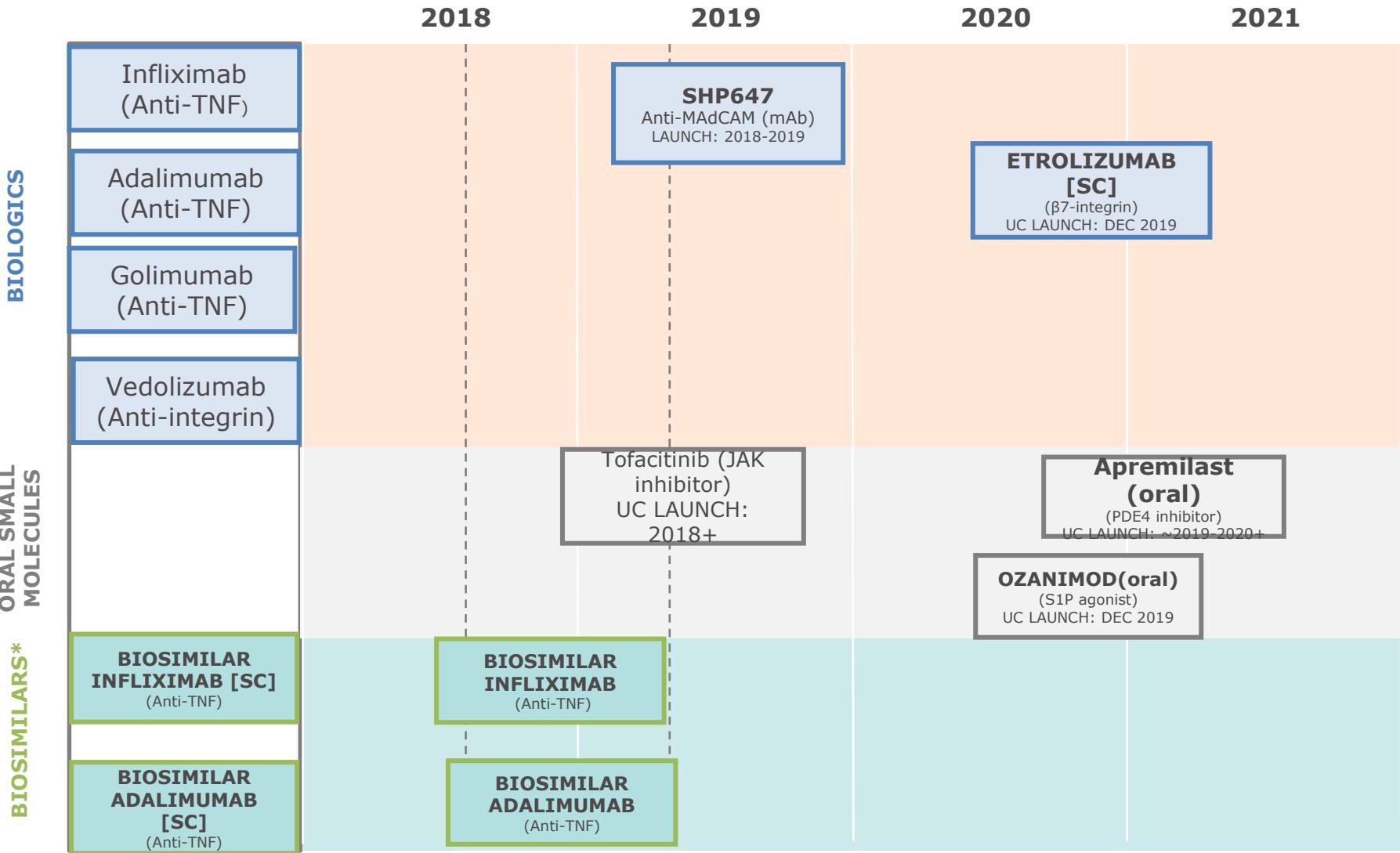
# **RECTO COLITE ULCERO- HEMORRAGIQUE**

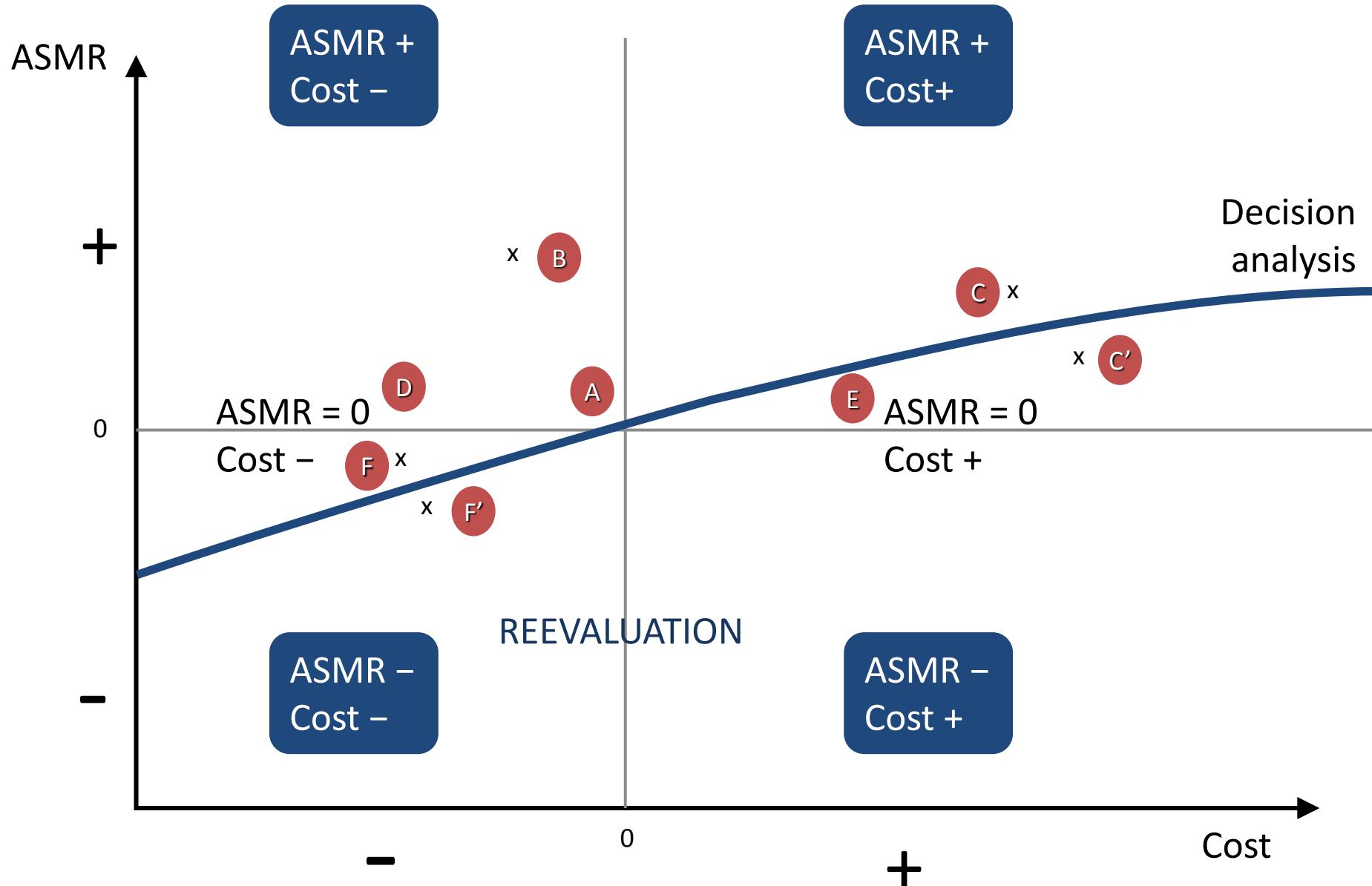
# TREATMENT ALGORITHM

## UC TREATMENT PATHWAY



# Multiple pipeline and biosimilar products are pursuing UC in the EU.





Maladie

Population  
à traiter

Population traitée

Population  
remboursable

ECR

Répondeurs