



Novel biomarkers for Crohn's disease drug development programs

Roadmap for biomarker qualification and precision medicine

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- Patient journey
 - Severe progressing disease vs mild disease
- Treatment options
 - Increased number of therapeutics
 - Traditional (salicylates, steroids, immunomodulators)
 - New generation (anti-TNF, anti-integrines, IL23p19, JAK)
 - Future (microbiome modulators,)
 - Efficacy ceiling
- Gap
 - Personalized/precision medicine approaches for clinical practice and drug development
 - “Right drug for right patient”

- Current status
 - Fecal Calprotectin (FCP) and C-reactive protein (CRP) are used in clinical practice and drug development
 - Research efforts in academia and industry
 - Pipeline of biomarkers
- Gaps
 - FCP and CRP are used in clinic and drug development, however not fully understood and not qualified as DDTs for CD
 - Large amounts of data available among institutions but not shared
 - Pipeline of biomarkers exists, however context of uses are not defined
 - No clear path to qualification

CD Biomarker pre-Consortrium (CDBpC)

- ✓ 1. Establish collaborative project across academia and industry to enable qualification of biomarkers for CD
- ✓ 2. Identify gaps in Crohn's disease drug development programs
- ✓ 3. Determine in what context a tool could be used to fill a gap within drug development program (COU)
- ✓ 4. Apply biomarkers to COU / Gaps
- ✓ 5. Biomarker Readiness Review
- ✓ 6. Redefine contexts of use based on biomarker readiness review
7. Align project with regulatory agencies
8. Prepare for full Consortium: Project Plan, Regulatory Submission, Publications

Deliverables:

1. An agreed upon hierarchical list of biomarkers to be pursued by the consortium to support unmet drug development needs in CD with input from stakeholders
2. Establishment of the project plan for the Crohn's Disease Biomarker Consortium based on the strategic focus set out by the pre-Consortium

ID Drug Development Gaps

Apply Biomarkers to COU

Redefine COU

Write up



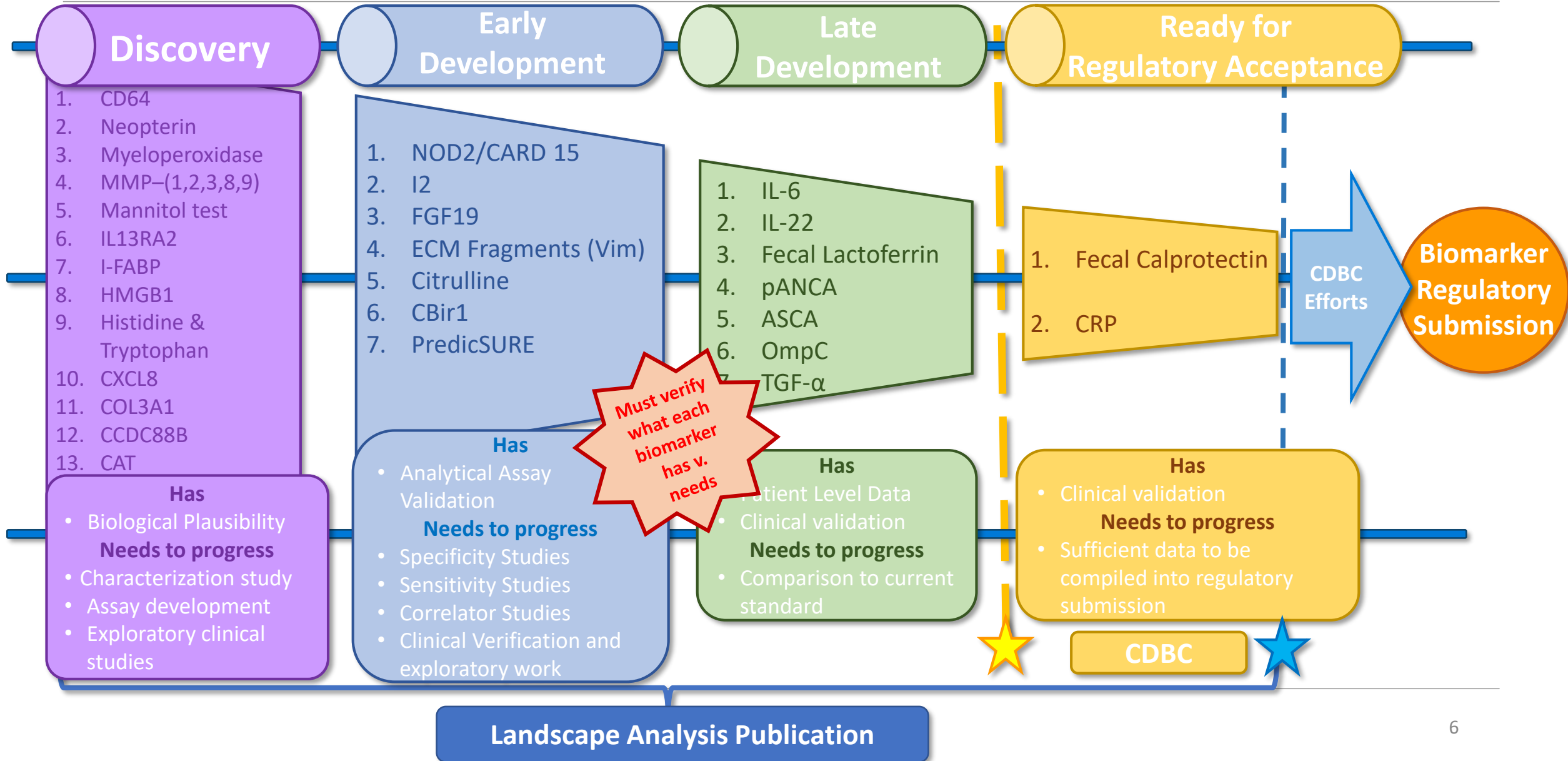
Disease Activity

- Biomarker approaches that will reduce need for endoscopies, stratify severity, determine active vs. remissive states.

Predictive/Prognostic & Treatment Options

- Biomarkers and/ or sets of biomarkers to aid in predicting complications, response to therapies or determine courses of precision medicine.

Verification CD Biomarker Stratification & Pipeline



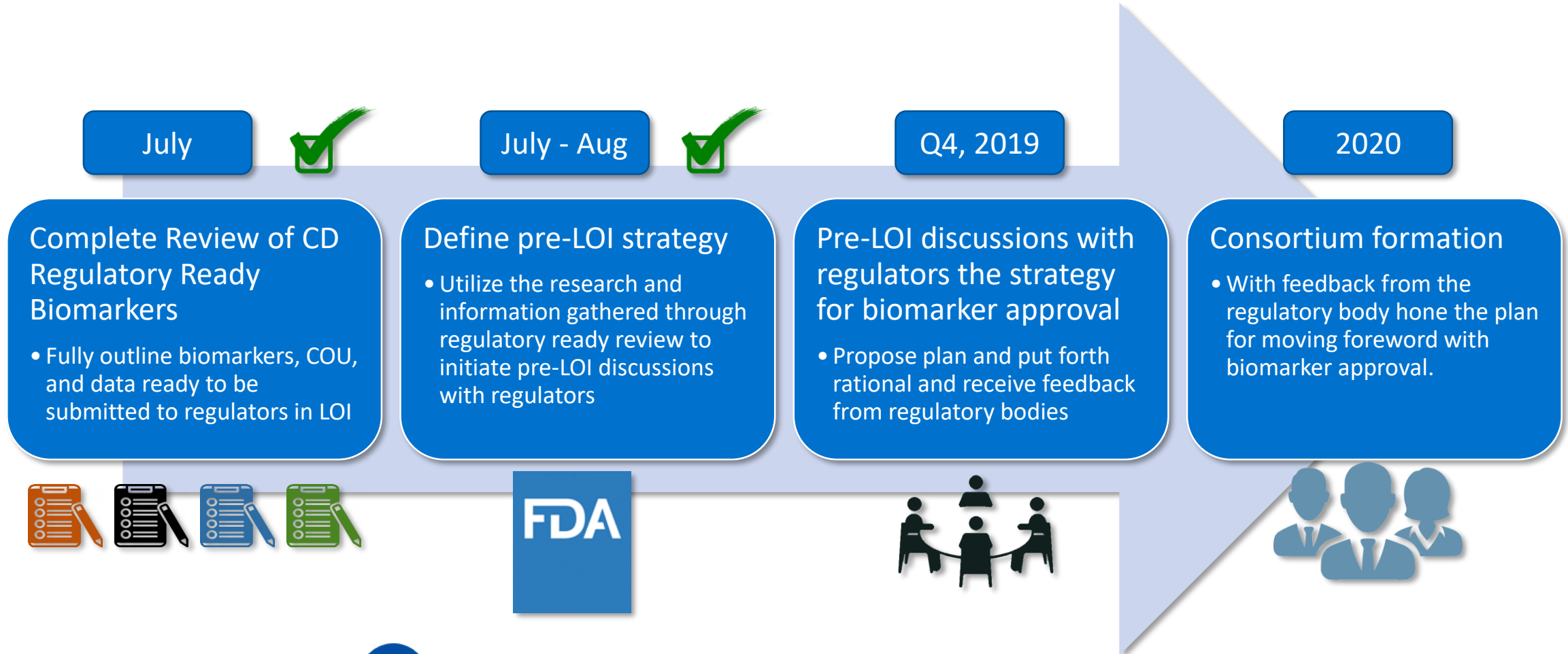
- **COU: (Fecal Calprotectin)** as a biomarker that **predicts long term remission**, following induction therapy in patients in clinical trials with Crohn's disease by **quantifying the degree of inflammation as measured by ileocolonoscopy**.
- **COU: (Fecal Calprotectin)** as an **enrichment biomarker** to **stratify patients** with Crohn's disease at high risk for progressive increase in disease activity by **assessing the degree of inflammation by ileocolonoscopy** for inclusion in clinical trials.
- **COU: (Fecal Calprotectin/ CRP)** for use as a **pharmacodynamic response** biomarker able to **identify probability** when a patient with Crohn's disease has **achieved endoscopic response/ healing** categorizing the patient as in remission in clinical trials.

CD Biomarker COU Clinical Data

CRP		
NCT #	Sponsor or Collaborator	Biomarker Context
NCT01235689	Abbvie	Diagnostic/ Pharmicodynamic / Remission
NCT01464333	Abbvie	Pharmicodynamic / Clinical Trial Endpoint
NCT01768858	Abbvie	Pharmicodynamic / Clinical Trial Endpoint
NCT01958827	Abbvie	Pharmicodynamic / Clinical Trial Endpoint
NCT02015793	AbbVie	Pharmicodynamic / Clinical Trial Endpoint
NCT02148718	AbbVie	Pharmicodynamic / Clinical Trial Endpoint
NCT02499783	AbbVie	Pharmicodynamic / Clinical Trial Endpoint
NCT02065570	AbbVie	Pharmicodynamic / Clinical Trial Endpoint
NCT02896985	Abbvie	Pharmicodynamic / Clinical Trial Endpoint
NCT03261102	McGill Uni. / Abbvie	Pharmicodynamic
NCT01369329	Janssen	Diagnostic/ Pharmicodynamic / Predictive
NCT03362736	Janssen	Stratifying/Pharmicodynamic
NCT03464136	Janssen	Pharmicodynamic / Clinical Trial Endpoint
NCT01349920	Merck	Pharmicodynamic
NCT03088449	Merck, AbbVie, Pfizer, CORE, Napp	Diagnostic/ Stratification/ Pharmicodynamic
NCT01276509	Pfizer	Diagnostic/ Pharmicodynamic
NCT01287897	Pfizer	Diagnostic / Pharmicodynamic / Pharmacodynamic
NCT01393899	Pfizer	Diagnostic/ Pharmicodynamic / Remission
NCT01393626	Pfizer	Diagnostic / Pharmicodynamic
NCT01470599	Pfizer	Diagnostic / Pharmicodynamic
NCT03710486	Takeda	Pharmicodynamic
NCT02764762	Takeda	Pharmicodynamic / Clinical Trial Endpoint

Fecal Calprotectin		
NCT #	Sponsor or Collaborator	Biomarker Context
NCT02015793	AbbVie	Pharmicodynamic
NCT02499783	AbbVie	clinical trial endpoint/ Pharmicodynamic
NCT02065570	AbbVie	clinical trial endpoint/ Pharmicodynamic
NCT01759264	AbbVie	Monitoring/ Pharmicodynamic/ Clinical trial endpoint
NCT02896985	Abbvie	Monitoring/ Pharmicodynamic/ Clinical trial endpoint
NCT02148718	Abbvie	Pharmicodynamic
NCT01393899	Pfizer	Diagnostic/ Pharmicodynamic / Remission
NCT01393626	Pfizer	Diagnostic / Pharmicodynamic
NCT01470599	Pfizer	Diagnostic / Pharmicodynamic
NCT01369329	Janssen	Monitoring
NCT03464136	Janssen	Diagnostic / Pharmicodynamic
NCT03710486	Takeda	Diagnostic / Pharmicodynamic
NCT02764762	Takeda	Diagnostic / Pharmicodynamic

Continuing Activities



- Establish consortium of stakeholders to qualify biomarkers as DDT for CD
- FCP and CRPO serves a blueprint for qualification of CD biomarkers
- Consortium will become partner of choice for others to qualify CD biomarkers