Genomics Impact on Pharma R&D: Next Generation Drugs, Co-Diagnostics and Patient Solutions

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Our Vision

To eliminate disease through developing highly innovative medical solutions for people around the world
Research Strategy

- Focus on areas of highest unmet need & compelling science
- Integrate internal & external science
- Companion diagnostics
- Disease interception approaches
- Patient solutions
Creating Value Through Innovation
End-to-End Strategy Focused on Five Therapeutic Areas

IMMUNOLOGY
- Inflammatory bowel disease
- Rheumatoid arthritis
- Psoriasis
- Pulmonary

NEUROSCIENCE
- Alzheimer’s disease
- Mood disorders
- Schizophrenia
- Chronic pain

INFECTIOUS DISEASES & VACCINES
- HIV
- HCV
- Respiratory
- Vaccines

CARdiovascULAR & METABOLISM
- Cardiovascular disease
- Diabetes

ONCOLOGY
- Prostate
- Lung
- B-cell malignancies

GENOMICS/INFORMATICS/BIOMARKER DISCOVERY
JANSSEN COMPANION DIAGNOSTICS
FDA Approved Oncology Companion Diagnostics

- Single gene markers or mutations in the drug target (or gene) in the targeted signaling pathway
- No complex molecular profiles approved yet as companion diagnostics
  - Need very large sample size at efficacious dose to detect reproducible profile
  - Challenges with obtaining sufficient tumor samples
  - Challenges with assay sensitivity
  - Ph 2 endpoints (tumor shrinkage) don’t always translate to Ph 3 endpoints (survival)

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Circulating Tumor Cells (CTC): Advancing Towards Personalized Medicine in Oncology

• CTC numbers are prognostic for disease outcomes & treatment response
• Next gen device will enable CTC capture and characterization
• Tumor molecular profiling at diagnosis and relapse

Non-Invasive, Real-Time CTC Characterization

Cell Morphology & Gene Expression

Molecular Characterization

Chromosomal Abnormalities

ex-vivo culture
Single Cell Analysis Reveals Tumor Heterogeneity

Rheumatoid Arthritis: A Destructive and Debilitating Systemic Immune Disease

- Early swelling leads to severe pain, and disability that is partially reversible
- Synovitis leads to joint destruction, loss of function and decreased quality of life
- Chronic inflammatory response results in joint structure degradation, permanent disability and co-morbidities including lymphoma and CV disease
Few Rheumatoid Arthritis Patients Achieve Complete Remission

**INCIDENCE**
- Steady over time
- ~0.25/1000

**Susceptible**
- Trigger

**PREVALENCE**
- 4.3M RA Patients (G7)
- Bio-eligible (1.5MM)
- On Biologics (850K)
- Remission @ 5% (43K)

**OUTCOMES**
- Disability 20-30% after 2-3 yrs
- Work disability 10x normal
- Hospitalization 2x normal
- Economic burden: $34.2B US cost of illness
- Multiple organ involvement: CV, pulmonary, renal, hematologic, skin and eyes
- Premature mortality

**REMISsion @ 5% (43K)**
RA Treatment Paradigm Shifts

Prognostic Markers
Network Pharmacology
Early Disease Identification

Predictive Biomarker Co-Dx
Best drug for initial treatment

Monitoring Biomarker Dx
Digital Health Care
Optimize Patient Outcomes

Disease Interception
New Therapies
Novel Mechanisms

Genome Sequencing and
Molecular Profiling
Biomarkers and Personalized Medicine in Rheumatoid Arthritis

Discovering new Solutions for RA Patients

- BATTER-UP consortia for anti-TNF responses in RA
- Whole genome sequencing of RA patients

Enriched for high likelihood of response
ACR50 = 80%

Current Benchmark
ACR50 = 40%
Inflammatory Bowel Disease (IBD): Crohn’s Disease and Ulcerative Colitis

Environmental triggers (infection, microbiome)

Moderately inflamed

Failure to down-regulate

Chronic uncontrolled inflammation = IBD

Down-regulate

Normal gut controlled inflammation

Normal gut controlled inflammation

Deep Ulceration

Stricture

Perianal Fistula

Anterior Uveitis

Proctocolectomy

Proctocolectomy
Profiling the Microbiome

Defining New Solutions for IBD Patients

• The gut, largest immune organ in the body

• Dysfunctional microbiome-host interactions in IBD

• Microbiome profiling initiatives:
  – Second Genome
  – Janssen clinical trials
    • Microbiota Sequencing
    • Informatics
    • Microbial biology
    • Immunology
Companion-Dx for Anti-TNF Treatment in UC

Discovering New Solutions for IBD Patients

- Gene expression profiling of tissue biopsies in ulcerative colitis (UC) in REMICADE® and SIMPONI® trials
- Identified predictor of response to anti-TNF treatment for personalized medicine
- Prospective validation trial underway

Genomics Impact on Pharma R&D

- Unprecedented opportunity to understand disease and create new medicines/solutions
- To fully apply genomic information to drug development we need:
  - Bioinformatics, computing and network pharmacology expertise to translate “big data” into knowledge
  - Cross disciplinary training programs
  - New business models; public/private consortia
  - Clear regulatory guidelines

“The patients are waiting!”

Dr. Paul Janssen