
# CONFLUENCE LIFE SCIENCES ACQUISITION

Dr. Neal Walker
President and CEO

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This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

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# Confluence Life Science Acquisition Summary

| | |
|---|---|
| ***Assets*** | • JAK inhibitors - oral and topical - (next generation)<br>• ITK inhibitors - oral and topical - (“anti-IL-17”)<br>• MK-2 inhibitor - oral - (“anti-TNF”) |
| ***Platform*** | • KINect™ platform – drug discovery engine<br>• Proprietary compound library and computational chemistry capability<br>• Medicinal chemistry, disease biology, immunology, pharmacology and preclinical development expertise |
| ***People*** | • Co-inventors of tofacitinib and former leaders of Pfizer kinase program (including JAK inhibitors)<br>• Kinome experts - chemists and biologists; combined 300+ years of drug discovery experience<br>• Significant experience in small molecule drug discovery through Phase II |

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# Transaction Founded on a Strategic Partnership

**Pre-transaction Aclaris**

- Oral and topical assets
- Robust intellectual property estate
- Drug development infrastructure
- Scientific leadership position in Hair Loss (Angela Christiano, Ph.D. / Columbia)
- Near Commercial A-101 Program
- Confluence Collaboration on Topical Soft JAK

**Confluence**

- Product pipeline that reinforces JAK leadership and expands inflammation/immunology franchise
- KINect™ Kinase Inhibitor Discovery Platform
- Drug development expertise
- Team composed of ex-Pfizer leadership in inflammation and immunology

**Fully Integrated Biopharmaceutical Company and Leading Developer of Small Molecule Therapeutics for Immunological Disorders of the Skin and other Organs**

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# Financial Highlights

| | |
|---|---|
| **Deal Terms** | • Confluence equityholders received an upfront payment of $10 million in cash and $10 million in common stock<br>• Up to $80 million in contingent payments upon achievement of certain development, regulatory and commercial milestones, plus additional low-single digit royalties |
| **Financial Implications for Aclaris** | • Acquired business is cash neutral to earnings for the six months ended June 30, 2017<br>• Integration of the Confluence Discovery Technologies CRO business as we incorporate personnel to more fully leverage the St. Louis based operations |
| **Confluence Discovery Technologies** | • Retain current talent and invest in growth and our internal capability expansion<br>• 80+ clients since founding spanning large biotech and pharma to smaller start-up biopharmaceutical companies; 90+ projects for 30+ clients in 2017<br>• Clients span large biotech and pharma to smaller start-up biopharmaceutical companies who utilize CDT to supplement their R&D for difficult-to-execute specialty skill bases and for programs which are difficult to source<br>• 40 Scientists: 40% Ph.D.; 60% B.S./M.S. |

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# Acquisition of Confluence Expected to Drive Future Growth

*Short term and Long term*

Synergies in drug discovery through Phase 2

*Internalizes preclinical research and development services which are currently outsourced*

CRO business facilitates cutting edge technology and disease expertise in immunology, pharmacology and biochemistry

*Cash neutral in near-term*

Supports and extends Aclaris' JAK kinase inhibitor programs

Enables targeted development of novel therapeutics for inflammation and immunology in dermatology and adjacent therapeutic areas

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# Confluence Assets

| | |
|---|---|
| **MK-2 Pathway Inhibitor CDD-450 "Oral Anti-TNF"** | • Psoriasis / Psoriatic Arthritis, RA, Chronic Inflammation<br>• Highly potent and designed to escape the tachyphylaxis associated with p38 kinase inhibitors |
| **JAK Inhibitors** | • Highly selective, covalent and non-covalent<br>• Oral and soft topical |
| **ITK Inhibitors "Oral Anti-IL17"** | • Psoriasis, Atopic Dermatitis<br>• Oral and soft topical |

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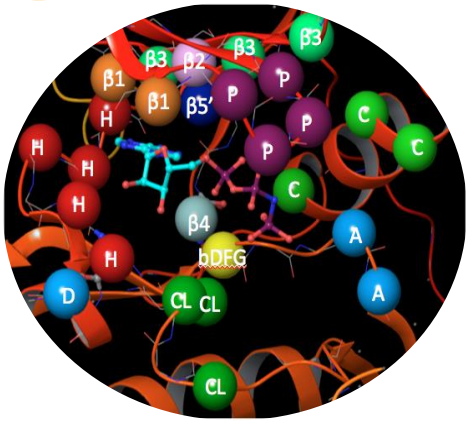
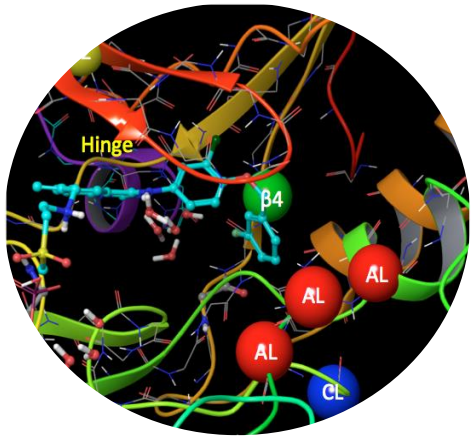
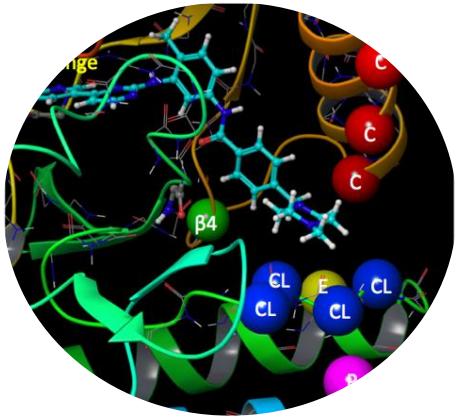
# Platform - KINect™ Innovation Engine




**Type 1 active conformation**
215 cysteine kinases

**Type 1.5 C-helix out conformation**
68 cysteine kinases




**Type 2 DFG out conformation**
128 cysteine kinases

- Concentrated effort in immunology: autoimmune disease and chronic inflammation
- Cysteinome targeted chemical library (60% of the kinome)
- Focused on a number of important but hard-to-drug kinases
- Structural analysis, KINect™ chemical library, screening in validated bioassays, SBDD (Schrödinger enabled) and medicinal chemistry
- KINect™ library interrogates both Type 1 and Type 2 kinases vs competitors who focus only on a few subgroups of Type 1 kinases
- KINect™ addresses both reversible and irreversible inhibitors

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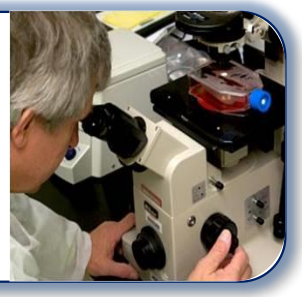
# Platform - Research and Development Capabilities

## BIOCHEMISTRY & ENZYMOLOGY

- Leaders in Mechanistic Enzymology
- Custom Assay Development
- Compound: Target Interaction
- Enzyme Inhibitor Mechanisms
- Direct Binding Kinetics
- High Throughput Screening

## CELL & MOLECULAR BIOLOGY

- Target Clone/Express/Purification
- Translatable Cellular Assays
- Target Modulation/Disease Assays
- Cell Pathway Interrogation
- Custom Assay Development
- Multiple Assay Platforms



## TRANSLATIONAL RESEARCH

- Biomarker Assay Development
- Clinical Biomarker Assessment
- *In vivo* Efficacy and PK Studies
- PK/PD Relationship
- Release Assay Validation

## IMMUNOLOGY & IMMUNO-ONCOLOGY

- Cytokine Expression
- Th Cell Differentiation/Activation
- CTL Differentiation and Function
- B Cell and NK cell Function
- Ag Specific Cell and *In Vivo* Models
- HWB/PBMC/Monocyte Assays

## BIOANALYTICAL CHEMISTRY

- Non-GLP Analytical
- Bioanalytical Method Development
- Bioanalytical Method Validation
- Pharmacokinetic/Toxicokinetic Analysis
- Ab Solubility and Aggregation

## COMPUTATIONAL & MEDICINAL CHEMISTRY

- Schrödinger ™ Enabled Structure Based Drug Design
- Computational Chemistry
- Library Design
- Compound Synthesis

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# Confluence People - Ex-Pfizer “Kinase and JAK experts”

| **Walter Smith**<br>*CEO* | **Joseph Monahan, PhD**<br>*CSO/Founder* | **Jon Jacobsen, PhD**<br>*Chemistry Director* | **Paul Changelian, PhD**<br>*Biology Director* |
|---|---|---|---|
| Former VP Research & Global Head, Pfizer Inflammation, co-leader of Pfizer Licensing Team<br>Delivered 8 clinical candidates, 6 INDs and 1 NDA in inflammation and cancer | Former Executive Director, Pfizer Inflammation Research and Leader of Global Kinase Technology Team<br>>95 publications and patents (>30 total on kinases) | Former Research Fellow and Director, Pfizer Chemistry<br>>100 publications and patents (15 total on kinases)<br>Project Lead for PFE JAK Program | Immunologist/drug discovery leader at pharma (Pfizer) & biotech (Lycera, Infinity)<br>Validated JAK 1/3 as target for transplant/RA/psoriasis, leading to approval of Xeljanz® |

***Program Initiation*** → ***Hit*** → ***Lead*** → ***Candidate*** → ***IND***

**BIOLOGY and COMPOUND PROFILING**
- Enzyme/Cellular assay development and screening
- Immunology models
- *In vivo* efficacy studies
- *In vitro* ADME
- *In vitro /In vivo* Metabolite profiling
- *In vivo* DMPK
- *In vivo* toxicology

**CHEMISTRY**
- Structure based drug design
- Medicinal Chemistry
- API synthesis
- Process Development
- Pre-Clinical cGMP API production
- CMC generation
- Patent filing

**PRE-CLINICAL IND ENABLING STUDIES (GLP)**
- GLP Analytics
- Drug-Drug Interaction
- Genetic toxicology
- Safety pharmacology
- Definitive PK
- General toxicology
- Biomarker development

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# The Kinase Opportunity – Rational Targeted Drug Discovery

***Creating New Medicines Targeting Previously Inaccessible Parts of the Kinome***

**KINect™ Technology Platform**

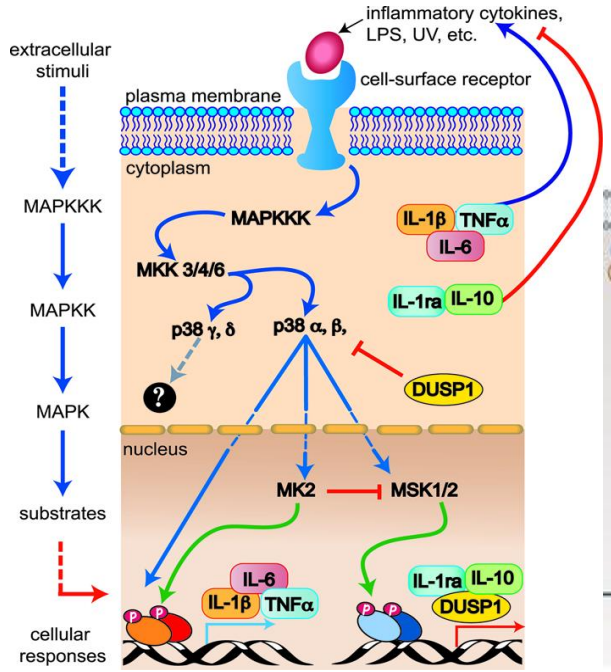
**Proprietary chemical library and integrated capabilities for interrogating the Kinome**

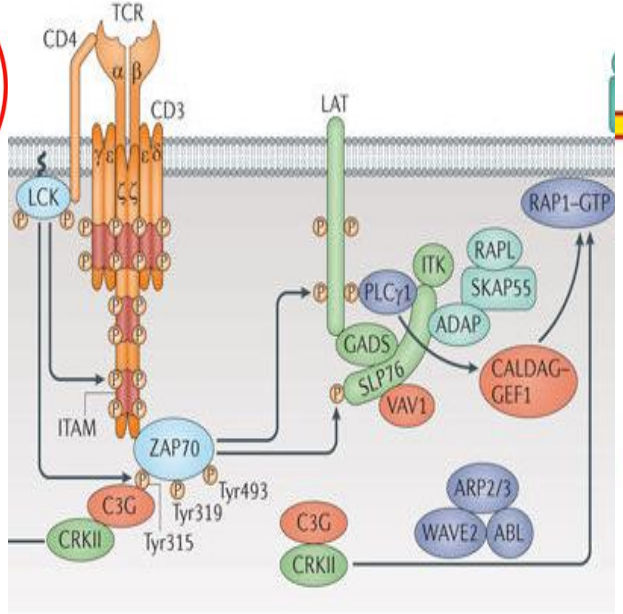
- Solves challenges encountered in the class
  - Selectivity
  - Biochemical efficiency
- Validity of targeting kinases is commercially established
- Plethora of validated kinase targets are inadequately drugged
- Kinect™ platform allows rational targeting of validated kinase targets

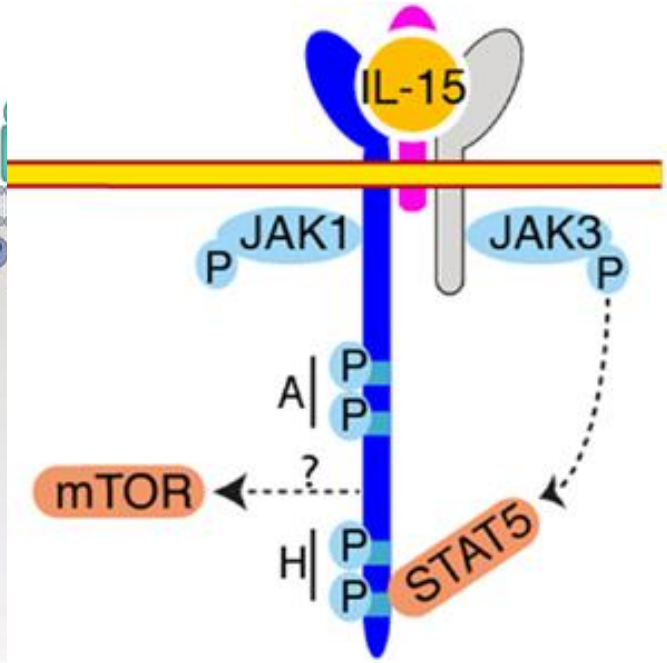
**Kinase Drugs Represented $240B in Aggregate Global Sales from 2011-2015**


***500 member class, representing 2% of the human genome***

# Confluence Pipeline




**MK2:** Innate immune response – clinically validated by Humira®, Actemra®, Kineret®

**ITK:** T-cell receptor dependent autoimmune disease – clinically validated by Neoral®, Prograf®, Orencia®

**JAK:** Inflammatory cytokine dependent inflammation – clinically validated by Xeljanz®, Jakifi®

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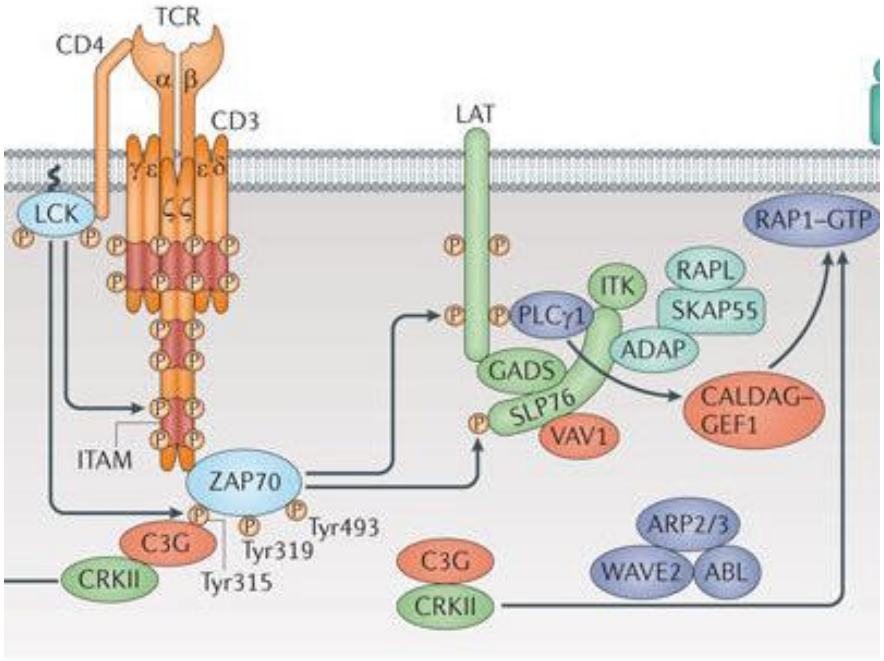
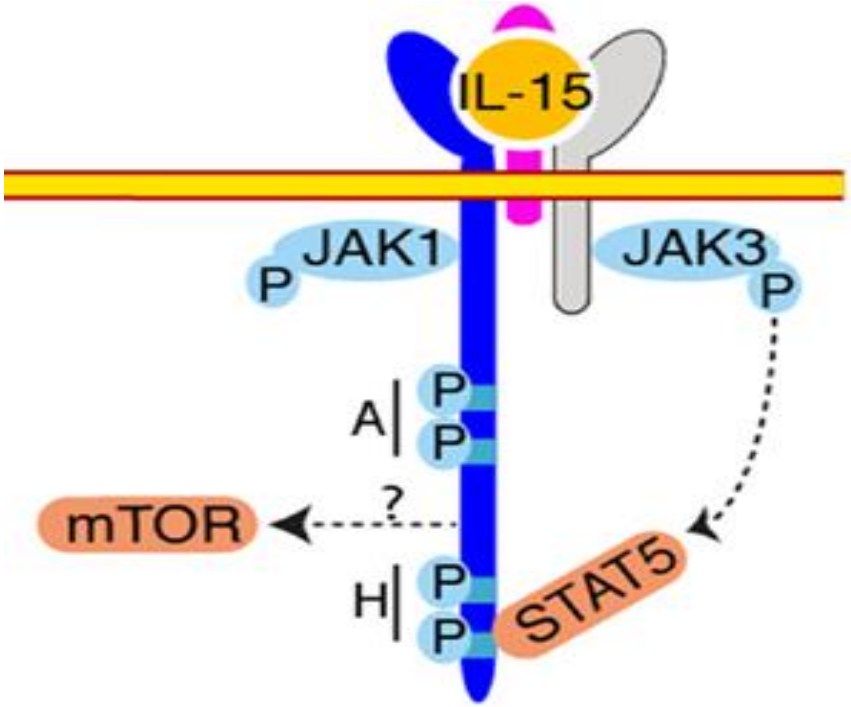
# Confluence Pipeline: Antigen and Cytokine Receptor Signaling Inhibitors for Dermatology




- **Alopecia Areata:** IFNγ (JAK1/2) and IL-15 (JAK1/3)
- **Vitiligo:** IFNγ (JAK1/2) and IL-15 (JAK1/3)
- **Psoriasis:** IFNγ (JAK1/2), IL-12/23 (JAK2/Tyk2), IL-22 (JAK1/Tyk2) and IL-21 (JAK1/3)
- **Atopic Dermatitis**: IFNγ (JAK1/2), TSLP (JAK1/2), IL-22 (JAK1/Tyk2) and IL-4/IL-21 (JAK1/3)
- All autoimmune disease driven by antigen recognition/T cell receptor (ITK)

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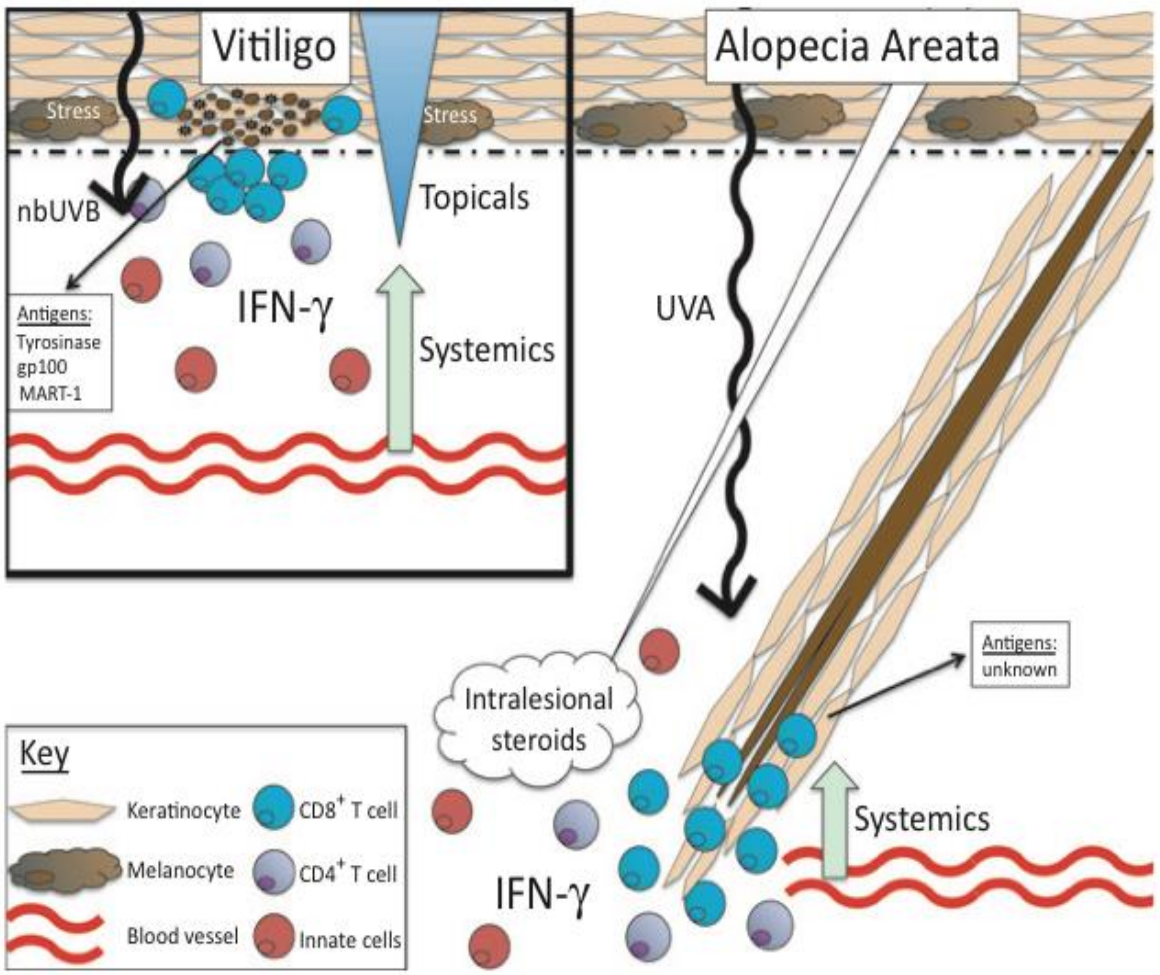
# Benefits of Targeted, Topical Soft Drugs

- Improved understanding of cytokine pathways in skin enables targeted pharmacology
- Differential formulations allow skin penetration to depth of disease activity
- Topical soft drugs are designed to be:
  - Active in the skin
  - But, inactivated in the bloodstream

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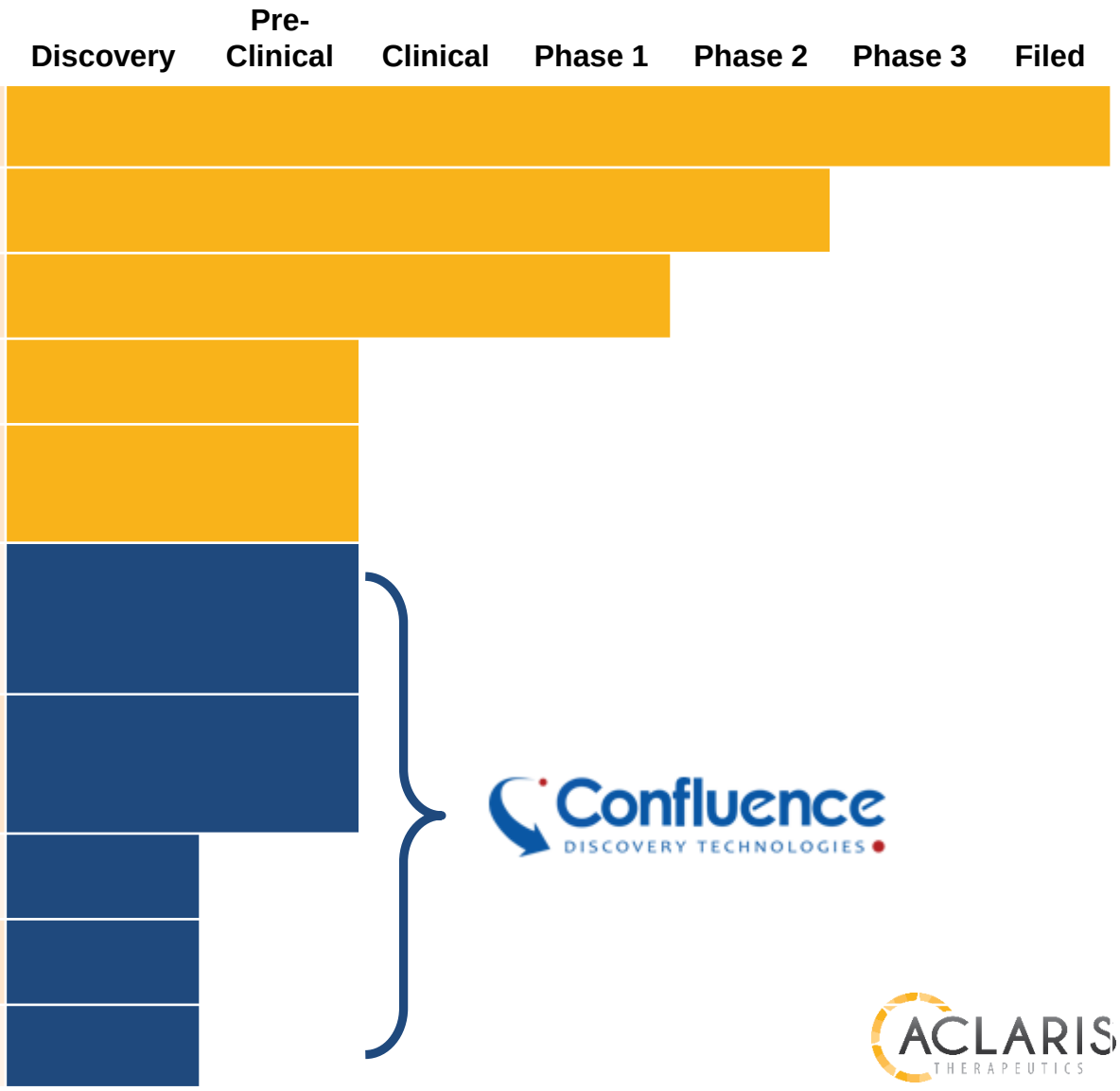
# Confluence Adds Complementary Pipeline

| Program | Indication(s) |
|---|---|
| **A-101 (40%)** *Topical* | **Seborrheic Keratosis** |
| **A-101 (45%)** *Topical* | **Common Warts** |
| **ATI-50001** *Oral* | **Alopecia Areata** |
| **ATI-50002** *Topical* | **Alopecia Areata** |
| **ATI-50001, ATI-50002** *Oral, Topical* | **Vitiligo** |
| **"Soft" JAK Inhibitor** *Topical* | **Hair Loss - androgenetic alopecia (AGA), Inflammatory Skin Disorders** |
| **MK-2 Inhibitor "Oral anti-TNF"** *Oral* | **Psoriasis, Psoriatic Arthritis, RA, Inflammatory Bowel Disease** |
| **ITK "Oral anti-IL17"** *Oral* | **Atopic Dermatitis, Psoriasis** |
| **ITK "Topical anti-IL17"** *Topical* | **Atopic Dermatitis, Psoriasis** |
| **Additional Compounds Novel Targets** | **Undisclosed** |



# Building a Fully Integrated Biopharmaceutical Company

## Executive Team
Proven track record of R&D, commercial execution, and business development

## Research and Development
Scientific leadership in JAK and kinase inhibitor chemistry - innovative clinical and regulatory strategies

## Commitment to Patients
Focus on “white-space” or underserved diseases where treatment gaps exist

## KINect™ Technology Platform
Proprietary discovery engine enables targeted design of novel drug candidates

## Pipeline
Multiple therapeutic programs ranging from discovery to NDA filed

## Intellectual Property
US & Global IP estate consisting of >150 patents/applications (issued and / or pending)

## Commercial Infrastructure
50-60 person sales force with expected launch 2018

## Strong Cash Position
$170 million at the end of 2Q17
Cash runway through end of 2018

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