一流的生物医药数据助力
一流的生物医药科研活动

科睿唯安Integrity等数据库操作培训

任锋 大客户战略合作部经理

杨晓栋 大客户战略合作部总经理

科睿唯安生命科学与制药事业部

2019年11月22日 中国 广东

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欢迎参加
科睿唯安
暨南大学
数据库培训

暨南大学++科睿唯安

该二维码7天内(11月29日前)有效，重新进入将更新

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暨南大学图书馆Integrity数据库登录方式

https://lib.jnu.edu.cn/database/detail.aspx?id=541

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提纲

公司简介 01

操作培训 02

科研案例 03

现场演示 04

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01 公司介绍

柠檬？橘子？

二手车市场

变形金刚

乔治·阿克尔洛夫发表《柠檬市场：质量不确定和市场机制》
2001年获得诺贝尔经济学奖

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搜索 一站式检索本馆已购买的所有纸质、电子资源 搜 索 高级检索

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- 按学科导航
- 按资源类型导航
- 按语言导航
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内容分类： 期刊 期刊文献

学科分类： 哲学 经济学 法学 教育学 文学 历史学 理学 工学 农学 医学 军事学 管理学 艺术学

资源简介： Web of Science核心合集数据库收录了12,000多种世界权威的、高影响力的学术期刊，内容涵盖自然科学、工程技术、生物医学、社会科学、艺术与人文等领域。

IP地址： 125.88.6.72

https://lib.jnu.edu.cn/database/detail.aspx?id=203

SCI

科睿唯安致力于打破
科研创新领域的信息不对称

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积累了超过一个半世纪的高质量数据和专业洞察

1864

Zoological Records
由伦敦动物学会和
大英博物馆创建
科学与学术研究业务

1926

BIOSIS
由细菌学家和植物学会创建
科学与学术研究业务

1955

尤金·加菲尔德博士
发明了引文索引和引文检索
科学与学术研究业务

1957

美国科学情报研究所
（ISI）成立
科学与学术研究业务

1963

Monty Hyams 开始在
他的小屋德温特销售
专利公报
专利和标准业务

1980s

汤姆森收购商标研究公司
Thomson & Thomson
以及 COMPUMARK
商标筛查与监测业务

1997

Web of Science 正式发布
科学与学术研究业务

2011

Cortellis 正式发布
生命科学与制药业务

2012

汤森路透收购
域名与品牌保护服务商
MARKMONITOR
域名与品牌保护业务

2016

原汤森路透知识产权
与科技业务被出售后，
正式成立科睿唯安公
司并在全球独立运营
科睿唯安

2017

收购评审学术研究成果平台
Publons
科学与学术研究业务

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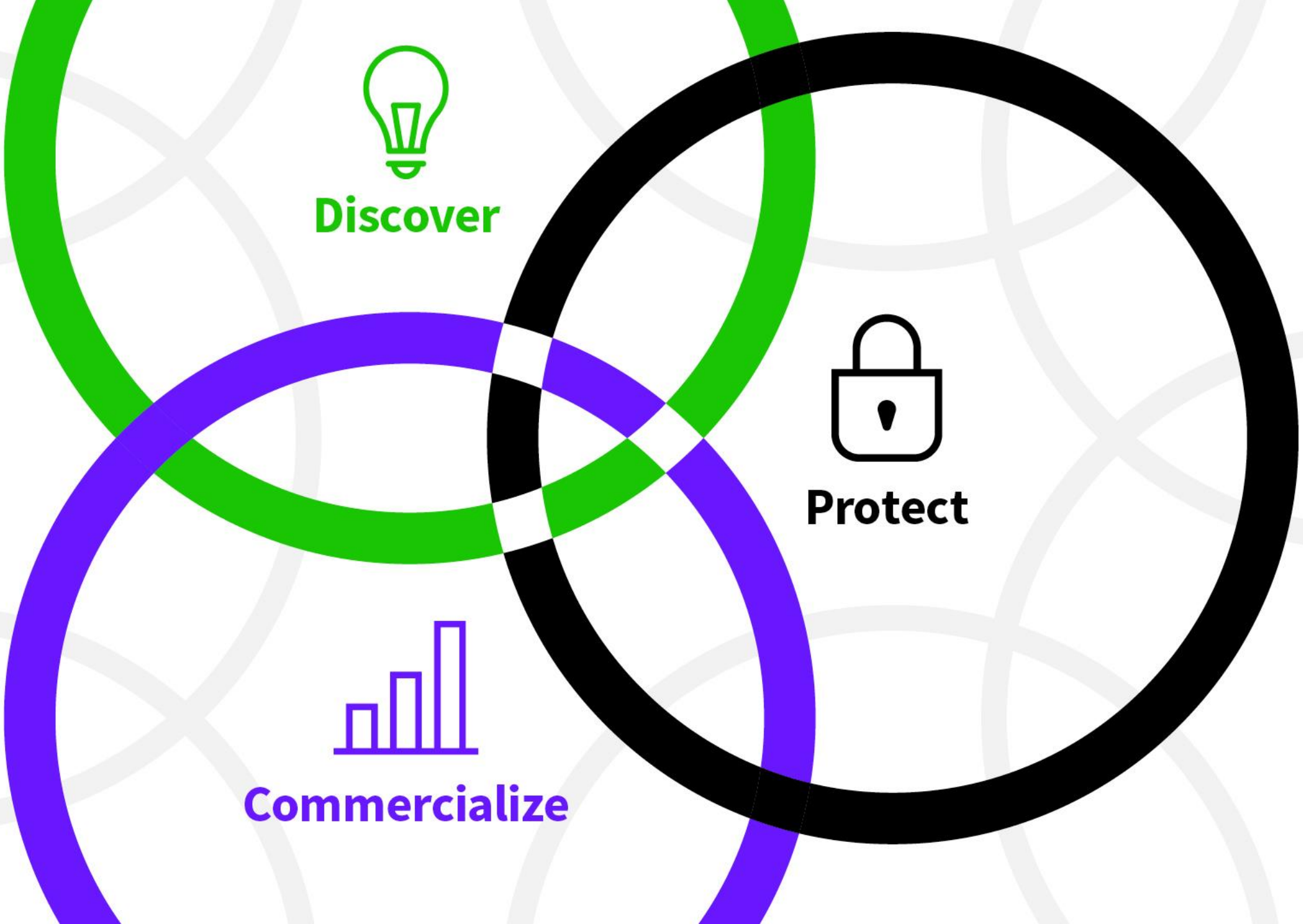

科睿唯安通过发现新想法、保护创新、助力创新成果的商业化，从而推动创新进程的稳步向前。

一系列备受全球业界信赖的品牌

科学与学术研究

专利与标准

生命科学与制药

商标筛查与监测

域名与品牌保护

知识产权管理

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谁在使用我们的产品与服务？

Academic institutions

Commercial enterprises

Governments

全球**50**家领先制药企业中有**49**家
在使用 Cortellis

超过一半的
财富 100 强企业在使用 MarkMonitor

每**10**个全球最有价值的品牌中就有**9**个
使用 CompuMark

40+ 家全球专利审查机构
在使用 德温特世界专利索引

通过 Web of Science 可以检索超过**10亿**条
引文数据

Clarivate Analytics | 科睿唯安 Analytics

哪些国内外生物医药机构在用？

Japan Science and Technology Agency
CNRS CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE
National Cancer Institute U.S. National Institutes of Health | www.cancer.gov
中国科学院 CHINESE ACADEMY OF SCIENCES
国药集团 SINOPHARM
BAYER
novo nordisk
UNITED STATES PATENT AND TRADEMARK OFFICE DEPARTMENT OF COMMERCE
Europäisches Patentamt European Patent Office Office européen des brevets
恒瑞 WWW.HRS.COM.CN
天士力制药 TASLY PHARM.
康弘药业 KANGHONG PHARMACEUTICAL
正大天晴医药
sanofi aventis
MERCK
Johnson & Johnson
LUYE PHARMA 绿叶制药
暨南大学 JINAN UNIVERSITY
新華
Bristol-Myers Squibb
gsk GlaxoSmithKline
Abbott
SPH 上海医药 SHANGHAI PHARMA
康宁杰瑞 ALPHAMAB
Roche
海思科药业 HAISCO PHARMACEUTICAL GROUP
Pfizer
Genentech IN BUSINESS FOR LIFE
NOVARTIS
华润医药 CR Pharmaceutical
HISUN 海正药业
Eisai
Takeda
AstraZeneca
药明康德 WuXi AppTec
齐鲁制药有限公司 QILU PHARMACEUTICAL CO., LTD.
JM Johnson Matthey
SCHERING making medicine work
Lilly
AMGEN
科伦集团 INDUSTRY GROUP
哈药集团有限公司 HARBIN PHARMACEUTICAL GROUP HOLDING CO.,LTD.
扬子江药业集团 Yangtze River Pharmaceutical Group
华海药业 HUAHAI PHARMACEUTICAL
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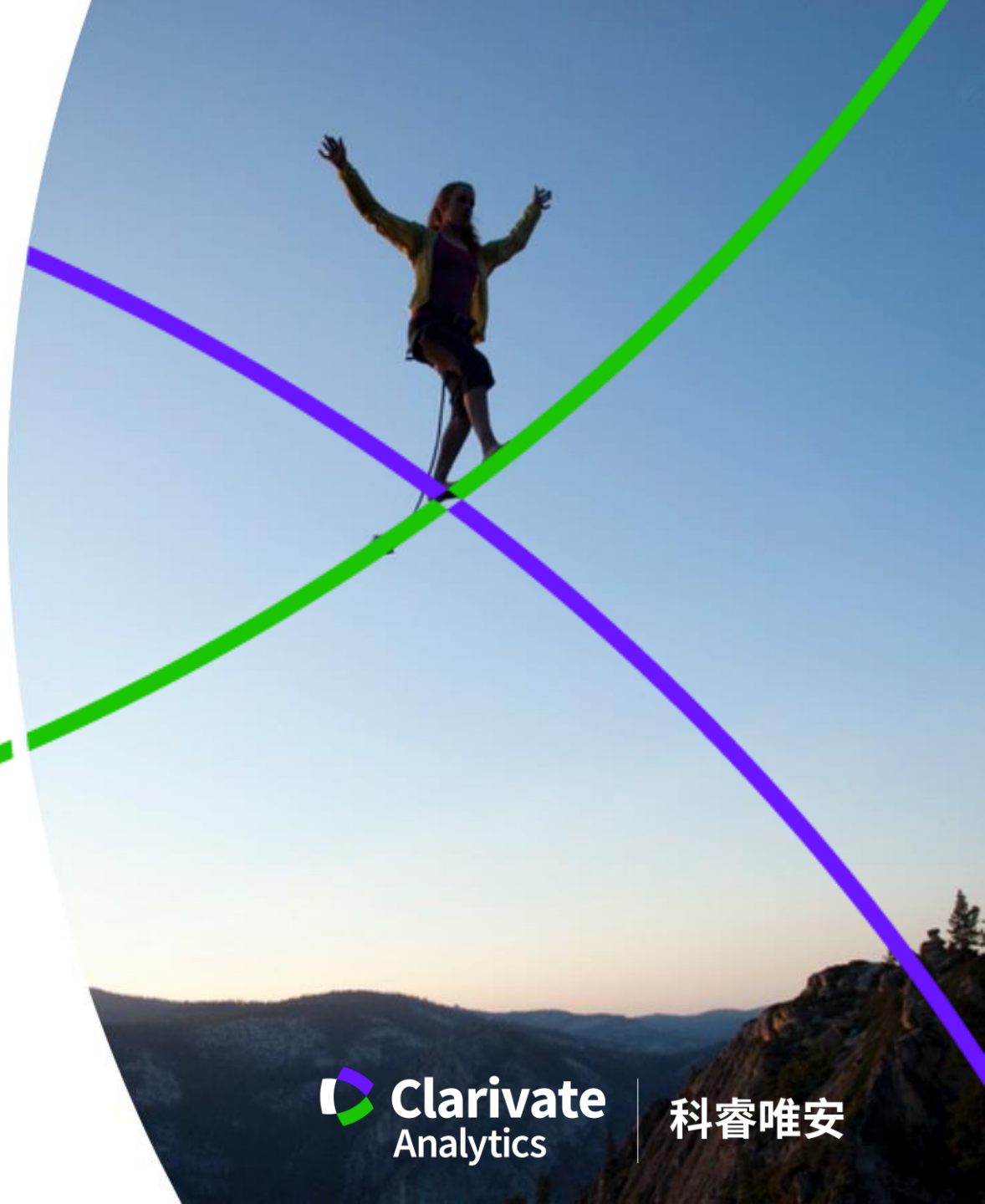
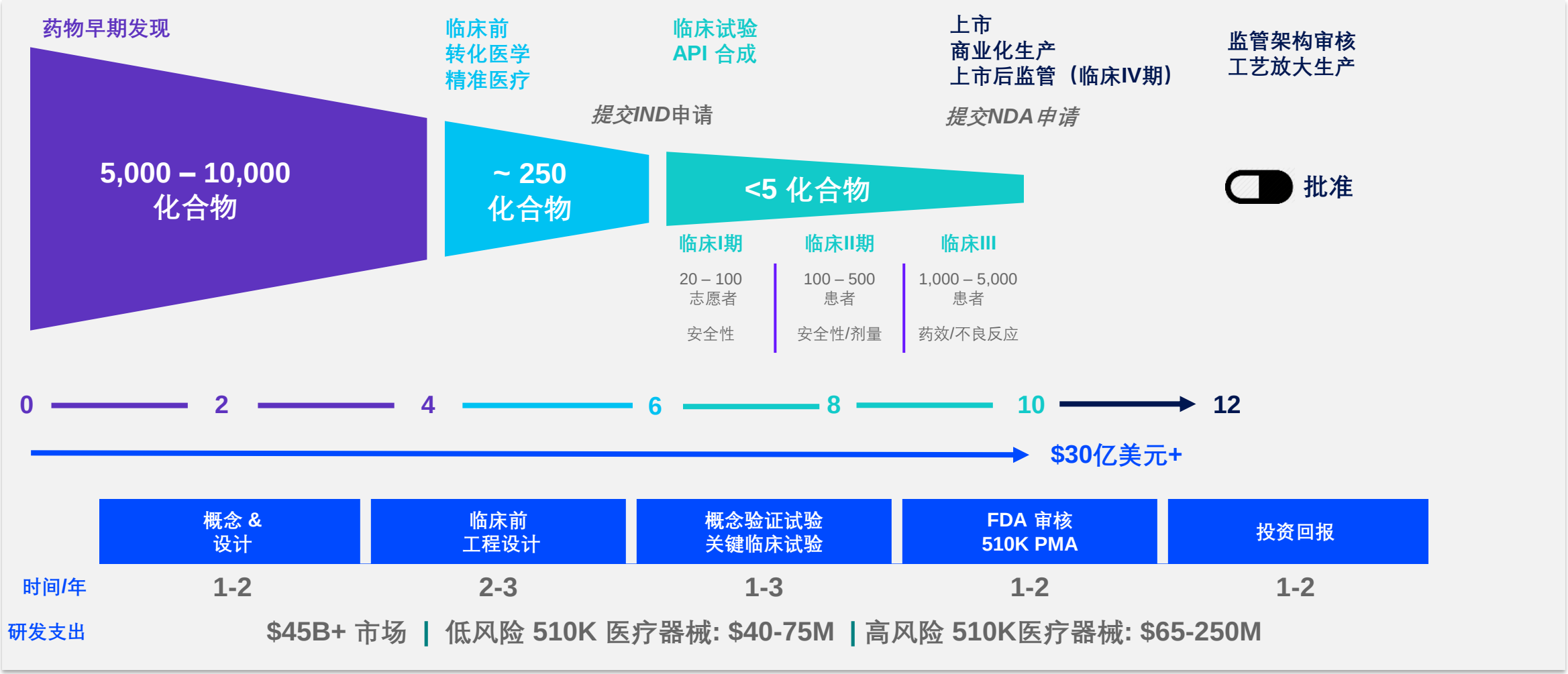
科睿唯安

我们是全球专业信息提供与分析服务领域的领导者。

我们帮助全球致力于创新的开拓者们，缩短将创意转变为颠覆性创新的时间，从而加速创新的进程。



整个药品开发生命周期长、花费高



研发新药的成本——新靶点与新方法呼之欲出

10-15

把一个药物从研发推向市场所用的时间

$3B

把一个药物从实验室研究推向市场所需的总费用[2]

$1.2B

新药研发的预估时间成本[1]

12%

自2003年以来，药物获批上市率已经下降了一半[1]

Sources:
1. Tufts Center for the Study of Drug Development
2. The Centre for Medicines Research

药物研发：不同节点的专业信息需求

Diseases 疾病信息	Discovery 研究数据挖掘	Pre-clinical 非临床研究数据	Clinical 临床研究信息	Regulatory 监管政策	Life-cycle Management 仿制药策略
• 疾病诊治信息 • 患者容量 • 市场潜力评估	• 探索疾病（药物）机制 • 挖掘潜在药物靶点 • 研究生物标志物	• 靶点成药性评估 • 综合研究数据 • 药物新闻	• 患者分层 • 临床路径 • 生物标志物应用	• 监管政策及比较 • 批准及指南	• 立项策略 • 市场竞争 • 专利信息 • API可及性

- 管线布局
- 研究进展及交易信息
- 产业动向新闻

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科睿唯安全流程产品及解决方案

Diseases 疾病信息	Discovery 研究数据挖掘	Pre-clinical 非临床研究数据	Clinical 临床研究信息	Regulatory 监管政策	Life-cycle Management 仿制药策略

- IPD数据库， 疾病预测报告Disease Forecast Report， 疾病综述Disease Briefing
- MetaCore， MetaDrug， KPA
- Integrity， 靶点挖掘DRA-TD， Drug News
- Cortellis 平台：Competitive Intelligence， Trial, Deal, Regulatory
- BioWorld, Biopharma Financing Report
- Newport

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02 操作培训

Integrity——专注创新药物研发信息支持

项目来源、思路

- 创新药做什么？

--Integrity数据库整合了大量处于不同研发阶段的生物药和化学药及其实验数据，及时更新，帮助研究者挖掘新靶点、新药物及相关数据，支持研发早期决策。

--***Integrity Biomarkers模块通过收集全球药物研发Biomarkers的相关信息，为新药研发提供多维支持。

研究指标、实验模板

- 创新药怎么做？

--Integrity模块提供及时且关键的研发信息，为创新药研发中的靶点发掘、药物优化（包含实验信息）、监测竞争对手、对标产品、了解竞争格局提供一手信息。

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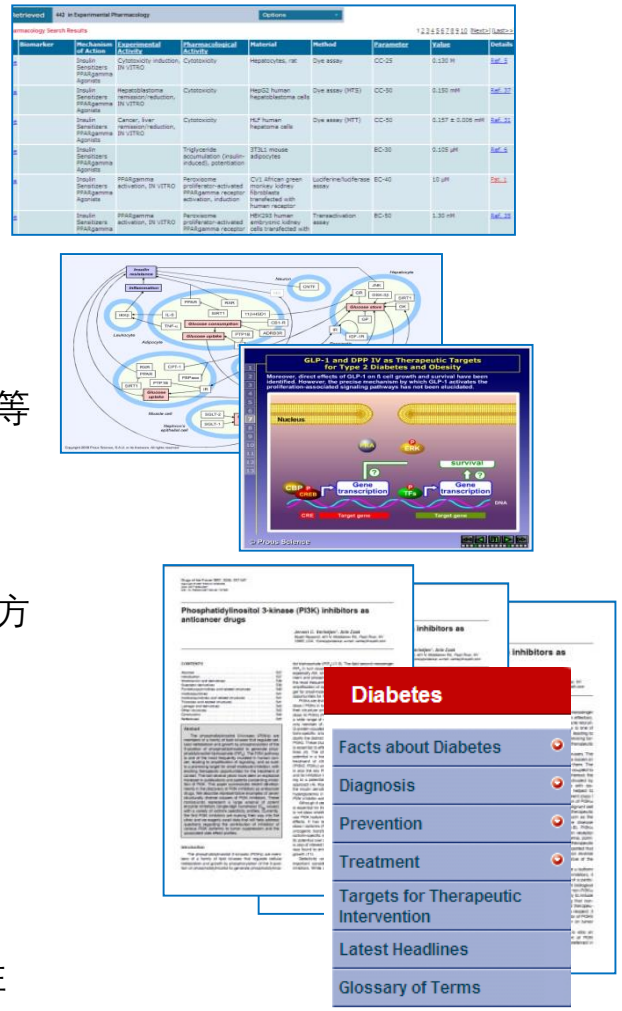
Integrity——多维度实用信息工具

- 监测国际最新研发动态
  - 及时获取国际上的研发新闻
  - 跟踪早期药物研发产品管线
  - 了解药物开发全貌和靶标、合成等最新进展
- 靶标进展报告和通路图
  - 了解某一靶标的研发进展、研究领域、作用机理等
  - 促进药物设计及基础机理的研究
- 疾病综述
  - 了解疾病研发历史、重要靶标、主流药物、治疗方法等
  - 申报资料的信息综述
  - 申请基金或课题时作为课题背景信息来源
- 药理学实验数据比较
  - 寻找具有某药理学特性的相关药物
  - 比较同一领域/类似结构等药物之间的药理学活性



- **快速识别**某一特定靶点上处于研发状态的药物
- **理解**临床选化合物如何从众多化合物中脱颖而出
- **发现最好**的评价临床前药物的动物模型，成功推动药物由动物向人的转化
- **发现和确认Biomarkers**为了跟踪药物治疗有效性、安全性，更好的理解疾病等

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Integrity模块主要结构及内容

化学药&生物药
靶点与通路
基因组
生物标记物
有机合成
实验药理学
药理实验模型
药动/药代
临床试验
疾病综述
公司/研究机构
文献
专利

常见问题
学习中心
操作手册
视频课程

专家观点
官方网站

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Integrity——庞大数据信息经整合后为研发人员提供多重帮助

特点 1　整合数据，更新及时

Integrity中的数据量（2019年2月统计）		Integrity数据收录时间
药物（化学药与生物药）	>562,025 (>506,552结构式)	1988
药物靶标&通路	>6,561	2004
基因组	>47,429	2001
生物标志物	>41,423	2007
化学全合成途径	>34,511	1970s
药理/毒理试验证据	>2,533,895	1998
试验模型	>120,979	2012
药代/药动试验数据	>984,037	2000
临床试验	>371,684	2000
疾病综述	160	2000
研发单位	>30,462	2000
文献	>2,556,804	1988
专利	>427,410	1988

* 药物数据是从1988年开始收录的; 但是同时也精选了1500余种1988年之前的重要化合物进行收录，供用户参考。

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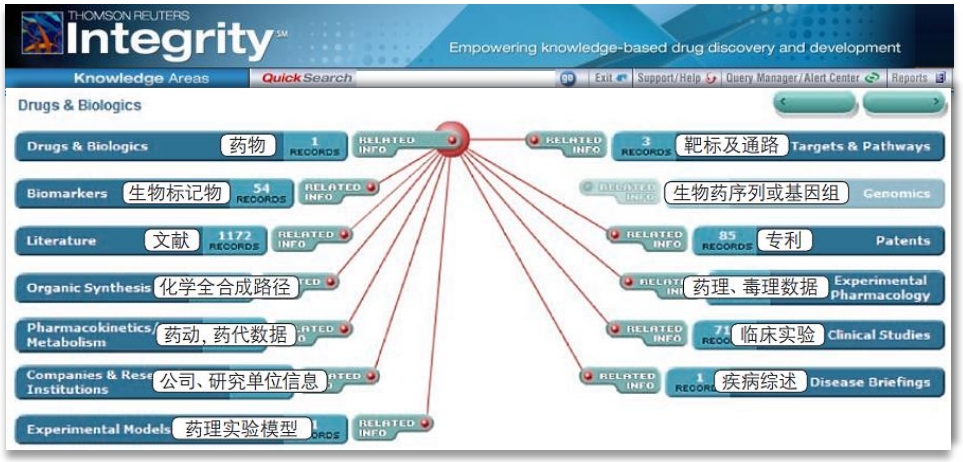
Integrity——数据关联度高、可溯源，便于分析和再探索

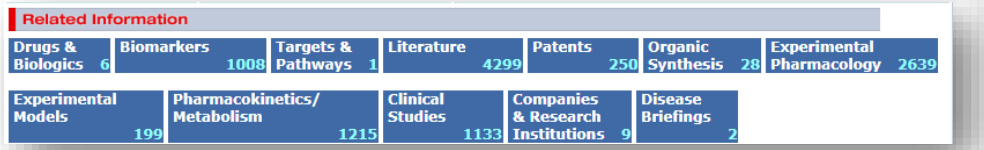
特点 2　高度关联，由点到面

- ✓ 早期研发药物产品管线
- ✓ 疾病综述、靶点评估
- ✓ 实验设计的参考与评价
- ✓ 药物研发的药理药代数据
- ✓ 临床、疾病、文献、专利等

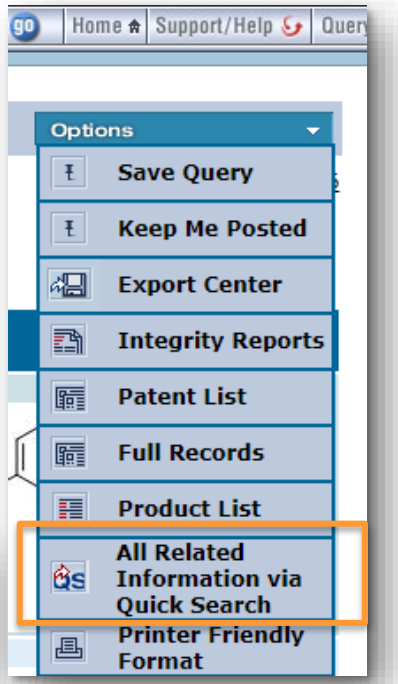
✓ 快速检索全面呈现关联数据



✓ 靶点/药物报告提供详尽关联信息



✓ 关联数据直接检索



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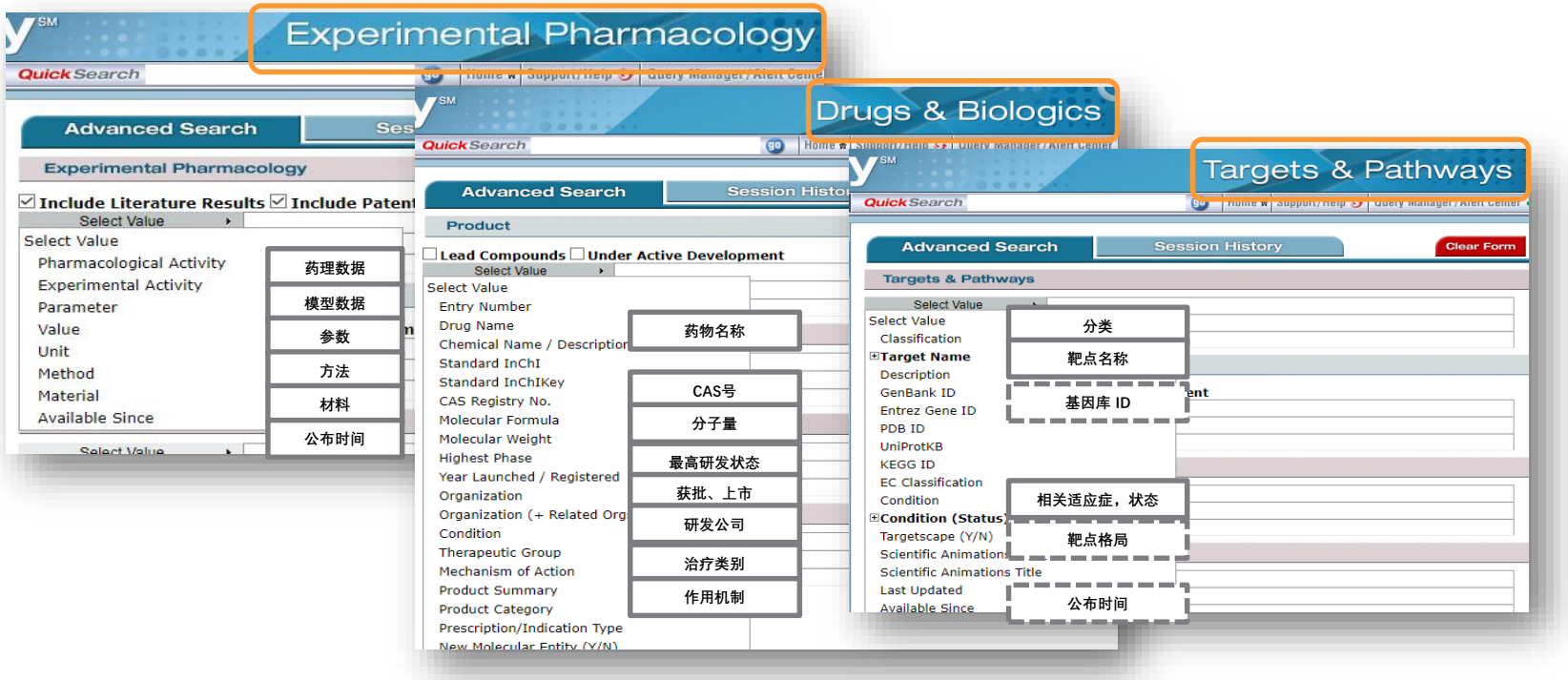
Integrity——针对不同专业，制定灵活多样的检索策略

特点 3　灵活检索，快速获取



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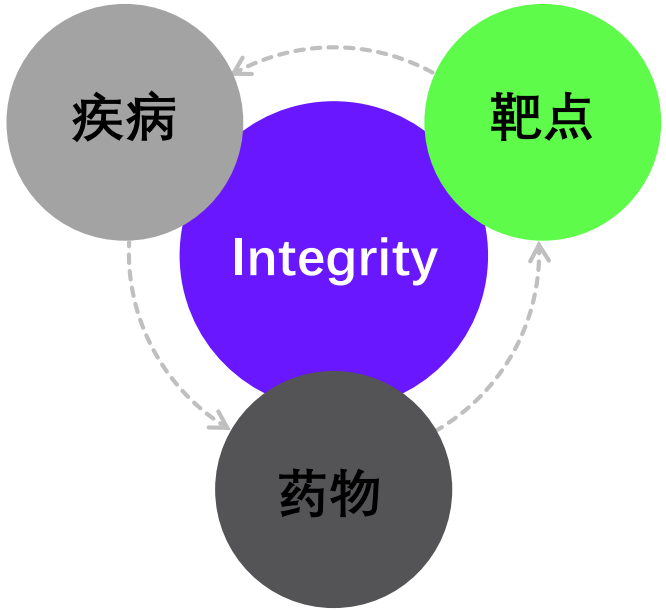
Integrity 在疾病、靶点和药物间构建网络关系，推进研究进程

信息	药物化学
文献	化合物信息
专利	有机合成
公司信息	生物
临床	疾病信息
临床研究	靶点和通路
代谢及安全性	基因信息
药理	辅助信息
化合物活性评价	疾病情况
生物标志物	药物研发情况
试验模型	上市药物情况



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Integrity

药理药效靶点
早期研发数据库

查询疾病、靶点信息最为全面和权威的工具

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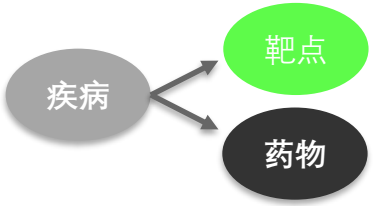
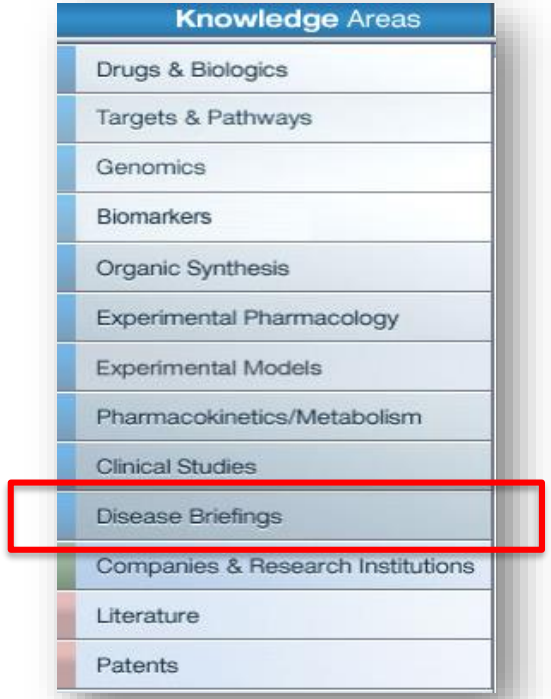
疾病综述：了解疾病的基本情况，为项目筛选立项调研奠定基础





提供160种疾病(涵盖20个治疗领域)的情报，包含：

- ✓ 病因
- ✓ 发病率/流行率
- ✓ 诊断
- ✓ 预防
- ✓ 治疗: 治疗类型、标靶(target)及相应的药品研发pipeline
- ✓ 已上市产品清单

每份报告另提供相关的辅助材料，如**临床指南**、词汇表(glossary)，多媒体插图列表和建议阅读。

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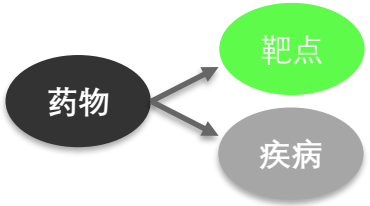
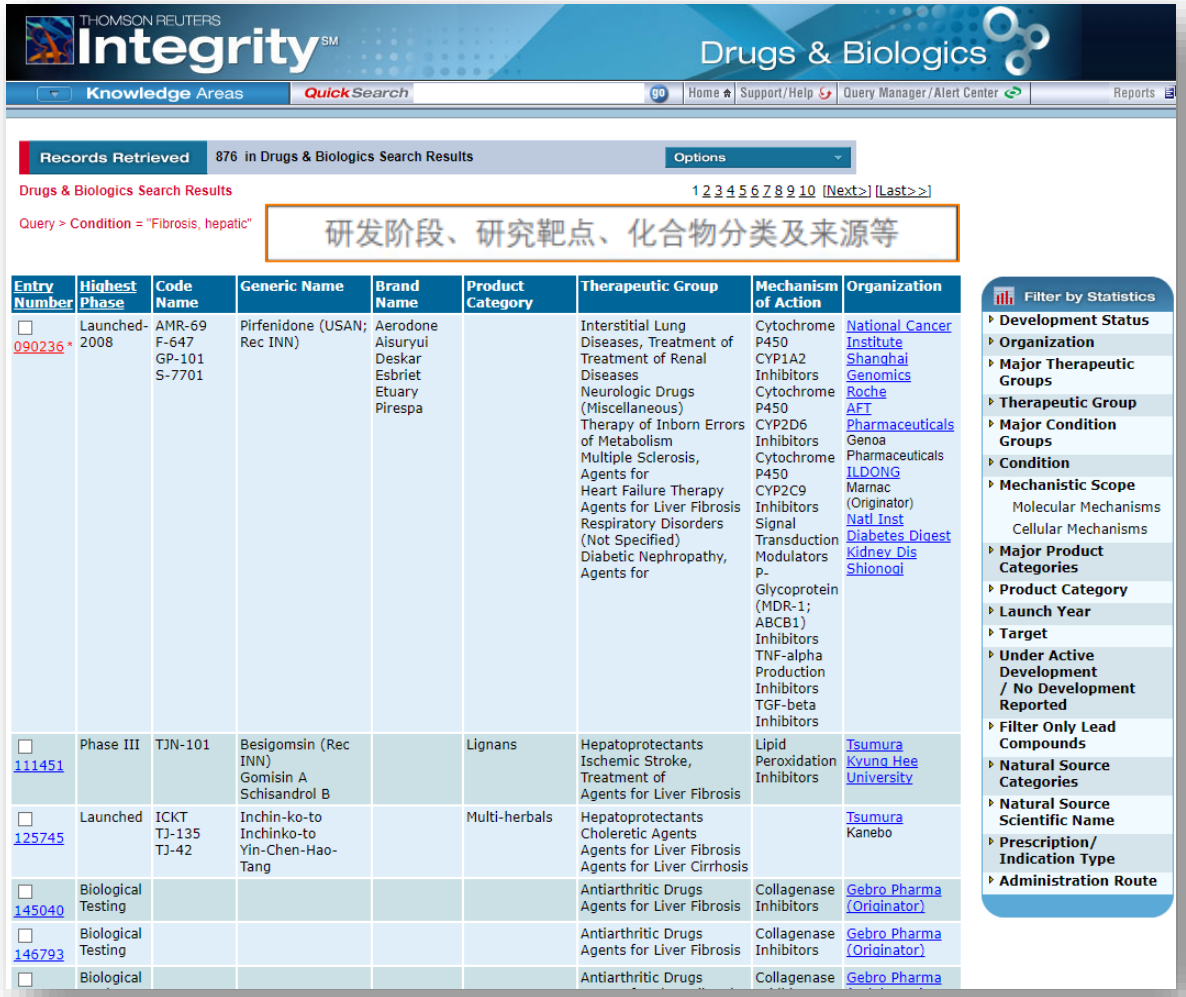
药物信息探索，根据筛选标签锁定检索目标





Entry Number	Highest Phase	Code Name	Generic Name	Brand Name	Product Category	Therapeutic Group	Mechanism of Action	Organization
090236 *	Launched-2008	AMR-69 F-647 GP-101 S-7701	Pirfenidone (USAN; Rec INN)	Aerodone Aisuryui Deskar Esbriet Etuary Pirespa		Interstitial Lung Diseases, Treatment of Treatment of Renal Diseases Neurologic Drugs (Miscellaneous) Therapy of Inborn Errors of Metabolism Multiple Sclerosis, Agents for Heart Failure Therapy Agents for Liver Fibrosis Respiratory Disorders (Not Specified) Diabetic Nephropathy, Agents for	Cytochrome P450 CYP1A2 Inhibitors Cytochrome P450 CYP2D6 Inhibitors Cytochrome P450 CYP2C9 Inhibitors Signal Transduction Modulators P-Glycoprotein (MDR-1; ABCB1) Inhibitors TNF-alpha Production Inhibitors TGF-beta Inhibitors	National Cancer Institute Shanghai Genomics Roche AFT Pharmaceuticals Genoa Pharmaceuticals ILDONG Marnac (Originator) Natl Inst Diabetes Digest Kidney Dis Shionogi
111451	Phase III	TJN-101	Besigomsin (Rec INN) Gomisin A Schisandrol B		Lignans	Hepatoprotectants Ischemic Stroke, Treatment of Agents for Liver Fibrosis	Lipid Peroxidation Inhibitors	Tsumura Kyung Hee University
125745	Launched	ICKT TJ-135 TJ-42	Inchin-ko-to Inchinko-to Yin-Chen-Hao-Tang		Multi-herbals	Hepatoprotectants Choleretic Agents Agents for Liver Fibrosis Agents for Liver Cirrhosis		Tsumura Kanebo
145040	Biological Testing					Antiarthritic Drugs Agents for Liver Fibrosis	Collagenase Inhibitors	Gebro Pharma (Originator)
146793	Biological Testing					Antiarthritic Drugs Agents for Liver Fibrosis	Collagenase Inhibitors	Gebro Pharma (Originator)
	Biological					Antiarthritic Drugs	Collagenase	Gebro Pharma

更多过滤分析标签

研发阶段

开发公司

治疗类别

适应症

作用机制

产品类别

上市时间

靶点类型

- 探索目标疾病相关药物开发和早期活性分子测试情况

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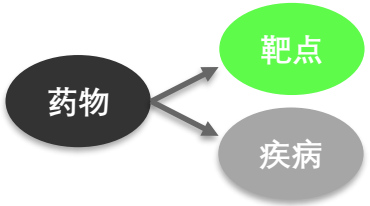
药物报告全面了解特定在研药物情况



Product Summary

REPORT

Pirfenidone is an orally active small-molecule
Shionogi received approval of pirfenidone in
InterMune (now Roche) received an approval
In 2010, the compound was recommended fo
assigned to the NDA. In 2014, InterMune res
obtained for IPF in 2011. The product is avail

The National Cancer Institute (NCI) is evalua
neurofibromatosis type I and progressive ple
and Kidney Diseases (NIDDK) is conducting
the treatment of diabetic nephropathy. The
evaluation by Shanghai Genomics, in phase
evaluating the compound in phase II clinica
ventricular ejection fraction. The company
Pudlak Syndrome and for the treatment of
development has been reported for these in

Pirfenidone may inhibit collagen synthesis,
and stimulation in response to cytokines.

Marnac licensed worldwide rights to develo
Japan, Korea and Taiwan where the drug is
designation by the FDA for the treatment o
In 2011, the compound was licensed to ILD
September 2014, InterMune was acquired

In 2013, orphan drug designation was assig
interstitial lung disease). In 2014, breakthr
idiopathic pulmonary fibrosis. Also in 2014,
idiopathic pulmonary fibrosis (IPF).

Records Retrieved 1 in Drugs & Biologics — Options

Drugs & Biologics Search Results 1

Entry Number	90236 UPDATES
Record Creation Date	Jun 12, 2002
Last Updated Date	Sep 22, 2017
CAS Registry No.	53179-13-8
Molecular Formula	C12 H11 N O
Molecular Weight	185.2218
Highest Phase	Launched - 2008
Under Active Development	

Chemical Structure — STRUCTURE FEATURES

Pirfenidone

Chemical Name/Description — METABOLITES

5-Methyl-1-phenylpyridin-2(1H)-one

Standard InChI

1S/C12H11NO/c1-10-7-8-12(14)13(9-10)11-5-3-2-4-6-11/h2-9H,1H3

Standard InChIKey

ISWRGOKTTBVCFA-UHFFFAOYSA-N

Code Name	Generic Name	Brand Name SALES
AMR-69 F-647 GP-101 S-7701	Pirfenidone (USAN; Rec INN)	Aerodone Aisuryui Deskar Esbriet Etuary Pirespa

Molecular Mechanism	Cellular Mechanism
Cytochrome P450 CYP1A2 Inhibitors Cytochrome P450 CYP2D6 Inhibitors Cytochrome P450 CYP2C9 Inhibitors P-Glycoprotein (MDR-1; ABCB1) Inhibitors TNF-alpha Production Inhibitors TGF-beta Inhibitors	Signal Transduction Modulators

Product Category	Therapeutic Group	Prescription/ Indication Type
	Interstitial Lung Diseases, Treatment of Treatment of Renal Diseases Neurologic Drugs (Miscellaneous) Therapy of Inborn Errors of Metabolism Multiple Sclerosis, Agents for Heart Failure Therapy Agents for Liver Fibrosis Respiratory Disorders (Not Specified) Diabetic Nephropathy, Agents for	Orphan Drug

Development Status Summary

DETAILS | MILESTONES | REGULATORY INFORMATION

Phase	Organization	Condition
Launched - 2008	Shionogi	Idiopathic pulmonary fibrosis
Phase III	Shanghai Genomics	Respiratory Disorders
Phase II	Natl Inst Diabetes Digest Kidney Dis	Focal segmental glomerulosclerosis
Phase II	Roche	Heart failure
IND Filed	Shanghai Genomics	Interstitial lung diseases
IND Filed	Shanghai Genomics	Nephropathy, diabetic

Related Information

Drugs & Biologics 5	Biomarkers 93	Targets & Pathways 6	Literature 680	Patents 86	Organic Synthesis 2	Experimental Pharmacology 108
Experimental Models 69	Pharmacokinetics/ Metabolism 436	Clinical Studies 188	Companies & Research Institutions 7	Disease Briefings 3		

主要进展

Development Status - Launched, Registered or Under Active Development

Country/Area	Phase	Organization	Brand Name	Condition	Indication	Admin. Route	Formulation
China	IND Filed	Shanghai Genomics	Etuary	Nephropathy, diabetic			
China	IND Filed	Shanghai Genomics	F-647	Interstitial lung diseases	Treatment of interstitial lung disease (ILD) with connective tissue disorder (CTD)		
China	Launched	Shanghai Genomics	Etuary	Idiopathic pulmonary fibrosis		oral	Capsules 100, 200 mg
China	Phase III	Shanghai Genomics	F-647	Respiratory Disorders	Treatment of radiation-induced pneumonitis		
European Union	Registered - 2011	Roche	Esbriet	Idiopathic pulmonary fibrosis	Treatment of mild to moderate idiopathic pulmonary fibrosis in adults	oral	Capsules 267 mg; Tablets, 267, 534 and 801 mg
France	Launched - 2012	Roche	Esbriet	Idiopathic pulmonary fibrosis	Treatment of mild to moderate	oral	Capsules

里程碑事件

Product Milestone History

Milestone Date	Milestone	Brand Name	Condition	Notes	Organization	Country/Area
Aug, 2017	Launched	Esbriet	Idiopathic pulmonary fibrosis	Treatment of mild to moderate idiopathic pulmonary fibrosis (IPF); Tablets, 267 mg	Roche	United Kingdom
Jun, 2017	MAA Approved	Esbriet	Idiopathic pulmonary fibrosis	Treatment of mild to moderate idiopathic pulmonary fibrosis in adults; Tablets 267, 534 and 801 mg	Roche	European Union
Mar, 2017	Phase II		Heart failure	In patients aged 40 years or older with heart failure and preserved left ventricular ejection fraction (HFpEF); Capsules	Roche	United Kingdom
2017	sNDA Approved	Esbriet	Idiopathic pulmonary fibrosis	Treatment of adult patients with idiopathic pulmonary fibrosis; Tablets, 267 mg of pirfenidone	Roche	United States
Dec, 2016	Phase II		Idiopathic pulmonary fibrosis	Treatment of patients with idiopathic pulmonary fibrosis and intermediate or high probability of group 3 pulmonary hypertension, in combination with sildenafil; Oral	Roche	

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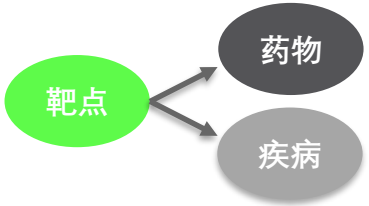
全面了解特定靶点信息



THOMSON REUTERS Integrity℠ Targets & Pathways

Records Retrieved | Records 1 to 2 of 2 retrieved | Options

Targets & Pathways Search Results

Query > Name = BTK

Target Name	Type	Major Conditio
Tyrosine-protein kinase BTK (isoform 1)	Protein	Major Condition Dermatological D Musculoskeletal Pain Renal Disorders Cardiovascular D Neurological Dis Gastrointestinal Eye Disorders Hematologic Dis Immunological D Respiratory Disc Endocrine Disor Infections Metabolic Diseas Cancer Other disorders
Tyrosine-protein kinase BTK (isoform 3)	Protein	Major Condition Dermatological D Musculoskeletal Pain Renal Disorders Cardiovascular D Neurological Dis Gastrointestinal Eye Disorders Hematologic Dis Immunological D Respiratory Disc Endocrine Disor Infections Metabolic Diseas Cancer Other disorders

Records Retrieved | 1 Record retrieved | Options

Targets & Pathways Search Results

Tyrosine-protein kinase BTK (isoform 1)

Last Updated Date	May 08, 2018
Type	Protein
Related Names	AGMX1; AT; ATK; Agammaglobulinaemia tyrosine kinase; B-cell progenitor kinase; BPK; BTK; Bruton Tyrosine Kinase (BTK); Bruton agammaglobulinemia tyrosine kinase; Bruton tyrosine kina variant 1; Dominant-negative kinase-deficient Brutons tyrosine kinase; IMD1; MGC126261; MGC126262; OTTHUMP00000023676; OTTHUMP00000063593; PSCTK1; Tyrosine-protein kinase BT
EC	2.7.10.2
Links	UniProtKB: Q06187 PDB: 1AWW, 1AWX, 1B55, 1BTK, 1BWN, 1K2P, 1QLY, 2GE9, 2Z0P
MetaCore	BTK, Bruton agammaglobulinemia tyrosine kinase
Description/Function	BTK is a non-receptor tyrosine kinase (EC 2.7.10.2) that is essential for B lymphocyte development and maturation. It mediates signal transduction initiated by the B cell receptor and IL-5 rece regulator of apoptosis. BTK inhibitors bind to and inhibit BTK activity, preventing B-cell activation and B-cell-mediated signaling. Thus, growth of malignant B cells that are overexpressed in a r
Targetscape	**Cancer** Colorectal Cancer Targetscape Non-Hodgkin Lymphoma (NHL) T-Cell Targetscape Bladder Cancer Targetscape Myelodysplasia Targetscape Glioblastoma Targetscape Pancreatic Cancer Targetscape **Dermatological Disorders** Skin Allergy Targetscape Urticaria & Angioedema Targetscape Pemphigus Targetscape **Immunological Disorders** Graft-versus-Host Disease (GVHD) Targetscape **Musculoskeletal and Connective Tissue Disorders** Rheumatoid Arthritis Targetscape 1 (Intercellular Crosstalk) **Other disorders (Systemic disorders)** Obesity Targetscape
Scientific Animations	Mast Cell Activation and Degranulation in Allergic and Inflammatory Responses
Condition (Status)	Collapse All / Expand All Cancer V (View Drugs) Cardiovascular Disorders E (View Drugs) Dermatological Disorders Endocrine Disorders E (View Drugs) Eye Disorders Gastrointestinal Disorders V 68 Conditions C 13 Conditions E 44 Conditions

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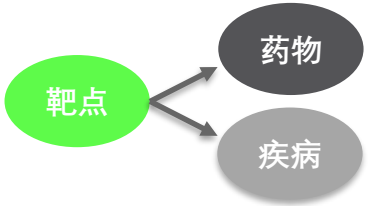
靶点-疾病关联信息

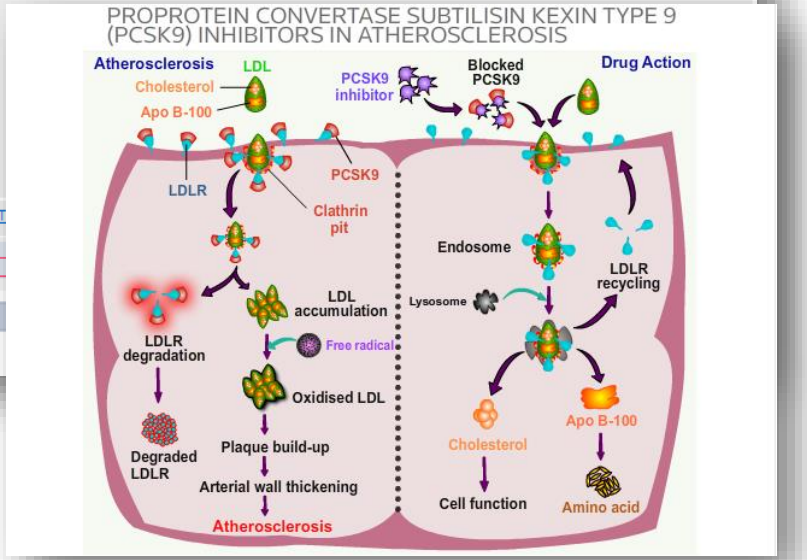


Proprotein convertase subtilisin/kexin type 9

Type	Protein
Related Names	FH3; HCHOLA3; Hypercholesterolemia autosomal dominant 3; LDLCQ1; NARC-1; NARC1; Neural apoptosis regulated convertase 1; PC9; PCSK9; Proprotein convertase PC9
Links	UniProtKB: Q8NBP7
MetaCore	PCSK9, proprotein convertase subtilisin/kexin type 9
Description/Function	PC9 is a secreted enzyme belonging to the peptidase S8 family. It is involved in cholesterol homeostasis by reducing the cellular uptake of plasma low-density lipoprotein (LDL) cholesterol. Inhibiting this protein may be effective in the treatment of lipoprotein disorders including atherosclerosis. It is also involved in the differentiation of cortical neurons and in regeneration of the liver.
Targetscape	Cardiovascular Disorders: Acute Coronary Syndrome (ACS) Targetscape; Metabolic Diseases: Dyslipidemia Targetscape
Scientific Animations	Proprotein Convertase Subtilisin Kexin Type 9 (PCSK9) Inhibitors in Atherosclerosis
Condition (Status)	Collapse All / Expand All; Cardiovascular Disorders (View Drugs); Diagnostics (View Drugs); Endocrine Disorders; Hematologic Diseases; Metabolic Diseases (View Drugs); Neurological Disorders; Other disorders (Systemic disorders); Renal Disorders; V 6 Conditions; C 2 Conditions; E 13 Conditions
Related Mechanisms	Anti-PCSK9 (Proprotein Convertase Subtilisin/Kexin-Type 9); Proprotein Convertase Subtilisin/Kexin-T
Products Under Development and Launched	Cardiovascular Disorders; Metabolic Diseases

Related Information

Drugs & Biologics 70 | Biomarkers 4 | Targets & Pathways 2 | Genomics 1 | Literature 14 | Patents 2 | Experimental Pharmacology 43 | Experimental Models 1



- 进一步了解病因：靶点-疾病关联
- 明确靶点干预产生的结果
- 建立用于研究验证的靶点-疾病治疗假说，指导开展实验

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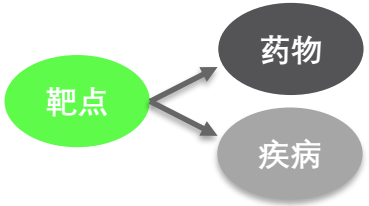
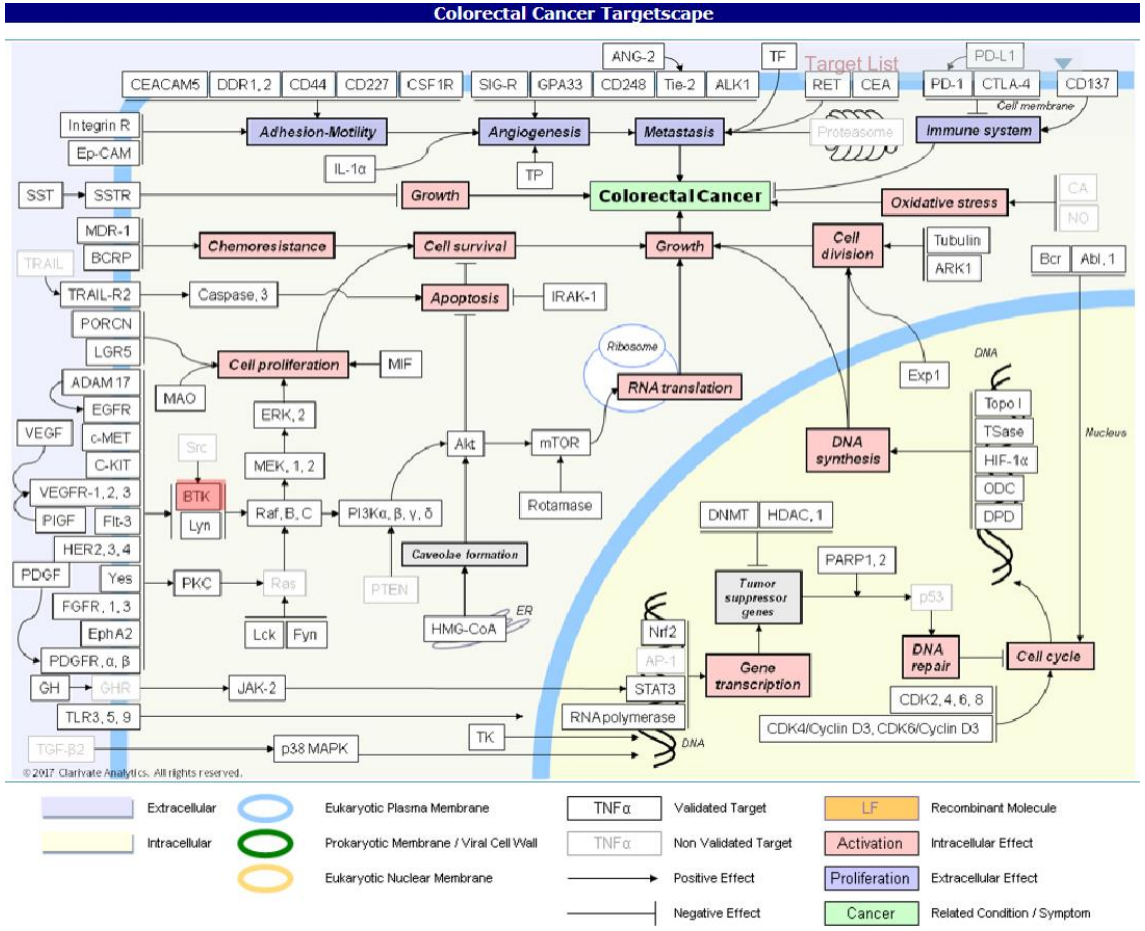
疾病靶点概览揭示与疾病进程相关的生理/病理过程





疾病进程相关的生理/病理过程

- 靶点直接相关的过程与临床终点的联系
- 靶点和不同治疗假说的联系
- 靶点的分布和定位差异，来自其他靶点的间接竞争
- 配合已知药物和指南明确现有药物的治疗方向

疾病涉及的器官组织，细胞类型

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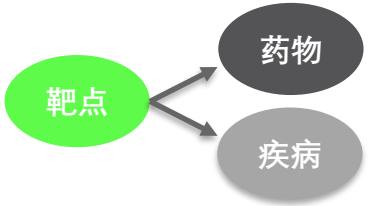
了解特定靶点对应的治疗药物情况



Proprotein convertase subtilisin/kexin type 9

Last Updated Date	Feb 24, 2017
Type	Protein
Related Names	FH3; HCHOLA3; Hypercholesterolemia autosomal dominant 3; LDLCQ1; NARC-1; NARC1; Neural apoptosis regulated convertase 1; PC9; PCSK9; Proprotein convertase PC9
Links	UniProtKB: Q8NBP7
MetaCore	PCSK9, proprotein convertase subtilisin/kexin type 9
Description/Function	PC9 is a secreted enzyme belonging to the peptidase S8 family. It is involved in cholesterol homeostasis by reducing the cellular uptake of plasma low-density lipoprotein (LDL) cholesterol. Inhibiting this protein may be effective in the treatment of lipoprotein disorders including atherosclerosis. It is also involved in the differentiation of cortical neurons and in regeneration of the liver.
Targetscape	**Cardiovascular Disorders**: Atherosclerosis Targetscape; Acute Coronary Syndrome (ACS) Targetscape. **Metabolic Diseases**: Dyslipidemia Targetscape
Scientific Animations	PCSK9 Inhibition; Proprotein Convertase Subtilisin Kexin Type 9 (PCSK9) Inhibitors in Atherosclerosis
Condition (Status)	Collapse All / Expand All; Cancer E (View Drugs); Cardiovascular Disorders V (View Drugs); Critical care medicine; Diagnostics E (View Drugs); Endocrine Disorders; Hematologic Diseases; Metabolic Diseases E (View Drugs); Neurological Disorders; Other disorders (Systemic disorders); Renal Disorders. V 10 Conditions; C 1 Conditions; E 15 Conditions
Related Mechanisms	Anti-PCSK9 (Proprotein Convertase Subtilisin/Kexin-Type 9); Proprotein Convertase Subtilisin/Kexin-Type 9 (PCSK9) Inhibitors; Proprotein Convertase Subtilisin/Kexin-Type 9 (PCSK9) Translation Inhibitors
Products Under Development and Launched	Cardiovascular Disorders; Endocrine Disorders; Metabolic Diseases

Related Information

Drugs & Biologics 100	Biomarkers 4	Targets & Pathways 2	Genomics 1	Literature 15	Patents 2	Experimental Pharmacology 70	Experimental Models 1

靶点相关药物纵览
•在研及上市的重点药物

Cardiovascular Disorders

EN	Drug Name	Mechanism of Action	Organization	Phases
661832	Evolocumab	Anti-PCSK9 (Proprotein Convertase Subtilisin/Kexin-Type 9)	Amgen	Pre-Registered

Arterial disease
Arteriosclerosis
Atherosclerosis

EN	Drug Name	Mechanism of Action	Organization	Phases
661832	Evolocumab	Anti-PCSK9 (Proprotein Convertase Subtilisin/Kexin-Type 9)	Amgen	Phase III
896528	AT-04A	Anti-PCSK9 (Proprotein Convertase Subtilisin/Kexin-Type 9)	AFFiRiS	Phase I
896536	AT-06A	Anti-PCSK9 (Proprotein Convertase Subtilisin/Kexin-Type 9)	AFFiRiS	Phase I

Coronary heart disease

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细节决定成败

多角度对比分析、最大程度挖掘和应用研究信息

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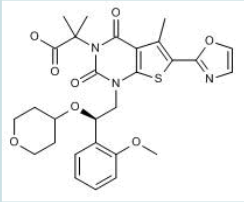
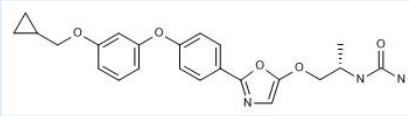
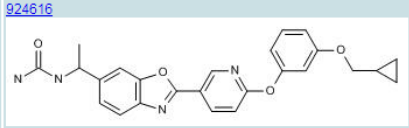
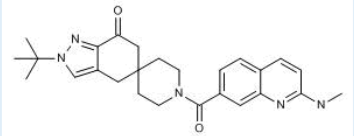
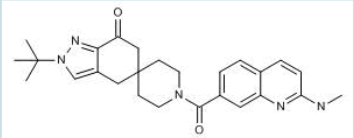
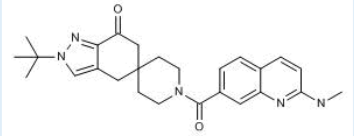
全面汇总药物专利信息，巧妙分析对比

Patents (Applicants)	Title	Subject Matter	Condition	Lead Compound
US 2017267690 WO 2017151816 * (Nimbus Apollo, Inc.)	Solid forms of a thienopyrimidinedione ACC inhibitor and methods for production thereof	Drug Substances Polymorphs	Acne vulgaris Non-alcoholic steatohepatitis	NDI-630 
WO 2016159049 * (Takeda Pharmaceutical Co., Ltd.)	Monocyclic compound	Drug Substances	Cancer Fibrosis, hepatic Hepatic steatosis	935977 
WO 2016084816 * EP 3225618 CN 107207444 (Takeda Pharmaceutical Co., Ltd.)	Bicyclic compound	Drug Substances	Cancer Non-alcoholic steatohepatitis	924616 
US 2015336958 * (Pfizer Inc.)	Substituted acetyl-CoA carboxylase inhibitors	Drug Substances	Diabetes type 2 Insulin resistance Non-alcoholic fatty liver disease (NAFLD) Obesity	792943 
US 2015112068 * (Pfizer Inc.)	Substituted acetyl-CoA carboxylase inhibitors	Drug Substances	Diabetes Insulin resistance Non-alcoholic fatty liver disease (NAFLD)	792943 
US 2014323730 * (Pfizer Inc.)	Substituted acetyl-CoA carboxylase inhibitors	Drug Substances	Diabetes type 2 Insulin resistance Non-alcoholic fatty liver disease (NAFLD)	792943 

- WO EU US CN JP KR IN
- 快速比较不同专利中的典型化合物结构
- 分析不同专利间的关联程度及参考关系
- 利用关联检索，获取专利化合物活性数据
- 专利报告：公司/药物链接; 专利PDF文档

Title

Imidazole and indole-based IDO1 inhibitors, preparation method and application thereof

Applicant	Inventor
China Pharmaceutical University (Nanjing [CN]) Nanjing University (NJU) (Nanjing [CN])	Lai, Y. Sun, Q. Zou, Y. Xu, Q. Guo, W. Wang, Y. Wang, F. Li, Y.

Patent Number	Publication Date	Legal Status Links	Priority Data	Priority Date
CN 107501272 *	Dec 22, 2017	INPADOC	2017 CN 10798280	Sep 5, 2017

Last Updated Date

Jan 26, 2018

Subject Matter	Conditions
Drug Substances	Autoimmune disease Cancer Cataract Depression Infection, viral Neurodegeneration Transplant rejection

Original Abstract

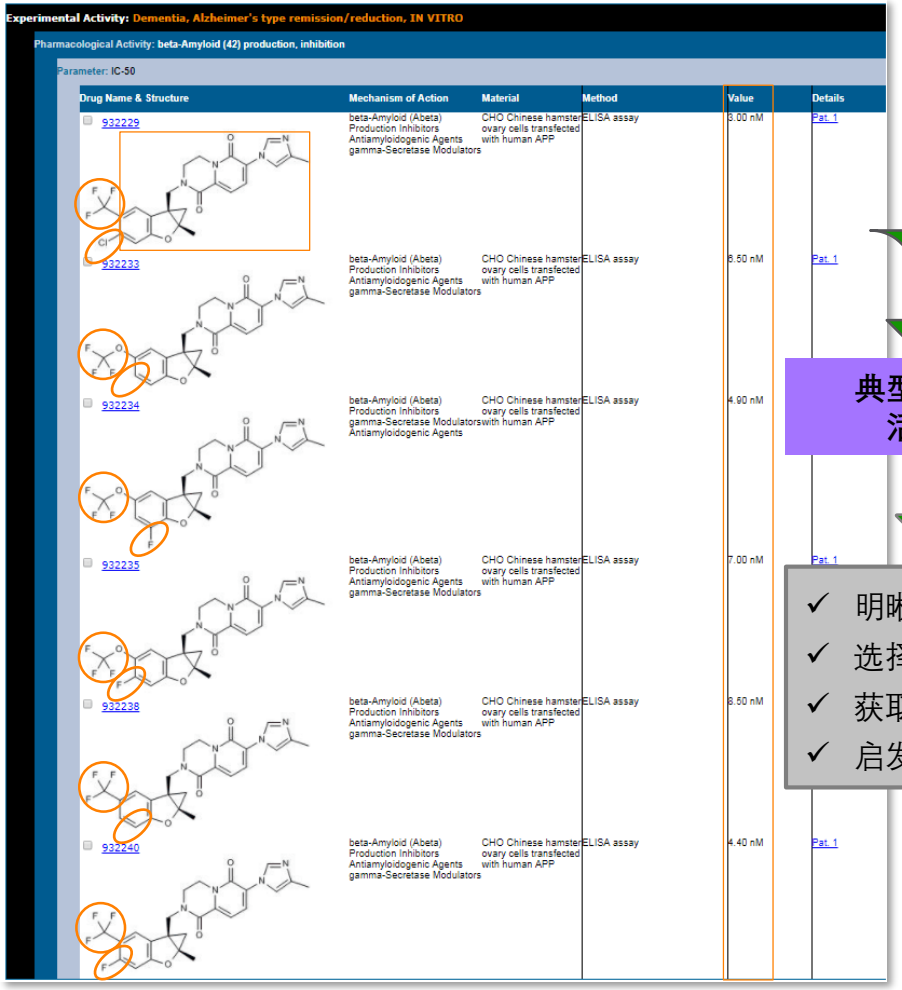
This invention belongs to pharmaceutical field, specifically claims a imidazole with formula (I) structure and the indole compound, its stereoisomer, or a pharmaceutically acceptable salt thereof, processes for their preparation, and their use as indoleamine 2, 3-dioxygenase 1 (IDO1) inhibitor. the experiment result shows that the compound of the invention has obvious inhibiting effect to activity of IDO1, can effectively promote T cell proliferation, inhibiting the initial differentiation of T cells into regulatory T cells, reverse IDO1 mediated immunosuppression. can be used for treating a disease associated with IDO1 mediated by kynurenine metabolic pathway pathological characteristics, including cancer, viral infections, neurodegenerative disorders, cataracts, organ transplant rejection, depression and autoimmune diseases.

Related Information

Drugs & Biologics 2 | Companies & Research Institutions 2

Clarivate Analytics

典型化合物与活性对照数据，启发化合物设计思路



Experimental Activity: Dementia, Alzheimer's type remission/reduction, IN VITRO

Pharmacological Activity: beta-Amyloid (42) production, inhibition

Parameter: IC-50

Drug Name & Structure	Mechanism of Action	Material	Method	Value	Details
932229	beta-Amyloid (Abeta) Production Inhibitors, Antiamyloidogenic Agents, gamma-Secretase Modulators	CHO Chinese hamster ovary cells transfected with human APP	ELISA assay	3.00 nM	Pat. 1
932233	beta-Amyloid (Abeta) Production Inhibitors, Antiamyloidogenic Agents, gamma-Secretase Modulators	CHO Chinese hamster ovary cells transfected with human APP	ELISA assay	6.50 nM	Pat. 1
932234	beta-Amyloid (Abeta) Production Inhibitors, gamma-Secretase Modulators, Antiamyloidogenic Agents	CHO Chinese hamster ovary cells transfected with human APP	ELISA assay	4.90 nM	
932235	beta-Amyloid (Abeta) Production Inhibitors, Antiamyloidogenic Agents, gamma-Secretase Modulators	CHO Chinese hamster ovary cells transfected with human APP	ELISA assay	7.00 nM	Pat. 1
932238	beta-Amyloid (Abeta) Production Inhibitors, Antiamyloidogenic Agents, gamma-Secretase Modulators	CHO Chinese hamster ovary cells transfected with human APP	ELISA assay	6.50 nM	
932240	beta-Amyloid (Abeta) Production Inhibitors, Antiamyloidogenic Agents, gamma-Secretase Modulators	CHO Chinese hamster ovary cells transfected with human APP	ELISA assay	4.40 nM	Pat. 1

典型化合物的活性数据

- ✓ 明晰目标化合物活性（体内/体外）
- ✓ 选择参考化合物
- ✓ 获取核心参考专利文献
- ✓ 启发化合物设计思路

- 利用关联检索，获取专利化合物活性数据
- 比较不同专利间化合物活性的活性，比较整体结构差异
- 比较同一专利内不同取代修饰对活性的影响
- 提供起始化合物设计思路，选取合适的参考化合物

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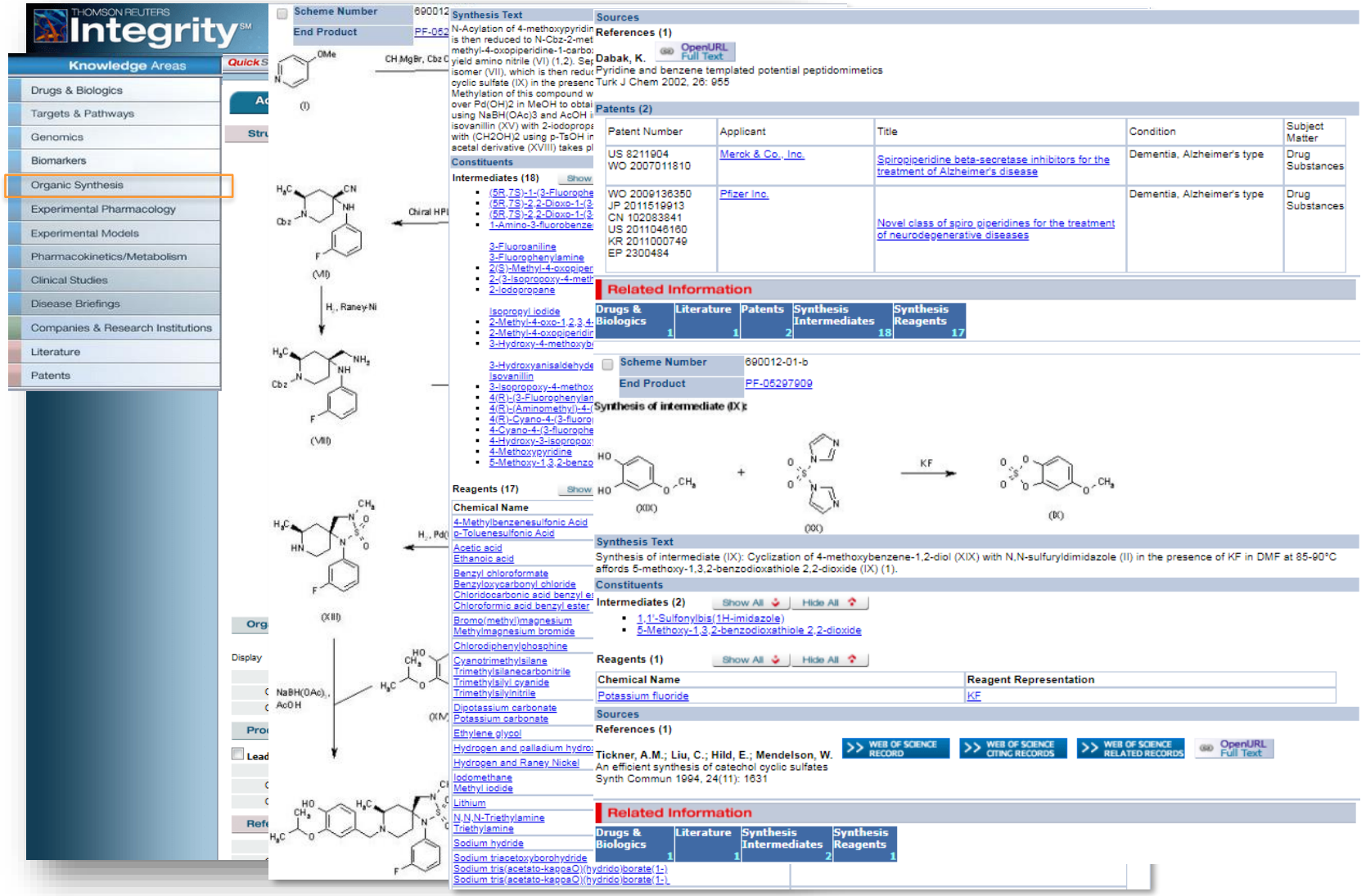
提供合成路线参考，由终产物反推中间体及试剂



- 支持结构检索
  - 次级结构检索
  - 相似度检索
- 合成路线
  - 终产物
  - 中间体
  - 试剂

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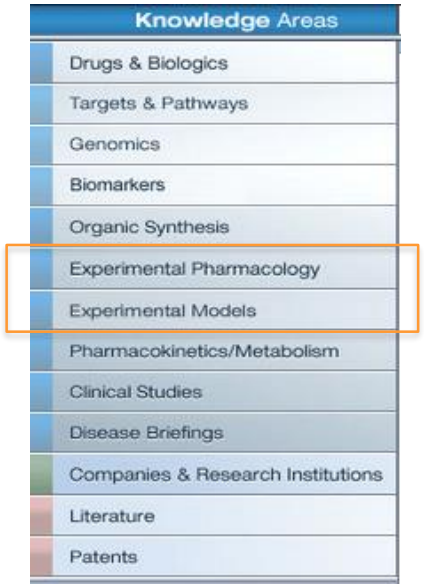
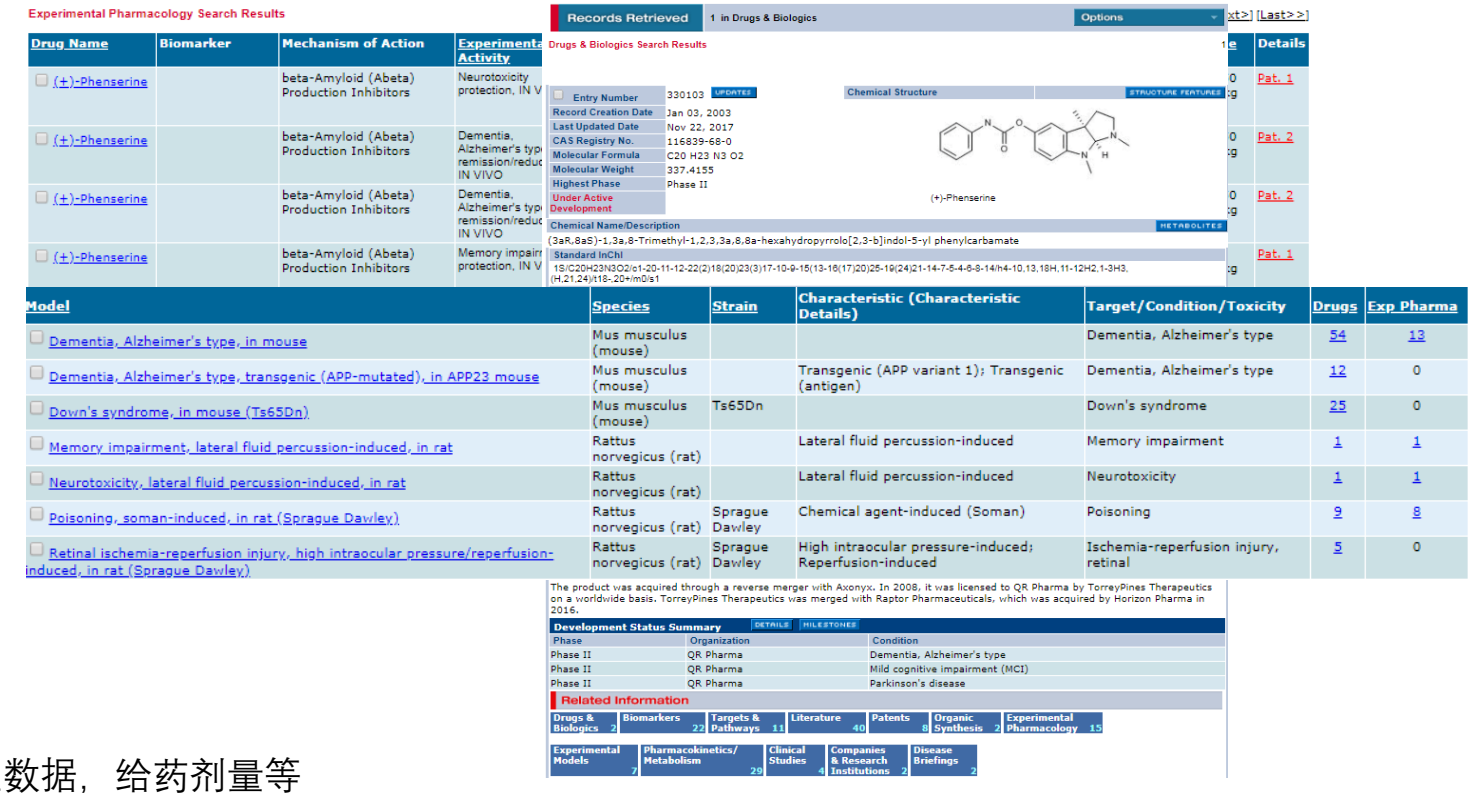
汇总、整理药理数据和实验模型





从靶点、化合物出发：

- 明确已知分子的活性数据，给药剂量等
- 挑选合适的体外/体内实验模型和方法
- 原始文献/专利引用出处

依据研发能力提前规划，缩短研发周期，评估研发风险

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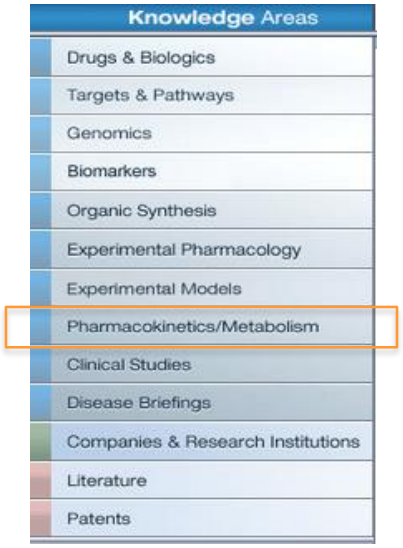
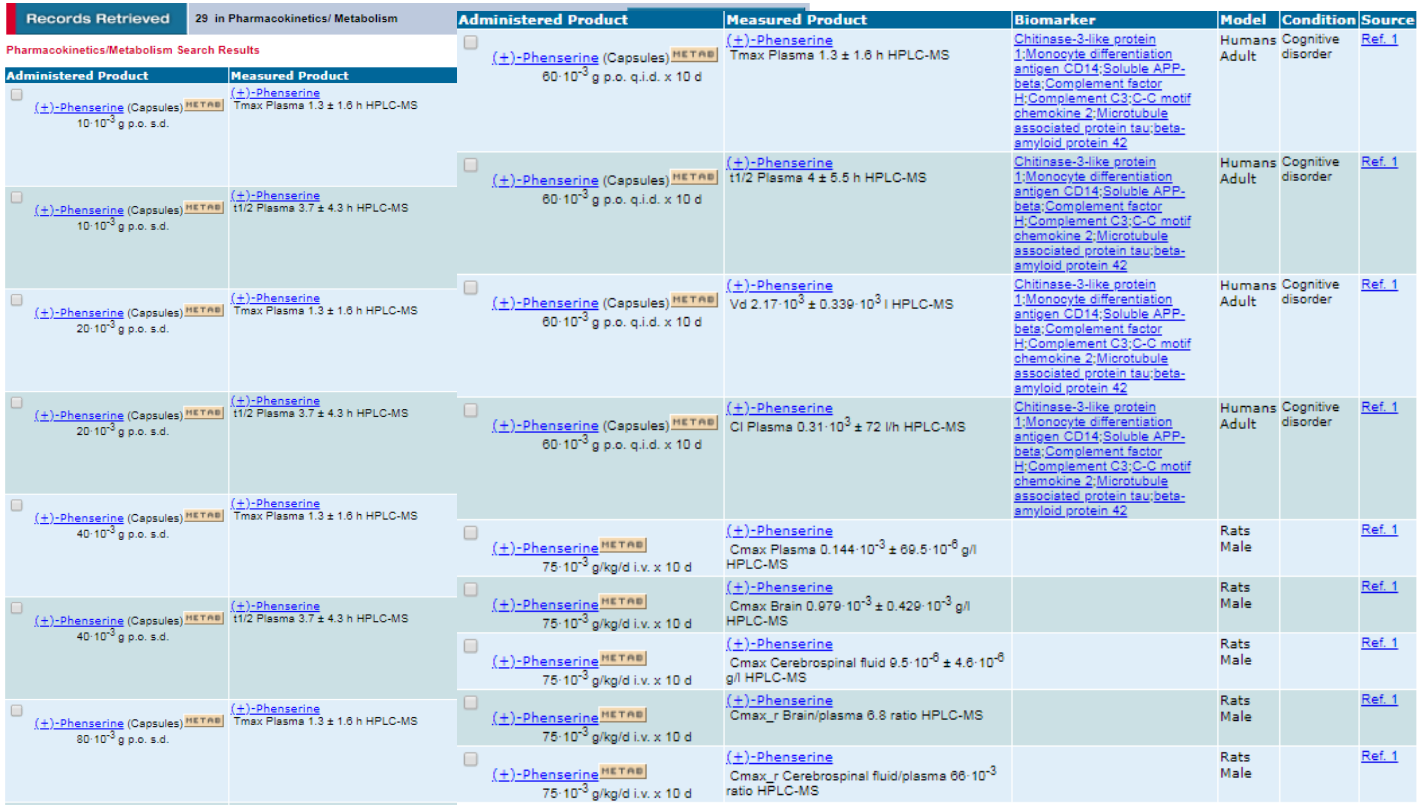
汇总药动和代谢数据，便于分析





Records Retrieved 29 in Pharmacokinetics/ Metabolism

Pharmacokinetics/Metabolism Search Results

Administered Product	Measured Product
(±)-Phenserine (Capsules) METAB $10 \cdot 10^{-3}$ g p.o. s.d.	(±)-Phenserine Tmax Plasma 1.3 ± 1.6 h HPLC-MS
(±)-Phenserine (Capsules) METAB $10 \cdot 10^{-3}$ g p.o. s.d.	(±)-Phenserine t1/2 Plasma 3.7 ± 4.3 h HPLC-MS
(±)-Phenserine (Capsules) METAB $20 \cdot 10^{-3}$ g p.o. s.d.	(±)-Phenserine Tmax Plasma 1.3 ± 1.6 h HPLC-MS
(±)-Phenserine (Capsules) METAB $20 \cdot 10^{-3}$ g p.o. s.d.	(±)-Phenserine t1/2 Plasma 3.7 ± 4.3 h HPLC-MS
(±)-Phenserine (Capsules) METAB $40 \cdot 10^{-3}$ g p.o. s.d.	(±)-Phenserine Tmax Plasma 1.3 ± 1.6 h HPLC-MS
(±)-Phenserine (Capsules) METAB $40 \cdot 10^{-3}$ g p.o. s.d.	(±)-Phenserine t1/2 Plasma 3.7 ± 4.3 h HPLC-MS
(±)-Phenserine (Capsules) METAB $80 \cdot 10^{-3}$ g p.o. s.d.	(±)-Phenserine Tmax Plasma 1.3 ± 1.6 h HPLC-MS

Administered Product	Measured Product	Biomarker	Model	Condition	Source
(±)-Phenserine (Capsules) METAB $60 \cdot 10^{-3}$ g p.o. q.i.d. x 10 d	(±)-Phenserine Tmax Plasma 1.3 ± 1.6 h HPLC-MS	Chitinase-3-like protein 1;Monocyte differentiation antigen CD14;Soluble APP-beta;Complement factor H;Complement C3;C-C motif chemokine 2;Microtubule associated protein tau;beta-amyloid protein 42	Humans Adult	Cognitive disorder	Ref. 1
(±)-Phenserine (Capsules) METAB $60 \cdot 10^{-3}$ g p.o. q.i.d. x 10 d	(±)-Phenserine t1/2 Plasma 4 ± 5.5 h HPLC-MS	Chitinase-3-like protein 1;Monocyte differentiation antigen CD14;Soluble APP-beta;Complement factor H;Complement C3;C-C motif chemokine 2;Microtubule associated protein tau;beta-amyloid protein 42	Humans Adult	Cognitive disorder	Ref. 1
(±)-Phenserine (Capsules) METAB $60 \cdot 10^{-3}$ g p.o. q.i.d. x 10 d	(±)-Phenserine Vd $2.17 \cdot 10^{3} \pm 0.339 \cdot 10^{3}$ l HPLC-MS	Chitinase-3-like protein 1;Monocyte differentiation antigen CD14;Soluble APP-beta;Complement factor H;Complement C3;C-C motif chemokine 2;Microtubule associated protein tau;beta-amyloid protein 42	Humans Adult	Cognitive disorder	Ref. 1
(±)-Phenserine (Capsules) METAB $60 \cdot 10^{-3}$ g p.o. q.i.d. x 10 d	(±)-Phenserine Cl Plasma $0.31 \cdot 10^{3} \pm 72$ l/h HPLC-MS	Chitinase-3-like protein 1;Monocyte differentiation antigen CD14;Soluble APP-beta;Complement factor H;Complement C3;C-C motif chemokine 2;Microtubule associated protein tau;beta-amyloid protein 42	Humans Adult	Cognitive disorder	Ref. 1
(±)-Phenserine METAB $75 \cdot 10^{-3}$ g/kg/d i.v. x 10 d	(±)-Phenserine Cmax Plasma $0.144 \cdot 10^{-3} \pm 69.5 \cdot 10^{-6}$ g/l HPLC-MS		Rats Male		Ref. 1
(±)-Phenserine METAB $75 \cdot 10^{-3}$ g/kg/d i.v. x 10 d	(±)-Phenserine Cmax Brain $0.979 \cdot 10^{-3} \pm 0.429 \cdot 10^{-3}$ g/l HPLC-MS		Rats Male		Ref. 1
(±)-Phenserine METAB $75 \cdot 10^{-3}$ g/kg/d i.v. x 10 d	(±)-Phenserine Cmax Cerebrospinal fluid $9.5 \cdot 10^{-6} \pm 4.6 \cdot 10^{-6}$ g/l HPLC-MS		Rats Male		Ref. 1
(±)-Phenserine METAB $75 \cdot 10^{-3}$ g/kg/d i.v. x 10 d	(±)-Phenserine Cmax_r Brain/plasma 6.8 ratio HPLC-MS		Rats Male		Ref. 1
(±)-Phenserine METAB $75 \cdot 10^{-3}$ g/kg/d i.v. x 10 d	(±)-Phenserine Cmax_r Cerebrospinal fluid/plasma $66 \cdot 10^{-3}$ ratio HPLC-MS		Rats Male		Ref. 1

- 了解在研化合物的药动、代谢数据
- 通过高级检索快速查找特殊类型的DMPK数据，明确化合物标准
- 从数据分析推断竞品的PK-PD关系

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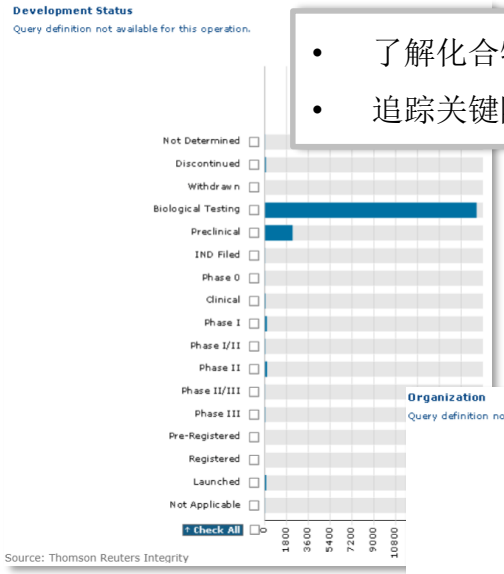
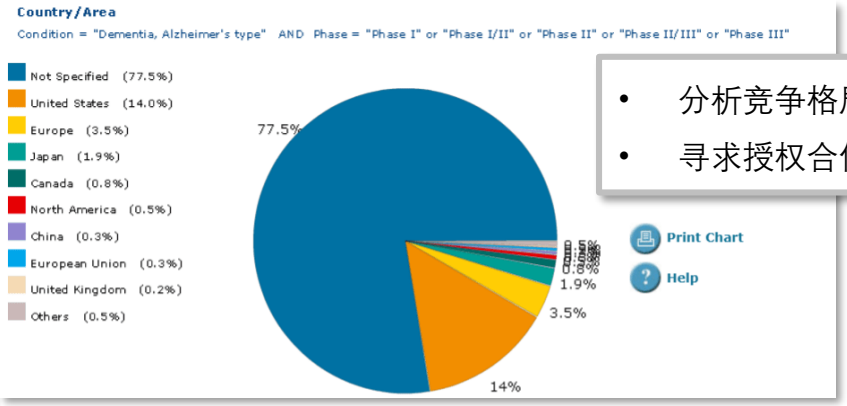
治疗药物产品管线分析

研发阶段



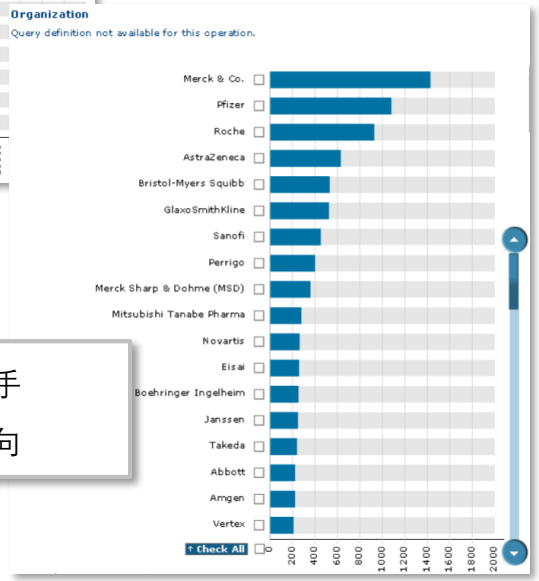
- 了解化合物研发阶段分布
- 追踪关键阶段化合物进展

国家/地区



- 分析竞争格局
- 寻求授权合作机会

研发公司



- 了解主要的竞争对手
- 选择合适的竞争方向

药物靶点

- 了解热门靶点
- 单个靶点的化合物集中比较
- 靶点前景预测
- 深入探索单个靶点

- 了解疾病相关在研药物研究的竞争格局，选择合适的切入时机，提前布局

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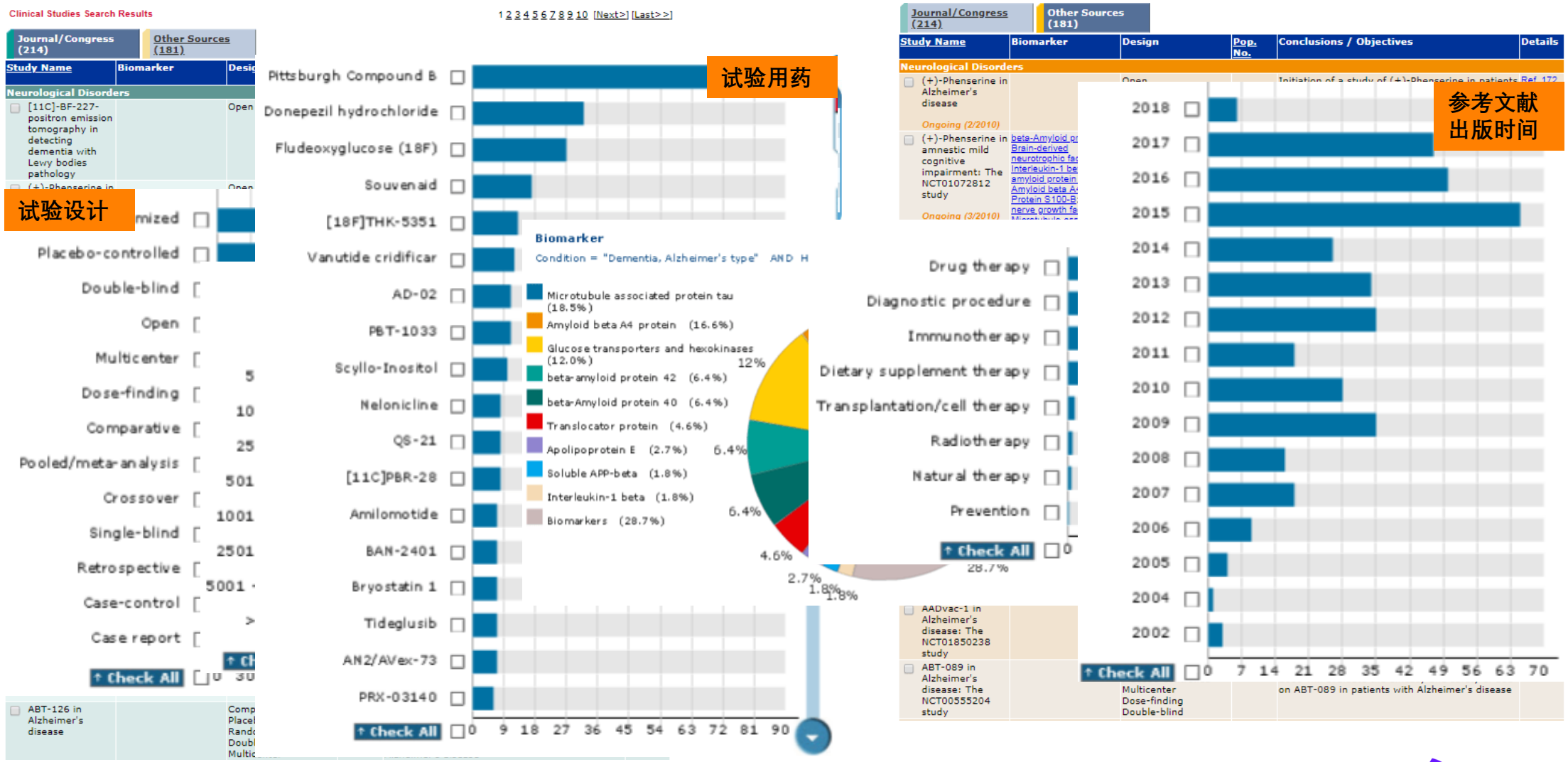
临床试验：支持未上市药物临床试验情况检索



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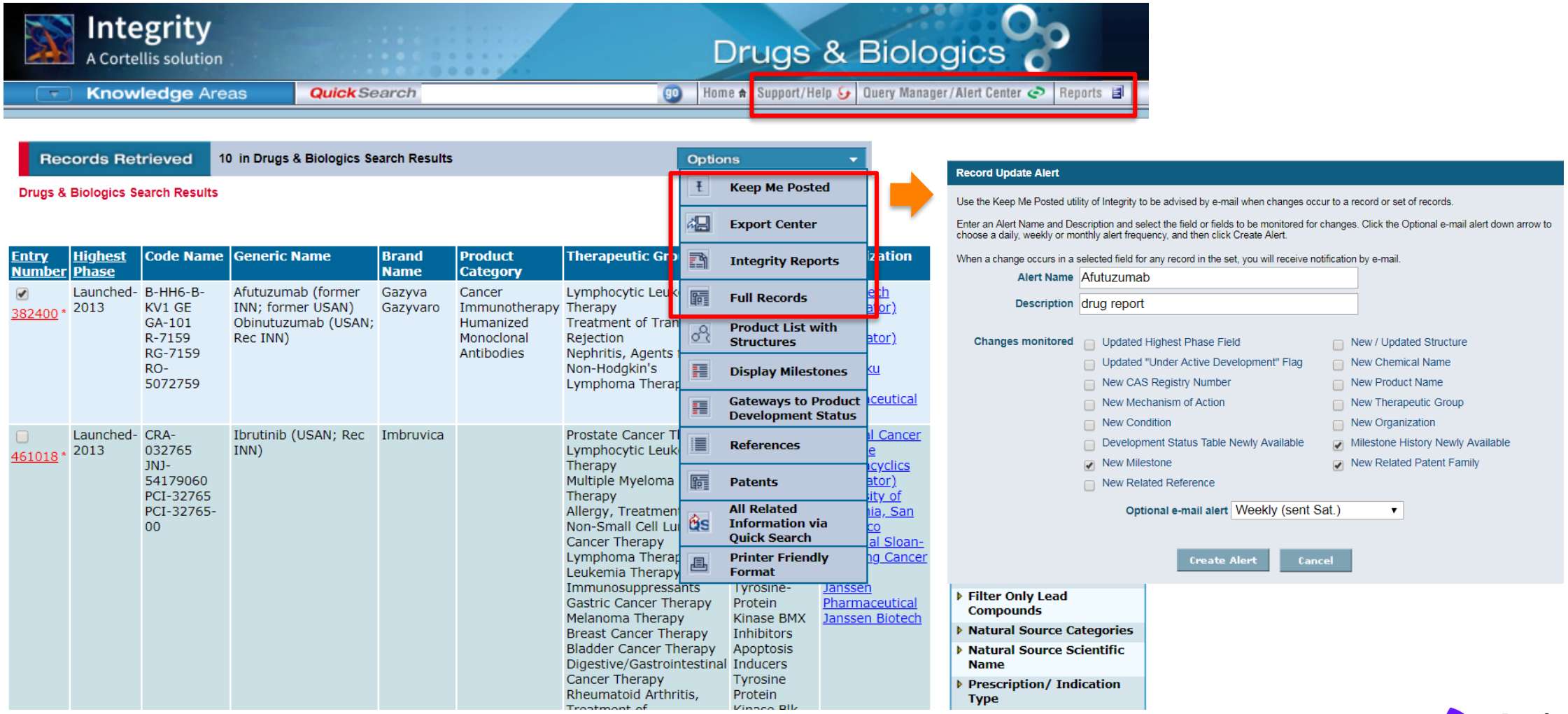
更新提醒（Alert）与报告导出



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03 科研案例

ReFRAME 药物再定位

药物再定位被证明是一种成功的策略在广泛的领域中应用

Drug	Innovator	Mechanism	Original Indication	Repurposed Indication
Gemcitabine	Eli Lilly	Inhibition of DNA synthesis	Antiviral	Anticancer
Raloxifene	Eli Lilly	Estrogen agonist/antagonist	Breast cancer	Osteoporosis
Buproprion	GSK	Norepinephrine–dopamine reuptake inhibitor	Depression	Smoking cessation
Dapoxetine	Eli Lilly	Selective serotonin reuptake inhibitor SSRI	Analgesia	Premature ejaculation
Fluoxetine	Eli Lilly	SSRI	Depression	Premenstrual dysphoria
Hydroxychloroquine	Sanofi	Lysosomal alkalinization; TLR inhibitor	Antiparasitic	Antiarthritic
Doxepin	Boehringer Mannheim (Roche)	Serotonin–norepinephrine reuptake inhibitor (SNRI)	Antidepressant	Antipruritic
Bimatoprost	Allergan	Prostaglandin analog	Glaucoma	Eyelash growth

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加利福尼亚医学研究中心：ReFRAME和PNAS

PNAS Proceedings of the National Academy of Sciences of the United States of America

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NEW RESEARCH IN Physical Sciences | Social Sciences

The ReFRAME library as a comprehensive drug repurposing library and its application to the treatment of cryptosporidiosis

Jeff Janes, Megan E. Young, Emily Chen, Nicole H. Rogers, Sebastian Burgstaller-Muehlbacher, Laura D. Hughes, Melissa S. Love, Mitchell V. Hull, Kelli L. Kuhen, Ashley K. Woods, Sean B. Joseph, H. Michael Petrassi, Case W. McNamara, Matthew S. Tremblay, Andrew I. Su, Peter G. Schultz, and Arnab K. Chatterjee

PNAS published ahead of print October 3, 2018 https://doi.org/10.1073/pnas.1810137115

Contributed by Peter G. Schultz, August 30, 2018 (sent for review June 14, 2018; reviewed by Nathanael S. Gray, John B. Hogenesch, and Peter S. Kim)

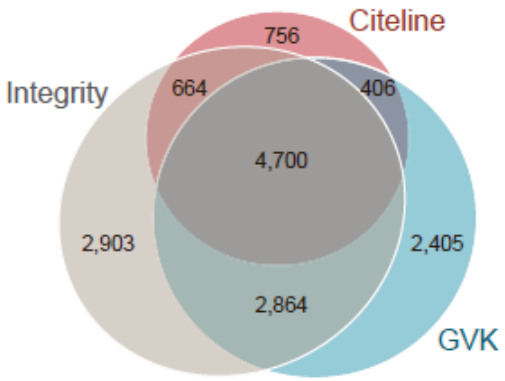


Fig. 1. Overlap of drug entries across all three primary data sources.

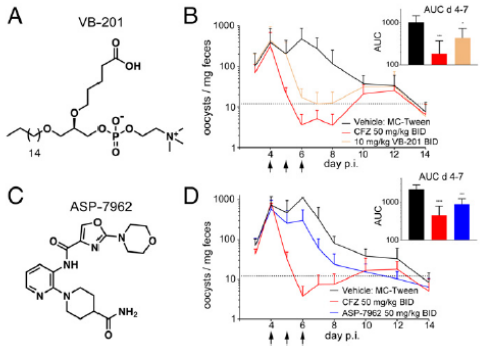
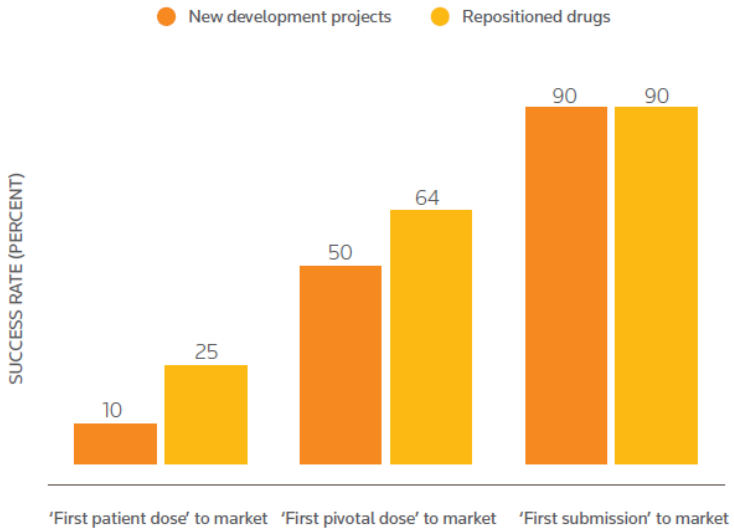


Fig. 3. ReFRAME library compounds with anticryptosporidial efficacy. (*A* and *C*) The structures of oxidized phospholipid VB-201 and TrkA inhibitor ASP-7962. ASP-7962 is a best-guess structure from a phase 2 trial. (*B* and *D*) Oocyst shedding trace of mice infected with 1×10^6 oocysts on day 0, then monitored for 2 wk. Line graph data are weight-adjusted mean oocyst counts ± SD ($n = 8$ over two separate experiments). (*B* and *D*, *Insets*) Bar graphs are oocyst counts ± SEM ($n = 4$) measured on day 7. These data were assessed with one-way ANOVA. Treatments were compared with the previously investigated compound clofazimine (CFZ) (50 mg/kg BID). AUC, area under the curve. $^*P < 0.05$; $^{***}P < 0.005$; $^{****}P < 0.001$.



1. 用科睿唯安部分Integrity数据跟加利福尼亚医学研究中心合作建立了一个小分子药物再利用库，名为 ReFRAME。
2. 通过ReFRAME，研究人员已经能够确定两种化合物，对可能危及生命的寄生虫（隐孢子虫属）有效。这项新研究的结果最近在美国国家科学院院刊PNAS上发表。
3. 同时科睿唯安从加利福尼亚医学研究中心拿到的数据也会加入到2019年的Integrity中。

CIRM CALIFORNIA'S STEM CELL AGENCY

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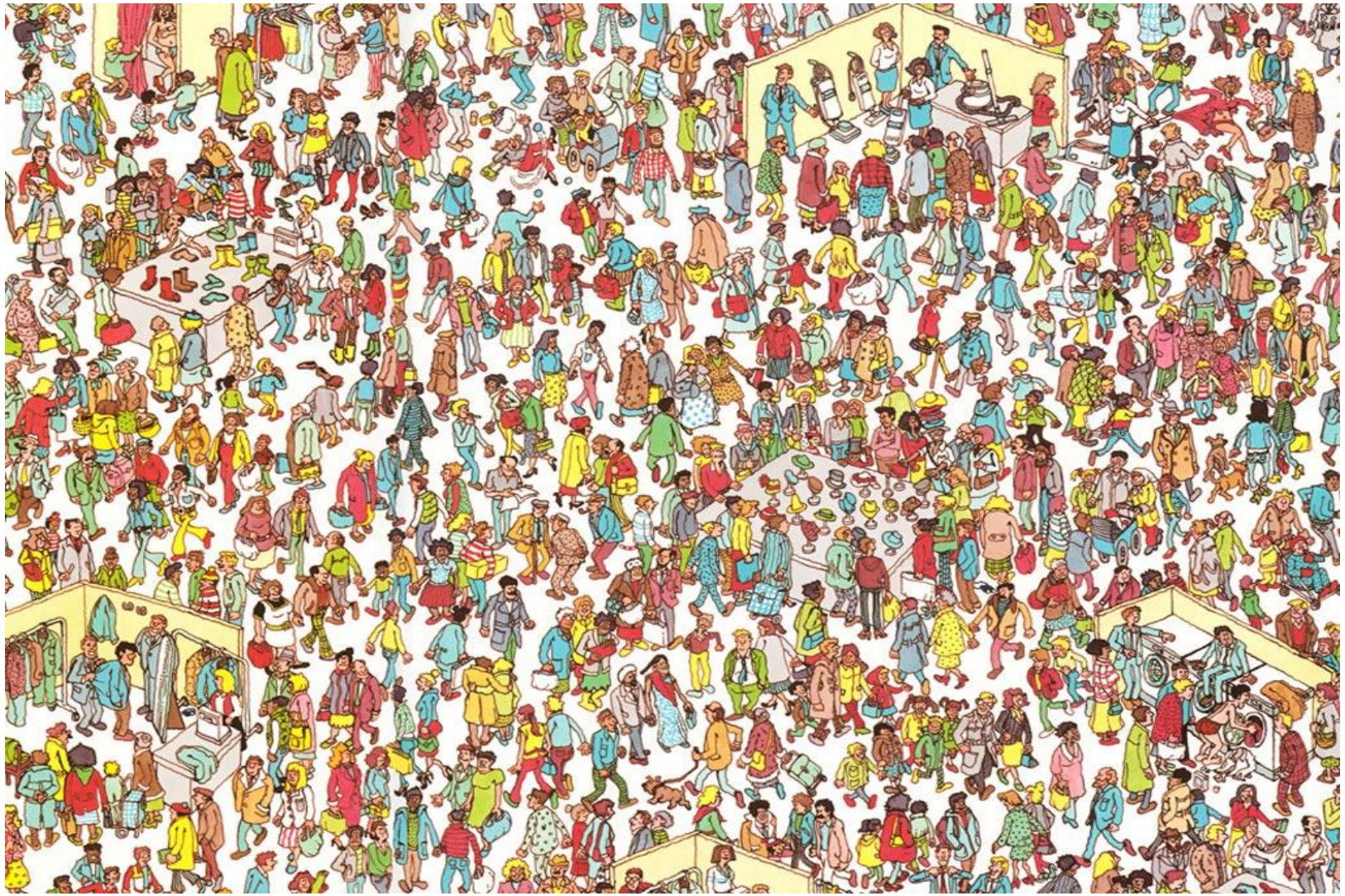
https://www.cirm.ca.gov/our-progress/institutions/california-institute-biomedical-research-0
https://www.scripps.edu/news-and-events/press-room/2018/20181003-reframe-calibr.html

人工智能训练集



Think of each person as a target....to identify whether this is a target that you wish to focus on you have to study each one...individually. In real terms that can mean **weeks of literature and patent reading**.

“我将于茫茫人海中访我唯一的灵魂伴侣，得之，我幸；不得，我命…” 徐志摩

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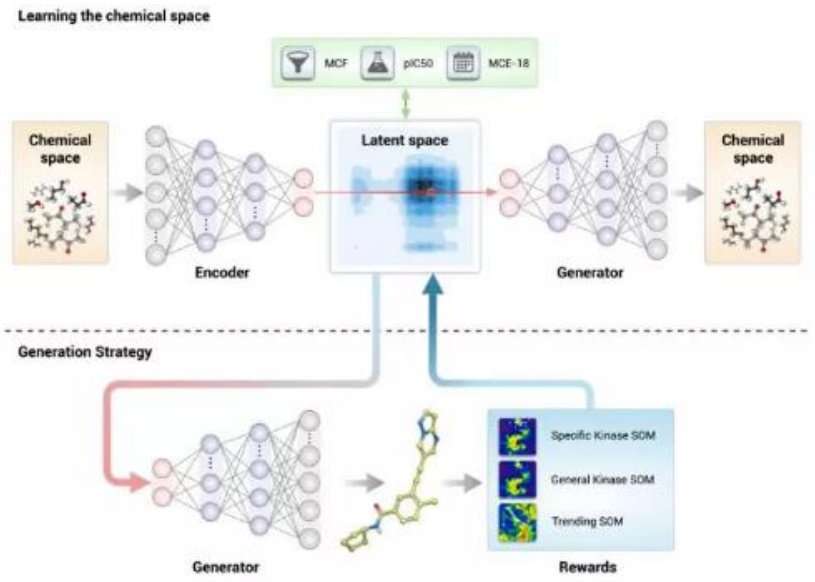
nature biotechnology

Brief Communication | Published: 02 September 2019

Deep learning enables rapid identification of potent DDR1 kinase inhibitors

Alex Zhavoronkov, Yan A. Ivanenkov, Alex Aliper, Mark S. Veselov, Vladimir A. Aladinskiy, Anastasiya V. Aladinskaya, Victor A. Terentiev, Daniil A. Polykovskiy, Maksim D. Kuznetsov, Arip Asadulaev, Yury Volkov, Artem Zholus, Rim R. Shayakhmetov, Alexander Zhebrak, Lidiya I. Minaeva, Bogdan A. Zagribelnyy, Lennart H. Lee, Richard Soll, David Madge, Li Xing, Tao Guo & Alán Aspuru-Guzik



本研究的算法示意图（上）以及采用的数据（下）

从选择一个靶点，到形成潜在的新药候选分子，这个过程需要多长的时间？过去的回答可能是数月，乃至数年。但在2019年今天，来自Insilico Medicine、药明康德、以及多伦多大学的科学家们在《自然》子刊*Nature Biotechnology*上给出了不同的答案。利用人工智能技术，将这一数字缩短到**21天**。

BRIEF COMMUNICATION

Methods

Pretraining data set. For the pretraining procedure, we have prepared a data set of structures using the Clean Leads set from the ZINC database[20] and proprietary databases from our partners. We have removed structures containing atoms other than carbon, nitrogen, oxygen, sulfur, fluorine, chlorine, bromine, and hydrogen. Routine medicinal chemistry filters were applied to exclude compounds with potentially toxic and reactive groups.

Kinase inhibitors and 'negative' data set. The data set of molecules that actively inhibit and do not inhibit various kinases was prepared using the data available in the Integrity and ChEMBL databases.

Alex Zhavoronkov et al., (2019), Deep learning enables rapid identification of potent DDR1 kinase inhibitors, Nature Biotechnology, DOI: https://doi.org/10.1038/s41587-019-0224-x

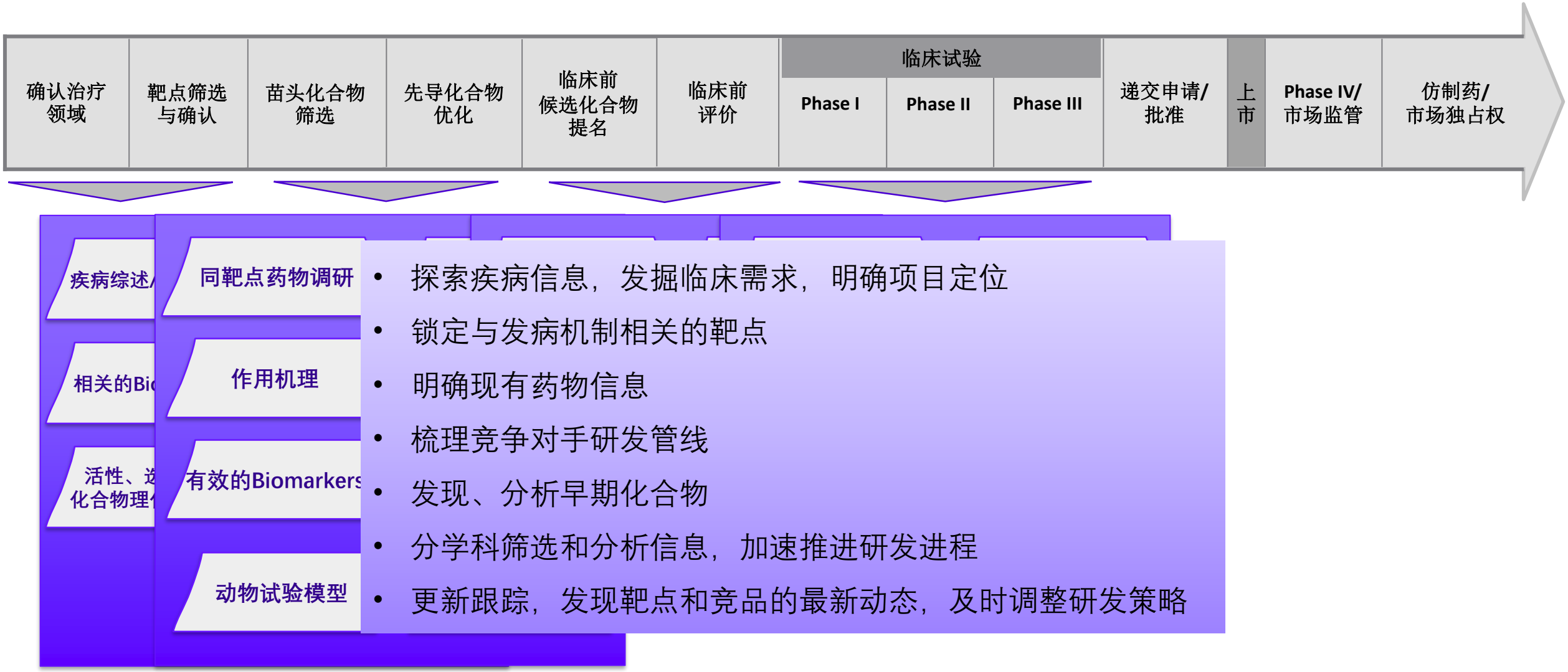
04 操作演示

Integrity
A Cortellis solution
Empowering knowledge-based drug discovery and development

登录网址： https://integrity.clarivate.com/integrity/xmlxsl/

Clarivate
Analytics

Integrity数据库：全面契合创新药物研发



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重要预告：
Integrity即将平台升级至
Cortellis Drug Discovery Intelligence（CDDI）

敬请期待！！！

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Clarivate Analytics | 科睿唯安

- **线上/线下培训：**为订购客户每年提供免费的培训交流活动；
- **科睿唯安在线学院：** http://clarivate.com.cn/e-Clarivate/
- **技术热线支持：**我们会为我们的客户提供400电话和Email咨询服务，保证您们在工作时间内有任何疑问都可以通过我们人工服务获得解答：

  TS技术支持团队：400 8822 031； ts.support.china@Clarivate.com

- 官方微信 扫描二维码 或 搜索 “科睿唯安生命科学与制药”

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预祝暨南大学师生
科研工作蒸蒸日上