



# Elsevier Life Science Solution

## 加速药物研发决策

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爱思唯尔生命科学客户顾问



# 内容

## ➤ Elsevier 生命科学解决方案

1. Reaxys对信息的提炼介绍，以及信息检索基础技巧
2. Reaxys专利检索策略
3. RMC辅助药物分子设计研发决策
4. PharmaPendium辅助药物临床研究

## ➤ 总结

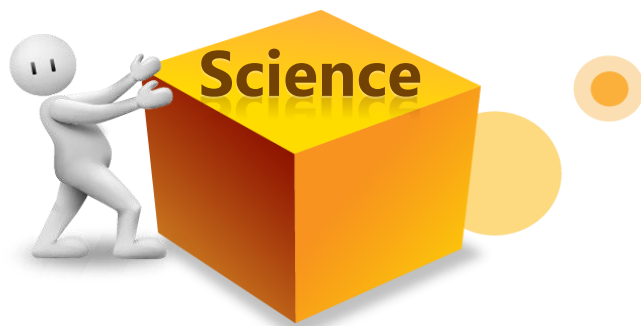
# 从数据库性质出发的分类方法



1. 注重速度
2. 数据整合
3. 缺乏系统化索引
4. 起到“告知”作用

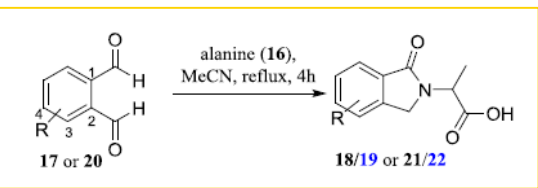
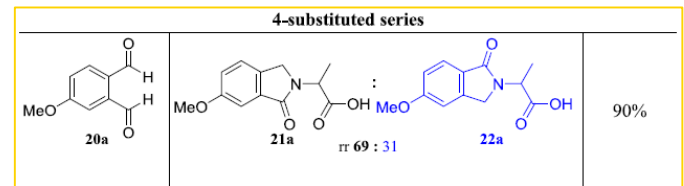
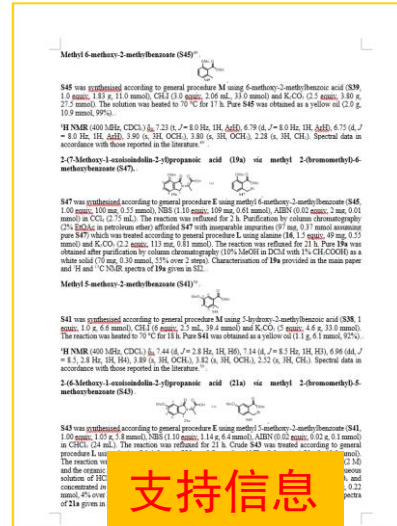
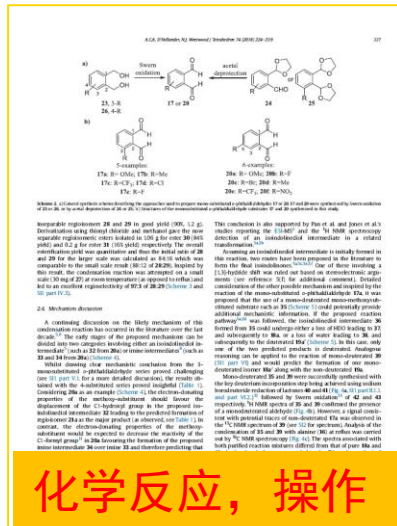
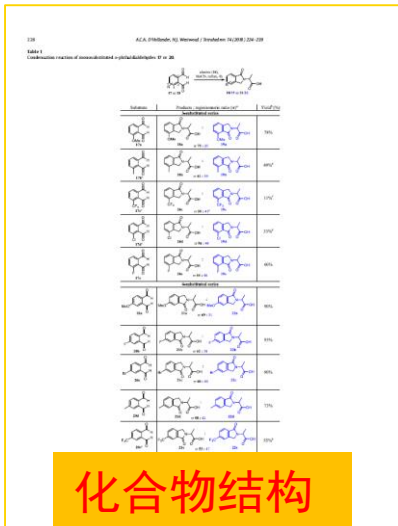
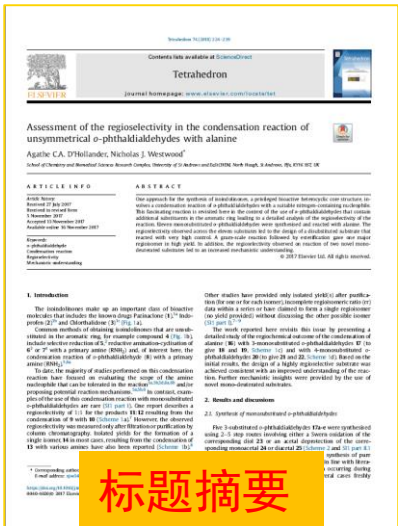


1. 注重宏观面
2. 更新速度慢
3. 参考作用
4. 定位“全局”作用



1. 主要支持研发
2. 主要来源期刊，专利
3. 完善的索引体系
4. 解决“为什么”，“怎么做”，“做什么”的问题

# 一篇全文期刊中的内容



Inseparable regioisomers **28** and **29** in good yield (90%, 1.2 g). Derivatization using thionyl chloride and methanol gave the now separable regioisomeric esters isolated in 1.06 g for ester **30** (84% yield) and 0.2 g for ester **31** (16% yield) respectively. The overall esterification yield was quantitative and thus the initial ratio of **28** and **29** for the larger scale was calculated as 84:16 which was comparable to the small scale result (88:12 of **28:29**). Inspired by this result, the condensation reaction was attempted on a small scale (30 mg of **27**) at room temperature (as opposed to reflux) and led to an excellent regioselectivity of **97:3** of **28:29** (Scheme 3 and S11 part IV.3).

## Supporting Information 中的内容

## 文献中包含的内容: 一些关键的概念

2-(6-Methoxy-1-oxoisindolin-2-yl)propanoic acid (**21a**) via methyl 2-(bromomethyl)-5-methoxybenzoate (**S43**).

**S43** was synthesised according to general procedure E using methyl 5-methoxy-2-methylbenzoate (**S41**, 1.00 equiv, 1.05 g, 5.8 mmol), NBS (1.10 equiv, 1.14 g, 6.4 mmol), AIBN (0.02 equiv, 0.02 g, 0.1 mmol) in  $CHCl_3$  (24 mL). The reaction was refluxed for 21 h. Crude **S43** was treated according to general procedure L using alanine (16, 1.5 equiv, 775 mg, 8.7 mmol) and  $NEt_3$  (2.2 equiv, 1.78 mL, 12.8 mmol). The reaction was refluxed for 2 h. Crude **21a** was basified using an aqueous solution of NaOH (2 M) and the organic impurities were extracted with DCM. The aqueous layer was acidified using an aqueous solution of HCl (1 M). The organics were extracted with DCM, combined, dried over  $MgSO_4$  and concentrated *in vacuo*. Pure **21a** was obtained after trituration in MeCN as a white solid (51 mg, 0.22 mmol, 4% over 2 steps). Characterisation of **21a** provided in the main paper and  $^1H$  and  $^{13}C$  NMR spectra of **21a** given in S12.

# 一篇典型的药物方面专利原文

United States  
Patent Application Publication  
Pub. No. US 2008/0676921 A1  
Haugberg et al.  
Pub. Date: Mar. 27, 2008

INHIBITORS OF BIRBENYL TYROSINE KINASE

Pub. No. US 2008/0676921 A1  
Pub. Date: Mar. 27, 2008

Figure 1: Normalized Proliferation vs Concentration for Compound 4 and Compound 15. The graphs show a dose-dependent decrease in proliferation as concentration increases from 0.1 to 10 μM.

US 2008/0676921 A1  
Mar. 27, 2008

INHIBITORS OF BIRBENYL TYROSINE KINASE

Background of the Invention

Summary of the Invention

Detailed Description

US 2008/0676921 A1  
Mar. 27, 2008

INHIBITORS OF BIRBENYL TYROSINE KINASE

Chemical structures and Markush definitions.

US 2008/0676921 A1  
Mar. 27, 2008

INHIBITORS OF BIRBENYL TYROSINE KINASE

Formulation and pharmaceutical compositions.

US 2008/0676921 A1  
Mar. 27, 2008

INHIBITORS OF BIRBENYL TYROSINE KINASE

Pharmaceutical compositions and methods of use.

US 2008/0676921 A1  
Mar. 27, 2008

INHIBITORS OF BIRBENYL TYROSINE KINASE

Pharmaceutical compositions and methods of use.

US 2008/0676921 A1  
Mar. 27, 2008

INHIBITORS OF BIRBENYL TYROSINE KINASE

Pharmaceutical compositions and methods of use.

## 典型药物专利中的内容：

1. 书目内容
2. 专利描述
3. Markush结构及实施例
4. 反应合成路线
5. 实施例的实验室数据
6. 实施例的应用数据





# Reaxys对这篇文献的索引—Key Word和题录摘要

Assessment of the regioselectivity in the condensation reaction of unsymmetrical o-phthaldialdehydes with alanine<sup>1</sup>

[D'Hollander, Agathe C.A.; Westwood, Nicholas J.](#) - [Tetrahedron, 2018, vol. 74, # 2, p. 224 - 239]

[Abstract](#) ^ [Index Terms](#) ^ [Substances](#) 103 v [Reactions](#) 236 v [Full Text](#) ↗

## Abstract

One approach for the synthesis of isoindolinones, a privileged bioactive heterocyclic core structure, involves a condensation reaction of o-phthaldialdehydes with a suitable nitrogen-containing nucleophile. This fascinating reaction is revisited here in the context of the use of o-phthaldialdehydes that contain additional substituents in the aromatic ring leading to a detailed analysis of the regioselectivity of the reaction. Eleven monosubstituted o-phthaldialdehydes were synthesised and reacted with alanine. The regioselectivity observed across the eleven substrates led to the design of a disubstituted substrate that reacted with very high control. A gram-scale reaction followed by esterification gave one major regioisomer in high yield. In addition, the regioselectivity observed on reaction of two novel monodeuterated substrates led to an increased mechanistic understanding.

## Index terms

**Author keyword:** Condensation reaction, Mechanistic understanding, o-phthaldialdehyde, Regioselectivity

**EMTREE drug term:** alanine, phthalaldehyde

**EMTREE medical term:** Article, esterification, polymerization, priority journal, regioselectivity, synthesis

**Reaxys Index Terms:** Swern oxidation, condensation reaction, esterification, pure, reactivity, regioselectivity, separation method, tautomerization

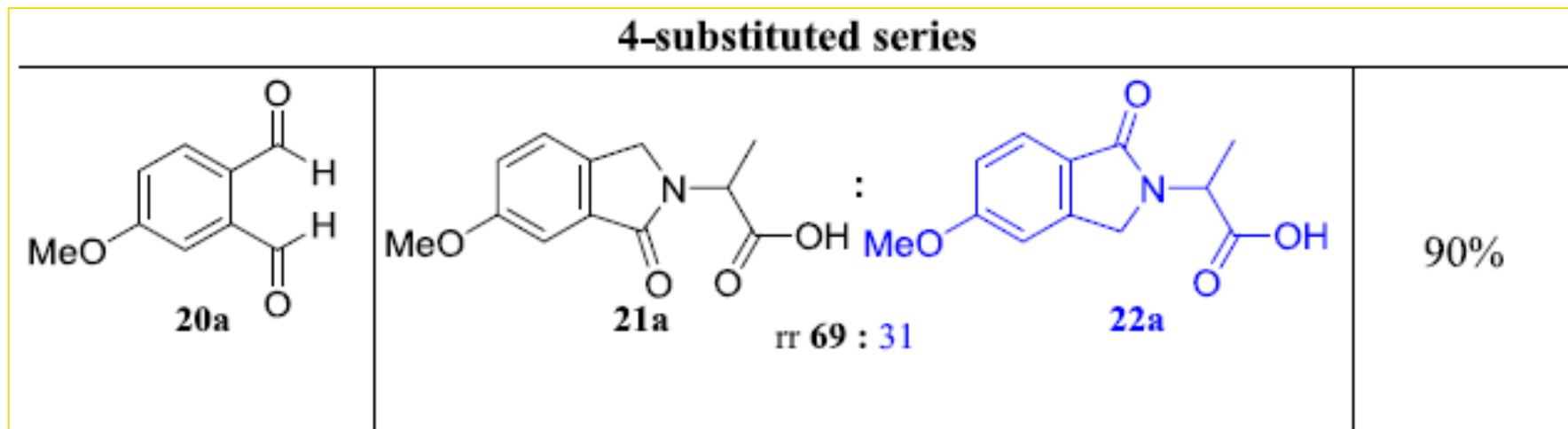


关键内容的提炼源自Elsevier不同的资源，Embase中的一级索引，EI索引，作者关键词，Reaxys自己的词库

# Reaxys对这篇文献的索引—物质与反应

Assessment of the regioselectivity in the condensation reaction of unsymmetrical o-phthalaldehydes  
1 with alanine  
[D'Hollander, Agathe C.A.; Westwood, Nicholas J.](#) - [Tetrahedron, 2018, vol. 74, # 2, p. 224 - 239]  
[Abstract](#) ▾ [Index Terms](#) ▾ [Substances](#) 103 ▾ [Reactions](#) 236 ▾ [Full Text](#) ↗

对于原文中出现的化合物21a，Reaxys都提取了什么信息



# Reaxys对文献中的化合物的深度提炼



2-(6-methoxy-1-oxoisindolin-2-yl)propanoic acid  
C<sub>12</sub>H<sub>13</sub>NO<sub>4</sub> 235.24 32021463

Hit Data - 7  
Identification  
Druglikeness

Physical Data - 2  
Spectra - 4  
Preparations - 7 >  
Reactions - 7 >  
Documents - 1 >

Hit Data - 7

- Substance Label - 1 hits out of 1
- Melting Point - 1 hits out of 1
- Crystal Property Description - 1 hits out of 1
- NMR Spectroscopy - 2 hits out of 2
- IR Spectroscopy - 1 hits out of 1
- Mass Spectrometry - 1 hits out of 1

Hit Data:  
在这篇文献中出现的和21a有关的重要数据



# Reaxys的深度提炼内容

## ^ Hit Data - 7

- ✓ Substance Label - 1 hits out of 1
- ✓ Melting Point - 1 hits out of 1
- ✓ Crystal Property Description - 1 hits out of 1
- ✓ NMR Spectroscopy - 2 hits out of 2
- ✓ IR Spectroscopy - 1 hits out of 1
- ✓ Mass Spectrometry - 1 hits out of 1

Reaxys重点提炼的是文献中的关键数据。

Label	Reference
21a	<a href="#">D'Hollander, Agathe C.A.; Westwood, Nicholas J.</a> - [Tetrahedron, 2018, vol. 74, # 2, p. 224 - 239] <a href="#">Full Text</a> ↗ <a href="#">Details</a> > <a href="#">Abstract</a> >

Melting Point, °C	Reference
194 - 196	<a href="#">D'Hollander, Agathe C.A.; Westwood, Nicholas J.</a> - [Tetrahedron, 2018, vol. 74, # 2, p. 224 - 239] <a href="#">Full Text</a> ↗ <a href="#">Details</a> > <a href="#">Abstract</a> >

Colour & Other Properties	Location	Reference
white	supporting information	<a href="#">D'Hollander, Agathe C.A.; Westwood, Nicholas J.</a> - [Tetrahedron, 2018, vol. 74, # 2, p. 224 - 239] <a href="#">Full Text</a> ↗ <a href="#">Details</a> > <a href="#">Abstract</a> >

Description (NMR Spectroscopy)	Nucleus (NMR Spectroscopy)	Solvents (NMR Spectroscopy)	Frequency (NMR Spectroscopy), MHz	Location	Reference
Chemical shifts, Spectrum	<sup>1</sup> H	d(4)-methanol	500	supporting information	<a href="#">D'Hollander, Agathe C.A.; Westwood, Nicholas J.</a> - [Tetrahedron, 2018, vol. 74, # 2, p. 224 - 239] <a href="#">Full Text</a> ↗ <a href="#">Details</a> > <a href="#">Abstract</a> >
Chemical shifts, Spectrum	<sup>13</sup> C	d(4)-methanol	125.8	supporting information	<a href="#">D'Hollander, Agathe C.A.; Westwood, Nicholas J.</a> - [Tetrahedron, 2018, vol. 74, # 2, p. 224 - 239] <a href="#">Full Text</a> ↗ <a href="#">Details</a> > <a href="#">Abstract</a> >

# Reaxys对原文反应的提炼 (21a)

Reaction ID: 47133770

The reaction scheme shows the synthesis of two regioisomers, 21a and 22a, from alanine and 4-methoxyphthalaldehyde. Alanine (16) reacts with 4-methoxyphthalaldehyde (20a) to produce a mixture of 21a and 22a. The reaction is regioselective, yielding 38 mg of product.

1 Conditions [Find Similar](#)

Yield	Conditions	Reference
In acetonitrile for 4h; Reflux; Inert atmosphere; Overall yield = 90 percent; Overall yield = 38 mg; regioselective reaction;	<a href="#">Experimental Procedure</a>	D'Hollander, Agathe C.A.; Westwood, Nicholas J. - [Tetrahedron, 2018, vol. 74, # 2, p. 224 - 239] <a href="#">Full Text</a> <a href="#">Details</a> <a href="#">Abstract</a>

General procedure: Alanine (16, 1.2 equiv.) was added to a solution of unsymmetrical o-phthalaldehyde (1.0 equiv.) in anhydrous MeCN (3.8 mL per mmol of o-phthalaldehyde). The reaction mixture was heated at reflux for 4 h under a nitrogen atmosphere. The solution was then cooled to rt before being concentrated in vacuo to afford the crude mixture of regioisomers.

原文中的General Procedure会被替换成对应的内容

4.3.9. 2-(6-Methoxy-1-oxoisoindolin-2-yl)propanoic acid (**21a**) with 2-(5-methoxy-1-oxoisoindolin-2-yl)propanoic acid (**22a**)  
A mixture of **21a** and **22a** was synthesised according to general procedure **B** using 4-methoxyphthalaldehyde (**20a**, 1.0 equiv., 30 mg, 0.18 mmol) and alanine (**16**, 1.2 equiv., 19 mg, 0.22 mmol). A

# Reaxys数据库对专利信息的提炼

专利中的实施例结构，反应，靶点

快速处理专利的生物活性数据

1 Documents with 196 Substances, 397 Reactions, 1 Targets

0 selected Limit To Exclude Export

Sort by Publication Year ↓

Heatmap

HETEROCYCLIC COMPOUNDS AS IMMUNOMODULATORS

1 Incyte Corporation; Wu, Liangxing; Qian, Ding-Quan; Lu, Liang; Lajkiewicz, Neil; Konkol, Leah C.; Li, Zhenwu; (...) Xiao, Kaijiong; Yao, Wenqing  
US2018/177784, 2018, A1  
Patent Family Members: TW2018/35073 A; US2018/177784 A1; US2018/177870 A1; US2018/179179 A1; US2018/179197 A1; ...

Abstract Claims Front Page Info Substances 196 Reactions 397 Targets Full Text ↗

专利中的发明描述

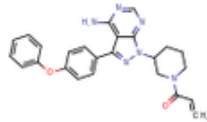
专利标记信息：族号，专利分类，公开日期等

原文链接

# Reaxys对这篇专利的提炼—实施例结构（其中一个实施例）

63 Substances out of 1 Documents, containing 15 Reactions, 4 Targets

0 selected Limit To Exclude Export Sort by No of References ↓ Heatmap

16  **1-[(3R)-3-[4-amino-3-(4-phenoxyphenyl)pyrazolo[3,4-d]pyrimidin-1-yl]piperidin-1-yl]prop-2-en-1-one**  
C<sub>25</sub>H<sub>24</sub>N<sub>6</sub>O<sub>2</sub> 440.505 13102237

Hit Data - 5 Druglikeness Physical Data - 4 Preparations - 7 >  
Identification Bioactivity (All) Spectra - 6 Reactions - 8 >  
Targets - 37 >  
Documents - 34 >

Hit Data - 5

- Substance Label - 1 hits out of 5
- Patent-Specific Data - 1 hits out of 4
- Crystal Property Description - 1 hits out of 3
- NMR Spectroscopy - 1 hits out of 3
- Mass Spectrometry - 1 hits out of 3

1. 物质在该专利中的标记
2. 物质在该专利中的特殊的数据（Markush相关）
3. 物质的晶体描述
4. 物质在该专利中的NMR数据
5. 物质在该专利中的Mass数据

# Reaxys对这篇专利的提炼—实施例细节

Hit Data - 5

- Substance Label - 1 hits out of 5
- Patent-Specific Data - 1 hits out of 4
- Crystal Property Description - 1 hits out of 3**
- NMR Spectroscopy - 1 hits out of 3
- Mass Spectrometry - 1 hits out of 3

Label	Reference
Compound 4	PHARMACYCLICS, INC. - <a href="#">US2008/76921</a> , 2008, A1 <a href="#">Full Text</a> <a href="#">Details</a> <a href="#">Abstract</a> Pharmacyclics LLC; Buggy, Joseph J.; Elias, Laurence; Fyfe, Gwe <a href="#">Full Text</a> <a href="#">Details</a> <a href="#">Abstract</a>

Related Markush Structure (RN)	Reference
13109621	PHARMACYCLICS, INC. - <a href="#">US2008/76921</a> <a href="#">Full Text</a> <a href="#">Details</a> <a href="#">Abstract</a>

Colour & Other Properties	Reference
white	PHARMACYCLICS, INC. - <a href="#">US2008/76921</a> , <a href="#">Full Text</a> <a href="#">Details</a> <a href="#">Abstract</a>

NMR Spectroscopy - 1 hits out of 3

Nucleus (NMR Spectroscopy)	Frequency (NMR Spectroscopy), MHz	Original Text (NMR Spectroscopy)	Comment (NMR Spectroscopy)	Signals, ppm	Reference
<sup>1</sup> H	400	<sup>1</sup> H-NMR (400 MHz): 8.26, s, 1H; 7.65, m, 2H; 7.42, m, 2H; 7.1-7.2, m, 5H; 6.7-6.9, m, 1H; 6.1, m, 1H; 5.5-5.7, n, 1H; 4.7, m, 1H; 4.54, m, 0.5H; 4.2, m, 1H; 4.1, n, 0.5H; 3.7, nm, 0.5H; 3.2, m, 1H; 3.0, m, 0.5H; 2.3, m, 1H; 2.1, m, 1H; 1.9, m, 1H; 1.6, m, 1H	Signals given	8.26	PHARMACYCLICS, INC. - <a href="#">US2008/76921</a> , 2008, A1 <a href="#">Full Text</a> <a href="#">Details</a> <a href="#">Abstract</a>

## Tips:

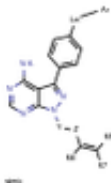
1. 利用物质标识，可以直接在专利全文中直接定位物质在专利中的位置。
2. Related Markush，直接给出实施例被保护的Markush结构
3. 晶体描述，核磁，质谱数据的直接给出

# Reaxys对这篇专利的提炼—Markush结构

1 Substances out of 1 Documents, containing 0 Reactions, 0 Targets

0     No of References ↓

1



Reaxys ID: 13109621  
13109621

Hit Data - 195 Documents - 1 >

Identification

Other Data - 193

^ Hit Data - 195

- Substance Label - 1 hits out of 1
- Patent-Specific Data - 1 hits out of 1
- Use - 193 hits out of 193

## Markush结构的具体描述

1. Markush结构在该专利中的标记
2. Markush结构该专利中的位置
3. Markush结构涉及的应用



# 内容

## ➤ Elsevier 生命科学解决方案

1. Reaxys对信息的提炼介绍，以及信息检索基础技巧
2. Reaxys专利检索策略
3. RMC辅助药物分子设计研发决策
4. PharmaPendium辅助药物临床研究

## ➤ 总结

# Reaxys检索方法总览

Reaxys<sup>®</sup> Quick search Query builder Results Synthesis planner History

Search for [icon] Import

Search Reaxys

Substance CAS Registry Number, e.g. 102625-70-7

AND

Feedback

**结构式索引化合物信息**

Reaxys<sup>®</sup> Quick search Query builder Results Synthesis planner History

Search in: Reactions > Targets > Substances > Documents >

Import Save Reset form Delete all

Structure Molecular Formula CAS RN Doc. Index

Document Basic Index is Document Basic Index

AND Patent Assignee is Patent Assignee

AND Patents: Main IPC is Main IPC

AND Patents: Date of publ... is

**综合信息的自定义模块化组合检索**

Reaxys<sup>®</sup> Quick search Query builder Results Synthesis planner History

Search for [icon] Import

Search Reaxys

Substance Molecular Formula, e.g. Pt(PPh<sub>3</sub>)<sub>3</sub>

AND

Feedback

**结构式索引反应信息**

Reaxys<sup>®</sup> Quick search Query builder Results Synthesis planner History

Search in: Reactions > Targets > Substances > Documents >

Import Save Reset form Delete all

Structure Molecular Formula CAS RN Doc. Index

Caco-2 permeability

Structure

Create Structure / Reaction Drawing

AND Cells/Cell Lines is 'Caco-2 cell line';Caco-2

AND Measurement Parameter is

**特殊信息的预设模块化组合检索**

# Reaxys结果集筛选方法总览

The image displays the Reaxys search results interface with several filter panels highlighted. The main search results area shows 37,826 reactions out of 12,016 documents containing 37,880 substances and 2,832 targets. A chemical reaction scheme is shown, and a 'Substance Classes' panel is open, listing various categories and their counts.

**Reaxys Filters (Left Panel):**

- Limit to > Exclude >
- By Structure
- Yield
- Reagent/Catalyst
- Solvent
- Catalyst Classes
- Solvent Classes
- Product Availability
- Reactant Availability
- Reaction Classes
- Document Type
- Publication Year
- Single step reactions only

**Substance Classes (213):**

- Substance Classes: 37,880
- Functional Group Classification: 36,399
- Ring Classification: 36,101
  - 6-membered rings: 36,042
  - 9-18-membered rings: 13,282
  - 5-membered rings: 9,221
  - 3-membered rings: 780
  - cyclopropane and derivatives: 529
  - cyclopropylcyclohexane and heteroatomic analogs: 334
    - cyclopropylbenzene and derivatives: 213
    - cyclopropylcyclohexane and heteroatomic analogs - not further classified: 76

**Reagent/Catalyst (Top Right Panel):**

- lithium aluminium tetr...: 17,292
- potassium carbonate: 5,997
- diisobutylaluminium hyd...: 4,406
- sodium tetrahydroborate: 4,142
- triethylamine: 4,112
- hydrogen: 3,822
- hydrogenchloride: 3,314

**Catalyst Classes (Right Panel):**

- Catalyst Classes: 37,826
- active center: 32,458
  - Al: 22,400
  - B: 10,432
  - Pd: 5,658
  - Cu: 2,079
  - Fe: 1,327
  - Si: 1,050
  - Zn: 711
  - Sn: 387
  - Ag: 377

**Index Terms (List) (Bottom Center Panel):**

- ozylation reaction: 486
- oxidation reaction: 469
- total synthesis: 427
- catalyst: 410
- catalytic reaction: 389
- reactivity: 312
- alkylation: 294
- ic50: 292
- hydrogenation: 290
- crystal structure: 274

**Document Type (Bottom Right Panel):**

- article: 7,168
- patent: 4,768
- conference paper: 26
- article in press: 21
- review: 18
- letter: 11
- retracted article: 1

# Case 1 化合物衍生物检索及其分析

- 检索以下列母核为基础的衍生化合物信息
- 快速获取其特定信息，核磁图谱，溶解度信息等
- 快速分析衍生物的大致结构式构成
- 快速获取某个特定结构的合成路线

The screenshot displays the Reaxys software interface. At the top, there are navigation tabs: "Quick search", "Query builder", "Results", "Synthesis planner", and "History". The user's name "Peng Wu" is visible in the top right corner. The main workspace is the "Structure editor" using "ChemAxon's MarvinJS". It features a toolbar on the left and a central canvas showing a chemical structure of a quinazolinone derivative (SMILES: Nc1nc2ccccc2n1). Below the canvas is another toolbar. On the right side, there is a search configuration panel titled "Search this structure as:". It includes radio buttons for "As drawn", "As substructure" (which is selected), and "Similar". Under "As substructure", there are radio buttons for "On all atoms" (selected) and "On heteroatoms". Below these are checkboxes for "Similar" options: "Tautomers", "Stereo", "Additional ring closures", "Related Markush", "Salts", "Mixtures", "Isotopes", "Charges", and "Radicals". At the bottom of the interface, there are buttons for "Clear", "Cancel", and "Transfer to query".

亚结构检索功能  
扩展所画结构为  
相关衍生物

这些选项却保，  
把相关的异构体  
也检索出来

# Case 1 化合物衍生物检索结果

96,884 K

Filters

Limit to > Exclude >

By Structure >

Measurement pX >

Highest Clinical Phases >

Targets >

Parameters >

Substance Classes >

96,884 Substances out of 21,106 Documents, containing 148,635 Reactions, 4,242 Targets

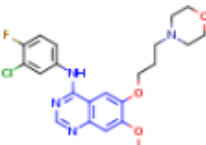
Reaxys - 96,884

0 selected Limit To Exclude Export

Sort by No of References ↓

Grid Heatmap

1



gefitinib  
C<sub>22</sub>H<sub>24</sub>N<sub>4</sub>ClFO<sub>3</sub> 446.909 8949523 184475-35-2

Identification	Bioactivity (All)	Spectra - 65	Preparations - 76 >
Druglikeness	Physical Data - 88	Other Data - 2,966	Reactions - 116 >
			Targets - 1,069 >
			Documents - 6,102 >

## ^ Spectra - 65

- ✓ NMR Spectroscopy - 38
- ✓ IR Spectroscopy - 9
- ✓ Mass Spectrometry - 12
- ✓ UV/VIS Spectroscopy - 5
- ✓ Raman Spectroscopy - 1

## ^ Physical Data - 88

- ✓ Melting Point - 25
- ✓ Association (MCS) - 5
- ✓ Chromatographic Data - 5
- ✓ Conformation - 1
- ✓ Crystal Phase - 7

## ^ Bioactivity (All)

- ✓ In vitro: Efficacy - 4878
- ✓ In vivo: Animal Model - 627
- ✓ Metabolism - 311
- ✓ Pharmacokinetic - 672
- ✓ Toxicity/Safety Pharmacology - 1393

# Case 1 化合物衍生物检索结果

^ Spectra - 65
✓ NMR Spectroscopy - 38
✓ IR Spectroscopy - 9
✓ Mass Spectrometry - 12
✓ UV/VIS Spectroscopy - 5
✓ Raman Spectroscopy - 1

Description (NMR Spectroscopy)	Nucleus (NMR Spectroscopy)	Coupling Nuclei	Solvents (NMR Spectroscopy)	Temperature (NMR Spectroscopy), °C	Frequency (NMR Spectroscopy), MHz	Original Text (NMR Spectroscopy)	Location	Comment (NMR Spectroscopy)	Signals, ppm	Kind of signal	Reference
Chemical shifts	<sup>1</sup> H		dimethylsulfoxide-d <sub>6</sub>		300		Paragraph 0096				<a href="#">Mingmin Full Text</a>
Chemical shifts	<sup>13</sup> C		dimethylsulfoxide-d <sub>6</sub>		75		Paragraph 0096				<a href="#">Shaanxi Wang, Liu WeiCN10 Full Text</a>
Chemical shifts	<sup>1</sup> H		dimethylsulfoxide-d <sub>6</sub>		400	1H NMR (400 MHz, d <sub>6</sub> -DMSO) $\delta$ 9.44 (s, 1H), 8.50 (s, 1H), 8.12 (dd, $J$ = 6.9, 2.7 Hz, 1H), 7.80 (m, 2H), 7.44 (t, 1H), 7.20 (s, 1H), 4.18 (t, $J$ = 6.7 Hz, 2H), 3.94 (s, 3H), 3.59 (t, $J$ = 4.4 Hz, 4H), 2.49 (t, $J$ = 6.9 Hz, 2H), 2.41 (bs, 4H), 2.00 (m, 2H).	Paragraph 0035				<a href="#">SCINOP LTD.; ZH, 2015, A1 Full Text</a>
Chemical shifts	<sup>13</sup> C		dimethylsulfoxide-d <sub>6</sub>		100	13C NMR (100 MHz, d <sub>6</sub> -DMSO) $\delta$ 156.48, 154.94, 153.57 ( $J$ = 241 Hz), 153.05, 148.74, 147.43, 137.33 ( $J$ = 3 Hz), 123.01, 122.77 ( $J$ = 7 Hz), 119.19 ( $J$ = 19 Hz), 116.90 ( $J$ = 21 Hz), 77.59, 66.43, 56.31, 55.35, 53.73, 26.13.	Paragraph 0035				<a href="#">SCINOP LTD.; ZH, 2015, A1 Full Text</a>

正文中位置

正文中具体数据

原文链接



# Case 1 化合物合成路线

1

购物车 合成路线

Shopping cart icon:    
 Search icon:   
 Home icon:   
 Synthesis icon:   
 Menu icon:

Synthesize ×

> Manually 手动

> **Autoplan** 自动

自动设计合成了路线参数设置

Substance Availability ×

- Accelrys' ACD
- CambridgeSoft ACX
- Labnetwork
- PharmaPendium
- Sigma Aldrich
- <sup>5g</sup>/<sub>\$100</sub> eMolecules

国内供应商

国际供应商

Create plans by autoplan ×

Number of plans to create  ∨ 合成计划数

Max. alternative branches  ∨ 每个计划中每步分支

Max. number of steps  ∨ 每个计划中多少步合成目标

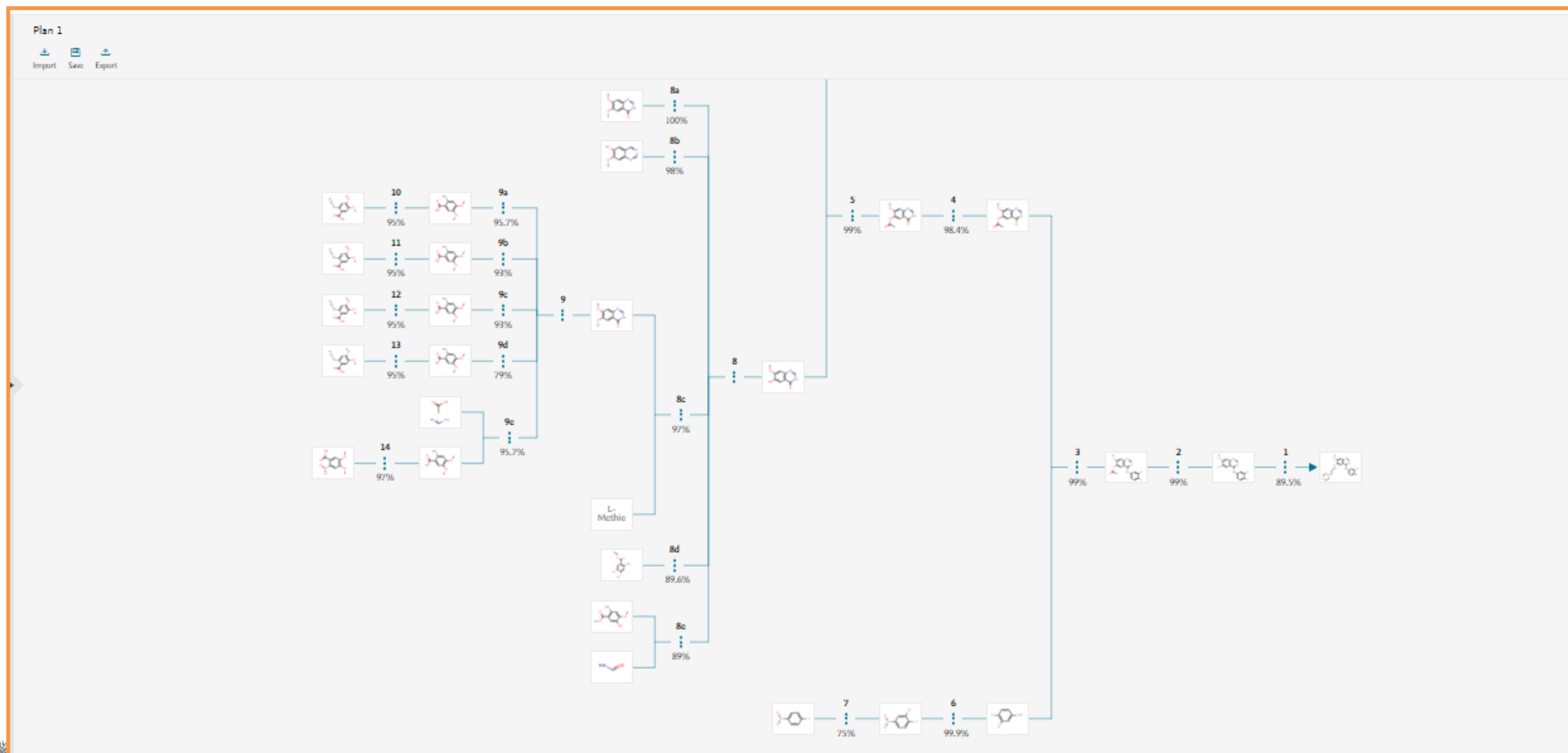
Stop searching if starting material is commercially available  Yes  No 当原料可购买时，是否停止设计

Default yield for reactions without a given yield  每步收率

Always show screen before creating autoplan

[Create Plans >](#)

# Case 1 化合物合成路线



# Case 1 衍生物结构式类型快速分析

Filters

96,884 Substances out of 21,106 Documents, containing 148,6

Limit to > Exclude >

By Structure >

Measurement pX >

Highest Clinical Phases >

Targets >

Parameters >

**Substance Classes >**

Molecular Weight >

Number of Fragments >

Availability >

Availability in other databases >

Available Data >

0 Limit To Exclude Export

1

2

### Substance Classes

Substance Classes	96,884
Functional Group Classification	90,750
Richter Classification	90,747
Ring Classification	90,747
6-membered rings	90,743
9-18-membered rings	90,722
5-membered rings	35,143
<b>3-membered rings</b>	
4-membered rings	
7-membered rings	
8-membered rings	

按官能团种类分  
按官芳香性种类分  
按官环结构种类分

#### 3-membered rings

- cyclopropane and derivatives
- (2-cyclopropylethyl)cyclohexane and heteroatomic analogs
  - (cyclopropylmethoxy)benzene and derivatives
  - N-benzylcyclopropanamine and derivatives
  - N-(biphenyl-3-ylmethyl)cyclopropanamine and derivatives
  - 7-(cyclopropylmethoxy)-N-phenylquinazolin-4-amine and derivatives
  - N-cyclopropyl-6-[3-[(cyclopropylamino)methyl]phenyl]quinazolin-4-amine and derivatives

Clear selected X

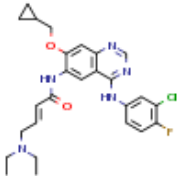
# Case 1 衍生物结构式类型快速分析

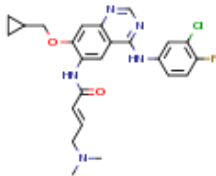
455 Substances out of 112 Documents, containing 346 Reactions, 52 Targets

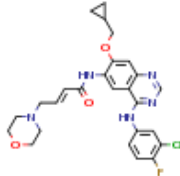
Reaxys - 455

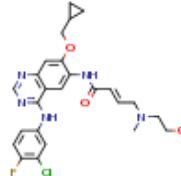
0 Limit To Exclude Export

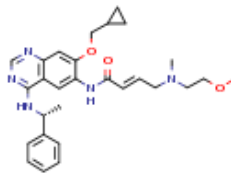
No of References ↓ List Heatmap

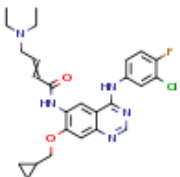
1 

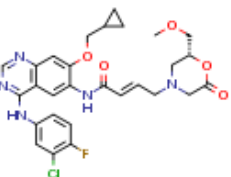
2 

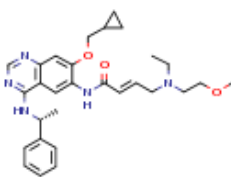
3 

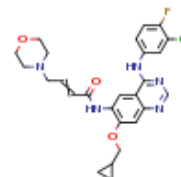
4 

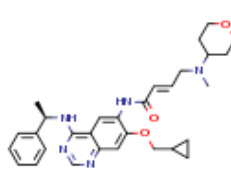
5 

6 

7 

8 

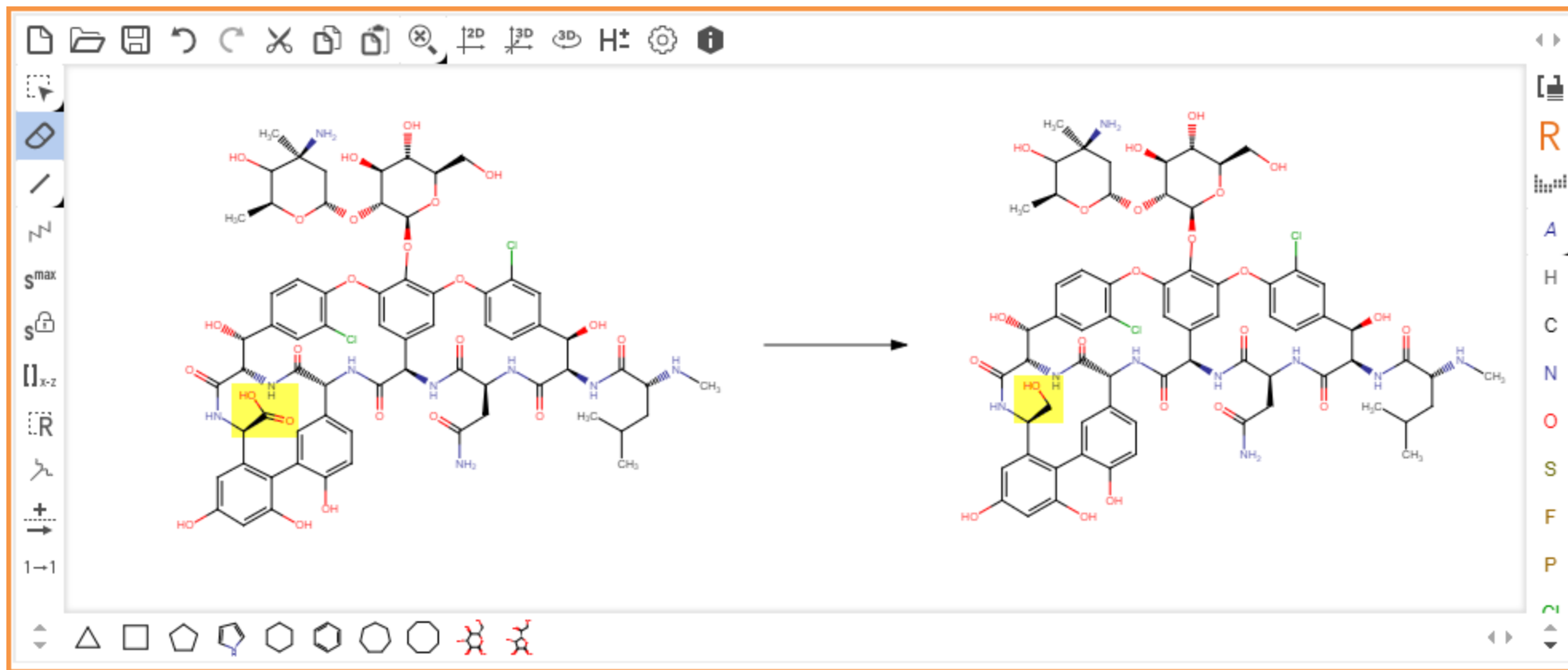
9 

10 

Feedback

## Case 2 同机理化学反应条件的检索

- 参与反应结构太复杂；结构太新颖。如何用同机理的反应条件检索知道实验？
- 如何快速分型最常用试剂？
- 如何快速获取特定催化剂？



## Case 2 同机理化学反应条件的检索

The screenshot displays the ChemAxon's MarvinJS structure editor interface. The main workspace shows a chemical reaction: benzoyl alcohol (left) reacts to form benzyl alcohol (right). The carbonyl carbon in benzoyl alcohol is highlighted with a red circle and labeled "对应反应前后反应位点" (Corresponding reaction site before and after the reaction). The hydroxyl hydrogen in benzyl alcohol is highlighted with a red circle and labeled "锁定该原子上只能是H" (Lock this atom, it can only be H). The search options panel on the right is open, with "As substructure" selected. The "On all atoms" sub-option is also selected. The "Similar" option is also selected. The "Transfer to query" button is visible at the bottom right.

Structure editor ChemAxon's MarvinJS

Create structure template from name >

Search this structure as:

- As drawn
- As substructure
  - On all atoms
  - On heteroatoms
- Similar

亚结构检索扩展为机理相同反应

对应反应前后反应位点

锁定该原子上只能是H

1-1

Clear Cancel Transfer to query >

+ More options Feedback



# Case 2 结果集的快速筛选

快速获取最常用试剂条件

快速获取特定试剂条件

The screenshot displays a chemical reaction database interface. On the left, a 'Filters' sidebar shows 13,744 results. The 'Reagent/Catalyst' and 'Catalyst Classes' filters are highlighted with orange boxes and arrows pointing to the text above. The main area shows 13,741 reactions out of 8,734 documents. A chemical reaction is shown: 4-bromobenzaldehyde reacts to form 4-bromobenzyl alcohol. Below the reaction, there are icons for shopping cart, zoom, and other actions. A table below the reaction provides conditions, yield, and reference information.

13,741 Reactions out of 8,734 Documents containing 20,523 Substances, 1,622 Targets

Limit To Exclude Export Syn-Plan

Reagents/Catalysts

Solvent

Catalyst Classes

Solvent Classes

Product Availability

Reactant Availability

Reaction Classes

Document Type

15 Conditions Find Similar Reaction ID: 2066982

Conditions	Yield	Reference
With sodium bis(2-methoxyethoxy)aluminium dihydride In toluene 1.) 10-20 deg C, 2.) room temperature, 10 min;	100%	Wells, Andy [Synthetic Communications, 1996, vol. 26, # 6, p. 1143 - 1147] Full Text Cited 1 times Details Abstract

## Case 2 常用试剂条件获取

Reagent/Catalyst ^

- lithium aluminium tetrah... 7,535
- diisobutylaluminium hyd... 1,664
- sodium tetrahydroborate 1,519
- water 1,345
- hydrogenchloride 1,007
- borane-thf 1,003
- sodium hydroxide 884

Filter by value v [View more](#)

把数万条操作步骤中的试剂，按使用频繁度排序

Reagent/Catalyst Clear selected x ↓ ↑ Sort by Occurrence v x

<input type="checkbox"/> lithium aluminium tetrahydride	7,535
<input type="checkbox"/> diisobutylaluminium hydride	1,664
<input type="checkbox"/> sodium tetrahydroborate	1,519
<input type="checkbox"/> water	1,345
<input type="checkbox"/> hydrogenchloride	1,007
<input type="checkbox"/> borane-thf	1,003
<input type="checkbox"/> sodium hydroxide	884
<input type="checkbox"/> potassium carbonate	883
<input type="checkbox"/> lithium borohydride	869
<input type="checkbox"/> sulfuric acid	668

1 2 3 ... 36 > Go to page > Limit to > Exclude >

# Case 2 特定试剂条件获取

Catalyst Classes

- active center 12,989
- heterogeneous 247
- organism / enzymes 9

[View more](#)

Catalyst Classes

▼ Catalyst Classes		13,741
> active center	有催化中心试剂	12,989
> heterogeneous	无催化中心试剂	247
> organism / enzymes	生物催化试剂	9

Catalyst Classes 1003

▼ Catalyst Classes		13,741
▼ active center		12,989
> AI		9,482
▼ B		4,086
<input type="checkbox"/> sodium tetrahydroborate		1,519
<input checked="" type="checkbox"/> borane-THF		1,003
<input type="checkbox"/> lithium borohydride		847
<input type="checkbox"/> dimethylsulfide borane complex		442
<input type="checkbox"/> boron trifluoride diethyl etherate		228
<input type="checkbox"/> borane		225

## Case 2 特定试剂条件获取

1,003 Reactions out of 1,745 Documents containing 1,645 Substances, 199 Targets

Limit To Exclude Export Syn-Plan Reaxys Ranking

1

通过试剂筛选，可以把特定条件，从所有报道过的条件中挑选出来

2 Hits ^ 6 Conditions v Find Similar > Reaction ID: 9591163

Conditions	Yield	Reference
With borane-THF In tetrahydrofuran at 0 - 20°C; Experimental Procedure v	94%	Jankowiak, Aleksandra; Obijalska, Emilia; Kaszynski, Piotr [Beilstein Journal of Organic Chemistry, 2013, vol. 9, p. 1873 - 1880] Full Text ^ Cited 5 times ^ Details > Abstract >

Feedback

# 内容

## ➤ Elsevier 生命科学解决方案

1. Reaxys对信息的提炼介绍，以及信息检索基础技巧
2. Reaxys专利检索策略
3. RMC辅助药物分子设计研发决策
4. PharmaPendium辅助药物临床研究

## ➤ 总结

# Reaxys中专利收录情况


Patent Offices	Time they cover	Indexed content
Various	1803 - 1980	<ul style="list-style-type: none"> <li>•Substance and reaction data</li> <li>•Patent citation information</li> <li>•Most organic chemistry</li> </ul>
English language patents from World, US, and European patent offices.	1976 - 2001 (automatic) 2001 - present (manual)	Includes the content above and: <ul style="list-style-type: none"> <li>•Markush substance display</li> <li>•All patent family members</li> <li>•Classification codes</li> </ul>
Asian patent offices in original language with English abstracts (China, Taiwan, South Korea, Japan)	2015 - present (manual: JP, KR) 2016 - present (manual: CN, TW)	Includes the same content as for WO, US and EP patent offices

1. 2015年以前，只有JP,KR的专利，没有申请WO, US,EP，则不被收录
2. 2016年以前，只有CN,TW的专利，没有申请WO, US, EP,则不被收录
3. 2015年以前，JP,KR；2016年以前CN,TW；具有WO,但是不具有英文版本，则不会摘录具体数据

- Reaxys中专利数据的抓取数据（2019年开始）
  - 专利公布，（通常3-10日，由专利局控制）获得专利局传递的数据
  - 文字内容：标题，摘要，claim，专利标记，授权人，发明人等，最迟10天内抓取入数据库
  - 化合物结构：包含名称结构的翻译，最迟1-1.5月内抓取入数据库（内容量影响抓取数据）
  - 生物活性数据等：最迟2月-2.5月内抓取入数据库（内容量影响抓取数据）

# 常用的综合检索专利的模块等

◇ Structure ✕

 Create Structure / Reaction Drawing

结构式

◇ Document Basic Index is ▼ Document Basic Index 🔍 ✕

关键词索引,  
可索引专利  
claim

◇ Patent Assignee is ▼ Patent Assignee 🔍 ✕

专利授权人

◇ Common Patent Number is ▼ Common Patent Number 🔍 ✕

通用专利号

◇ Patents: Main IPC is ▼ Main IPC 🔍 ✕

1级IPC

◇ Patents: Secondary IPC is ▼ Secondary IPC 🔍 ✕

2级IPC

◇ Patents: Date of publ... is ▼ Date of publication 🔍 ✕

公开日期（不分专  
利类型A或B，以最  
近的进行日期进行匹配）

## Case 3: 检索‘辉瑞’为授权者，并具有某‘特定结构专利’

The screenshot displays a chemical search interface. At the top, there are search filters for 'Reactions', 'Targets', 'Substances', and 'Documents'. Below these are utility buttons: 'Import', 'Save', 'Reset form', and 'Delete all'. On the right, there are icons for 'Structure', 'Molecular Formula', 'CAS RN', and 'Doc. Index'. The main search area is titled 'Structure' and contains a chemical structure of a benzimidazole derivative with an amino group (NH<sub>2</sub>) at the 2-position. To the right of the structure, the text reads: '只需要结构式+授权人组合即可' (Only need structure + assigner combination). Below the structure, the text says: '在指定授权人时，可以通尽可能过‘contain’逻辑来扩展授权人的‘全名’' (When specifying the assigner, you can use the 'contain' logic to expand the assigner's 'full name'). At the bottom, there is a search bar with the text 'Patent Assigner' and a dropdown menu showing search operators: 'contains', 'ends with', 'is', 'contains', and 'starts with'. The 'contains' operator is selected, and the search term 'pfizer' is entered. The Elsevier logo is visible in the bottom left corner.

Search in: Reactions > Targets > Substances > Documents >

Import Save Reset form Delete all

Structure Molecular Formula CAS RN Doc. Index

Structure

NH<sub>2</sub>

只需要结构式+授权人组合即可

On all atoms 在指定授权人时，可以通尽可能过‘contain’逻辑来扩展授权人的‘全名’

AND Patent Assigner contains pfizer

- contains
- ends with
- is
- contains
- starts with

ELSEVIER



# 设定条件都会去命中

112 Documents with 8,824 Substances, 7,789 Reactions, 59 Targets

0 selected Limit To Exclude Export Sort by Publication Year Heatmap

- SUBSTITUTED CARBONUCLEOSIDE DERIVATIVES USEFUL AS ANTICANCER AGENTS**  
1 **PFIZER INC.**; KUMPF, ROBERT ARNOLD; MCALPINE, INDRAWAN JAMES; MCTIGUE, MICHELE ANN; PATMAN, RYAN; RUI, EUGENE YUANJIN; TATLOCK, JOHN HOWARD; TRAN-DUBE, MICHELLE BICH; WYTHES, MARTIN JAMES TW2018/2074, 2018, A  
Patent Family Members: CA2969295 A1; US2017/348313 A1; WO2017/212385 A1; TW2018/2074 A; UY37274 A; ...  
[Abstract](#) [Claims](#) [Front Page Info](#) [Substances 653](#) [Reactions 1611](#) [Full Text](#)  
[Hit Substances 1](#)
- Antibodies to insulin-like growth factor I receptor**  
2 **Pfizer Inc.**; Amgen Fremont Inc.; Cohen, Bruce D.; Beebe, Jr., Jean; Miller, Penelope E.; Moyer, James D.; Corvalan, Jose Ramon; Gallo, Michael US9234041, 2016, B2  
Patent Family Members: HN2001000283 A; UY27087 A1; CA2433800 A1; DZ3494 A1; WO2002/53596 A2; ...  
[Abstract](#) [Claims](#) [Front Page Info](#) [Substances 18](#) [Full Text](#)  
[Hit Substances 1](#)
- Quinazoline derivatives**  
3 **Pfizer Products Inc.**; OSI Pharmaceuticals, LLC; Schnur, Rodney Caughren; Arnold, Lee Daniel EP2163546, 2016, B1  
Patent Family Members: NO961299 D0; HU9600834 D0; IL117598 D0; MA23831 A1; NO961299 A; ...  
[Abstract](#) [Claims](#) [Front Page Info](#) [Substances 196](#) [Reactions 236](#) [Full Text](#)  
[Hit Substances 129](#)

# 专利的信息摘取

## □ SUBSTITUTED CARBONUCLEOSIDE DERIVATIVES USEFUL AS ANTICANCER AGENTS

1 PFIZER INC.; KUMPF, ROBERT ARNOLD; MCALPINE, INDRAWAN JAMES; MCTIGUE, MICHELE ANN; PATMAN, RYAN; RUI, EUGENE YUANJIN; TATLOCK, JOHN HOWARD; TRAN-DUBE, MICHELLE BICH; WYTHES, MARTIN JAMES TW2018/2074, 2018, A

Patent Family Members: CA2969295 A1; US2017/348313 A1; WO2017/212385 A1; TW2018/2074 A; UY37274 A; ...

Abstract ▾ Claims ▾ Front Page Info ▾ Substances 653 ▾ Reactions 1611 ▾ Full Text ↗

Hit Substances 1 ▾

Assignees			Inventors (Authors)		
PFIZER INC.; KUMPF, ROBERT ARNOLD; MCALPINE, INDRAWAN JAMES; MCTIGUE, MICHELE ANN; PATMAN, RYAN; RUI, EUGENE YUANJIN; TATLOCK, JOHN HOWARD; TRAN-DUBE, MICHELLE BICH; WYTHES, MARTIN JAMES			KUMPF, ROBERT ARNOLD; MCALPINE, INDRAWAN JAMES; MCTIGUE, MICHELE ANN; PATMAN, RYAN; RUI, EUGENE YUANJIN; TATLOCK, JOHN HOWARD; TRAN-DUBE, MICHELLE BICH; WYTHES, MARTIN JAMES		
Patent No	Kind Code	Publ. Date	Application No	Filing Date	Indexed Patent
CA2969295	A1	2017/06/01	CA2969295	2017/06/01	
US2017/348313	A1	2017/06/02	US2017-612030	2017/06/02	
WO2017/212385	A1		WO2017-212385		
TW2018/2074	A		TW2018-2074		
UY37274	A		UY37274		
AR108763	A1		AR108763		
TW1637945	B	2018/10/11	TW2017-1637945		
TW2018/40570	A	2018/11/16	TW2018-40570		
AU2017279014	A1	2018/12/13	AU2017-279014		
SG112018104855	A	2018/12/28	SG112018-104855		
CO2018013105	A2	2018/12/28	CO2018-013105		
CL2018003504	A1	2019/02/01	CL2018-003504		
KR2019/15745	A	2019/02/14	KR2019-015745		

专利标记,  
便于查询  
该专利的  
授权情况

专利Claim  
便于理解  
专利的发明内容

Claims

1. A structure of formula (I) compound of formula or a stereoisomer thereof, tautomers or its pharmaceutically acceptable salt or solvate or prodrug:  
Wherein  
R<sub>1</sub> Selected from hydrogen, halogen, C<sub>1</sub> - C<sub>6</sub> Alkyl, C<sub>1</sub> - C<sub>6</sub> C alkoxy and C<sub>1</sub> - C<sub>6</sub> Haloalkyl;  
R<sub>2</sub> Selected from hydrogen, halogen, C<sub>1</sub> - C<sub>6</sub> C alkyl and C<sub>1</sub> - C<sub>6</sub> Haloalkyl;  
R<sub>3</sub> Is selected from:  
Each R<sub>3</sub> Independently selected from hydrogen, halogen, optionally substituted C<sub>1</sub> - C<sub>6</sub> Alkyl, C<sub>1</sub> - C<sub>6</sub> C alkoxy, amino or C<sub>1</sub> - C<sub>6</sub> Haloalkyl;  
R<sub>4</sub> For the group - (CHR<sub>4</sub>)<sub>2</sub> - (Y)<sub>2</sub> - (CHR<sub>7</sub>)<sub>2</sub> - R<sub>8</sub> ;  
R<sub>6</sub> , R<sub>7</sub> Independently selected from hydrogen, C<sub>1</sub> - C<sub>6</sub> Alkyl, hydroxy;  
C Y is selected from: C<sub>1</sub> - C<sub>6</sub> Alkyl, NH or O;  
R<sub>8</sub> C selected from optionally substituted C<sub>2</sub> - C<sub>8</sub> Heterocyclic alkyl, optionally substituted C<sub>3</sub> - C<sub>8</sub> Cycloalkyl, optionally substituted C<sub>2</sub> - C<sub>10</sub> Heteroaryl, substituted ethylenically H, C<sub>1</sub> - C<sub>6</sub> Alkyl, C<sub>2</sub> - C<sub>8</sub> Heterocyclic alkyl, C<sub>3</sub> - C<sub>8</sub> Cycloalkyl, - S(O<sub>2</sub>) C<sub>1</sub> - C<sub>6</sub> Alkyl, - S(O) C<sub>1</sub> - C<sub>6</sub> Alkyl, - C(O) (CH<sub>2</sub>)<sub>w</sub> C<sub>2</sub> - C<sub>8</sub> Heterocyclic alkyl, C<sub>2</sub> - C<sub>10</sub> Heteroaryl, C<sub>6</sub> - C<sub>10</sub> Aryl, hydroxy or halogen.  
W is selected from 0, 1, 2;  
S, t, u independently selected from 0, 1, 2.

2. In the formula (I) compound or its stereoisomers according to Claim 1, tautomers or its pharmaceutically acceptable salt or solvate or prodrug, characterized in that said R<sub>3</sub> Is selected from

3. In the formula (I) compound or its stereoisomers according to Claim 2, tautomers or its pharmaceutically acceptable salt or solvate or prodrug, characterized in that said R<sub>3</sub> Is selected from

4. In the formula (I) compound or its stereoisomers according to Claim 3, tautomers or its pharmaceutically acceptable salt or solvate or prodrug, characterized in that said R<sub>4</sub> Is - OCH<sub>2</sub> R<sub>8</sub> , - CH<sub>2</sub> R<sub>8</sub> , - R<sub>8</sub> ; R<sub>8</sub> Selected from the following group optionally substituted: oxa cyclopropane, oxetane, tetrahydrofuran, tetrahydro - 2H - pyran, pyran, azetidine, pyrrolidine, piperidine, morpholine, morpholine -3 - one or thiomorpholine 1, 1 - dioxide; substituted ethylenically H, C<sub>1</sub> - C<sub>6</sub> Alkyl, C<sub>2</sub> - C<sub>8</sub> Heterocyclic alkyl, C<sub>3</sub> - C<sub>8</sub> Cycloalkyl, - S(O<sub>2</sub>) C<sub>1</sub> - C<sub>6</sub> Alkyl, - S(O<sub>2</sub>) (CH<sub>2</sub>)<sub>w</sub> C<sub>3</sub> - C<sub>8</sub> Cycloalkyl, - S(O<sub>2</sub>) (CH<sub>2</sub>)<sub>w</sub> C<sub>2</sub> - C<sub>8</sub> Heterocyclic alkyl, - C(O) C<sub>1</sub> - C<sub>6</sub> Alkyl, - C(O) (CH<sub>2</sub>)<sub>w</sub> C<sub>3</sub> - C<sub>8</sub> Cycloalkyl, - C(O) (CH<sub>2</sub>)<sub>w</sub> C<sub>2</sub> - C<sub>8</sub> Heterocyclic alkyl, C<sub>2</sub> - C<sub>10</sub> Heteroaryl, C<sub>6</sub> - C<sub>10</sub> Aryl, hydroxy or halogen.

5. In the formula (I) compound or its stereoisomers according to Claim 4, tautomers or its pharmaceutically acceptable salt or solvate or prodrug, characterized in that said R<sub>4</sub> Selected from the following

# Case 4: 检索2019年2月，与CD137相关的，人用药，含抗原或抗体的医药配置品（生物药类专利）

The screenshot shows the Reaxys Query Builder interface. The search criteria are as follows:

- Group 1: Patents: Main IPC OR Patents: Secondary IPC, both containing 'a61k 39/00'.
- AND: Document Basic Index, containing 'cd137'.
- AND: Patents: Date of publication, containing '2019/02'.

Annotations on the screenshot:

- A box labeled "Contains 便于快速模糊检索" points to the "contains" dropdown menus.
- A box labeled "4个模块同时组合, 并设定需要逻辑" points to the overall query structure.
- A box on the right provides details: "IPC分类:人用药类A61K, 含抗体类39/00", "关键索引: CD137", and "公开日期: 2019年2月 (注: 该公开日期为专利的最后一个公开日期, 不一定是首发。可能是族号, 可能是不同版本的最新公开日期, 如, A1, A2, B)".

# 组合模块构建

Reaxys

Quick search Query builder Results Synthesis planner History

Search in: Reactions > Targets > Substances > **关键词模块**

Import Save Reset form Delete all

Structure Molecular Formula CAS RN **Doc. Index**

在Query Builder中只需要点击所需模块即可进行组合检索

Drag & Drop to build a new query

查询特定模块

Find search fields and forms  
Q ipc

Reaxys ^

- ◇ Patents: Main IPC
- ◇ Patents: Secondary IPC

Feedback

# 检索结果

METHODS AND COMPOSITIONS FOR PREPARING GENETICALLY ENGINEERED CELLS

2 JUNO THERAPEUTICS, INC.; BONYHADI, Mark L. WO2019/32929, 2019, A1

Patent Family Members: WO2019/32929 A1

Abstract  Claims  **Front Page Info**  Full Text [↗](#)

Claims hit: {...of CD28, CD137 (4-1-BB), OX40, or ICOS.42. The method of claim 41, wherein...}

Assignees		Inventors (Authors)	
JUNO THERAPEUTICS, INC.; BONYHADI, Mark L.		BONYHADI, Mark L.	
Patent No	Kind Code	Publ. Date	Application No
WO2019/32929	A1	2019/02/14	WO2018-US46151
Priority No	公开日期 授权状况		Priority Date
US2017-543359P			2017/08/09
Patent Classification			
Main IPC	A61K 39/00		
Secondary IPC	C12N 5/0783		
<b>IPC 分类</b>			

## Claims

### CLAIMS

#### WHAT IS CLAIMED:

1. A method for genetically engineering (a) incubating an input composition, or T cells, wherein the stimulating conditions or more intracellular signaling domains (b) introducing a nucleic acid encoding incubating.

2. A method for genetically engineering population of T cells comprising naive-like the stimulating conditions comprises the or more intracellular signaling domains

the incubating the input composition under stimulating conditions is performed prior to, during and/or subsequent to introducing a nucleic acid encoding a receptor.

3. The method of claim 1 or claim 2, wherein the incubating is carried out for at least 3 days.

4. The method of claim 1 or claim 2, wherein the incubating is carried out for at least 4 days.

5. The method of claim 1 or claim 2, wherein the incubating is carried out for at least 5 days.

6. The method of claim 1 or claim 2, wherein the incubating is carried out for at least 6 days.

7. A method for stimulating T cells, the method comprising:

(a) incubating, under stimulating conditions, an input composition comprising T cells comprising a culture-initiating amount of naive-like T cells or a CD8+ stimulated composition, wherein the stimulating conditions comprise the presence of a stimulatory reagent capable of activating one or more intracellular signaling components of a TCR complex and/or one or more intracellular signaling domains of one or more costimulatory molecules, thereby generating a stimulated

(b) introducing into the stimulated cell composition a nucleic acid encoding a genetically engineered recombinant receptor, wherein the method thereby generating

cells expressing the genetically engineered recombinant receptor.

专利‘Claim’部分的摘取和可索引，对于生物药类专利的检索非常有利。

通常生物药类的专利，不具有结构式，且专利标题和摘要一般会撰写得比较简单，造成了生物药类专利检索的困难

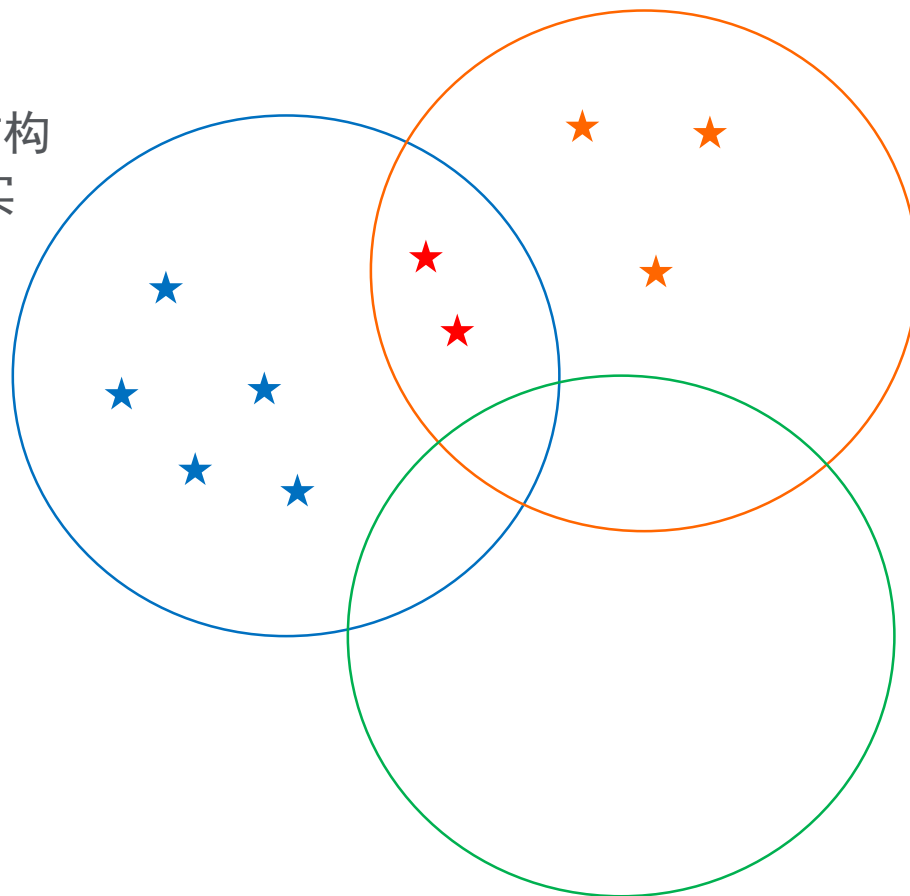


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# 基于全新化合物评估的Markush检索

- Markush检索概览

Markush A结构  
包含范围及实  
施例

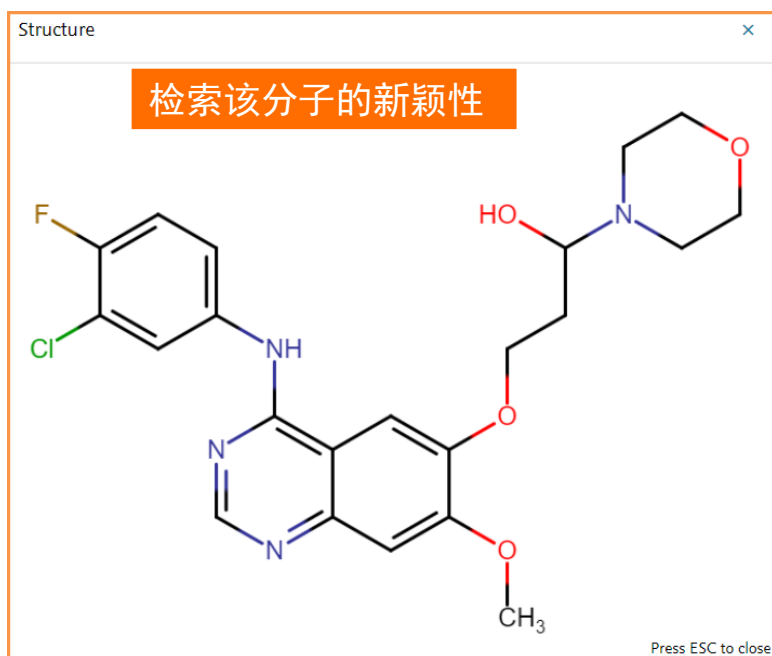


Markush B结构  
包含范围及实  
施例

Markush C结构包含  
范围，必须保证覆盖  
范围没有实施例，才  
有可能被授权

# Markush检索的基本模式

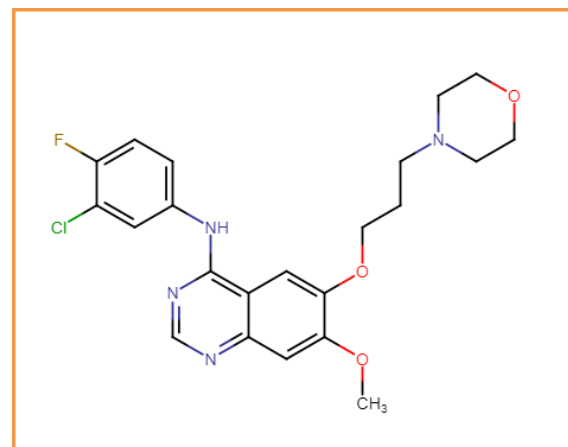
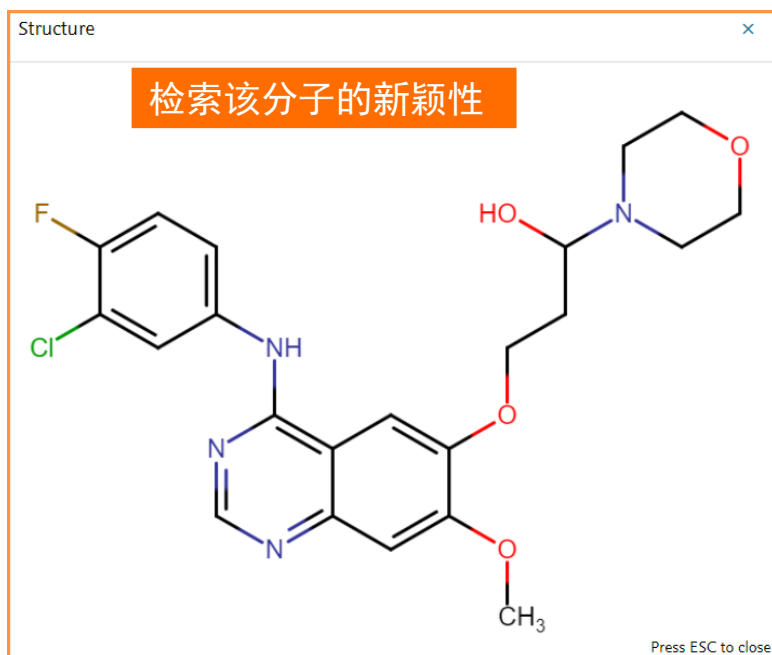
- Reaxys数据库中markush检索需要手动分辨结构分子的新颖性



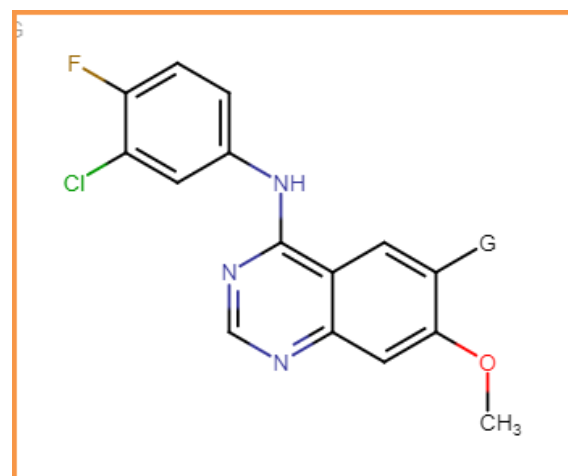
0	Substances	Structure :  as drawn	直接检索结果为零
0	Targets	Structure :  as drawn	
0	Substances	Structure :  average similarity; included: only absolute stereo, additional ring closures allowed, salts, mixtures, isotopes, charges, radicals	
0	Reactions	Reaction Query :  as drawn	

# Markush检索的基本模式

- 通过分析之后，可以通过相似已存在结构的markush锁定结果



方法1：相关性最高检索



方法2：限定一定范围的检索



# Markush检索的基本模式-方法1：最相关结构检索

Reaxys® Quick search Query builder Results Synthesis planner History Register > Sign in

Structure editor ChemAxon's MarvinJS Create structure template from name >

Search this structure as:

- As drawn
- As substructure
- Similar
- Tautomers
- Stereo
- Additional ring closures
- Related Markush
- Salts
- Mixtures
- Isotopes
- Charges
- Radicals

Markush检索，会把‘结构式’中确切的部分去匹配专利中的‘实施例结构’命中相关专利

整个分子都是确切结构

除开‘G’官能团的剩下部分是确切结构

注意关联Markush其余的‘异构体’选项请关闭以避免干扰

# Markush检索的基本模式-检索结果

Reaxys® Quick search Query builder Results Synthesis planner History Register > Sign in

11 Substances out of 6,211 Documents, containing 116 Reactions, 1,069 Targets

1 selected Limit To Exclude Export

1 gefitinib C22H24N4ClF03 44  
Identification  
Druglikeness  
Physical Data - 88  
Other Data - 2,972

2  
Reaxys ID: 11329531  
11329531  
Identification  
Other Data - 3

3  
Reaxys ID: 18419582  
18419582  
Identification  
Other Data - 42

4  
Reaxys ID: 20784707  
20784707  
Identification  
Documents - 1 >

Preparations - 76 >  
Reactions - 116 >  
Targets - 1,069 >  
Documents - 6,211 >

Sort by No of References ↓ Grid Heatmap

Feedback

排除第一个结构所包含的文献，即为10个Markush结构对应的专利

方法1：相关性最高检索检索结果中，除去第一个为所画结构本身，剩下的结构均为，包含该‘具体结构为实施例’的专利中‘Markush结构’

# Markush检索的基本模式-检索结果

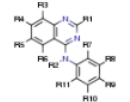
10 Substances out of 9 Documents, containing 0 Reactions, 0 Targets

10个 'Markush' 结构, 9篇专利

Reaxys - 10

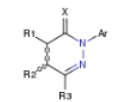
0 selected Limit To Exclude Export

Sort by No of References ↓ Grid Heatmap

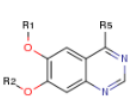
1 

Reaxys ID: 11329531  
11329531  
Identification  
Other Data - 3

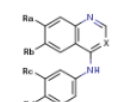
Documents - 1 >

2 

Reaxys ID: 18419582  
18419582  
Identification  
Other Data - 42

3 

Reaxys ID: 20784707  
20784707  
Identification

4 

Reaxys ID: 23992506  
23992506  
Identification  
Other Data - 5

9 Documents with 10 Substances, 0 Reactions, 0 Targets

Reaxys - 9

0 selected Limit To Exclude Export

Sort by Publication Year ↓ Heatmap

1 A preparation method of gefitinib (by machine translation)  
Lunan Pharmaceutical Group Co., Ltd.; Zhang Guimin; Dong Huaimin; Yu Junhou - CN108727284, 2018, A  
Abstract Claims Front Page Info Substances 9 Reactions 12 Full Text  
Hit Substances 2


2 Quinazoline derivatives and use thereof (by machine translation)  
Zhengzhou University The First Affiliated Hospital; Cheng Weiyan; Zhang Xiaojian; Tian Xin - CN106432202, 2017, A  
Patent Family Members: CN106432202 A; CN106432202 B  
Abstract Claims Front Page Info Substances 21 Reactions 19 Full Text  
Hit Substances 2

3 PROCESS FOR PREPARING QUINAZOLINE DERIVATIVE  
SCINOPHARM (CHANGSHU) PHARMACEUTICALS, LTD.; ZHANG, Xiaoheng; LV, Xizhou - WO2015/188318, 2015, A1  
Patent Family Members: CA2914990 A1; WO2015/188318 A1; AU2014389984 A1; TW2016/2085 A; CN105377820 A; ...  
Abstract Claims Front Page Info Substances 14 Reactions 28 Full Text  
Hit Substances 2

4 COMBINATION PRODUCTS WITH TYROSINE KINASE INHIBITORS AND THEIR USE  
NOVARTIS AG; TIEDT, Ralph; CHATENAY-RIVAUDAY, Christian; ITO, Moriko; PENG, Bin; GONG, Ying; AKIMOV, Mikhail - WO2013/149581, 2013, A1  
Patent Family Members: WO2013/149581 A1; CA2868202 A1; AU2013243097 A1; CN104245701 A; KR2015/1782 A; ...  
Abstract Claims Front Page Info Substances 6 Targets Full Text  
Hit Substances 2

5 SMALL MOLECULE COMPOUNDS FOR TARGETING INFLAMMATORY CONDITIONS  
Brooks, Marvin B. - US2013/281448, 2013, A1  
Patent Family Members: WO2013/158482 A1; US2013/281448 A1; US2015/31695 A1  
Abstract Claims Front Page Info Substances 5 Full Text  
Hit Substances 3

6 Method of Synthesizing 6,7-Substituted 4-Anilino Quinazoline  
Shih, Kae-Shyang; Hsieh, Yu-Jung; Liu, Ching-Wei - US2010/267949, 2010, A1  
Patent Family Members: CN101863844 A; US2010/267949 A1; CN101863844 B  
Abstract Claims Front Page Info Substances 27 Reactions 18 Full Text  
Hit Substances 2



ELSEVIER

# Markush检索的基本模式-方法2：一定范围扩展结构检索

➤ 需要进一步检索新颖性时，可进行一定范围限定的扩展检索



The screenshot displays the Reaxys software interface. At the top, there are navigation tabs: "Quick search", "Query builder", "Results", "Synthesis planner", and "History". On the right side, there are buttons for "Register" and "Sign in". The main workspace is the "Structure editor" using "ChemAxon's MarvinJS". It features a toolbar with various editing tools and a central canvas showing a chemical structure. The structure consists of a benzimidazole core. One benzimidazole nitrogen is bonded to a benzene ring substituted with a fluorine atom (F) and a chlorine atom (Cl). The other benzimidazole nitrogen is bonded to a benzene ring substituted with a methoxy group (-OCH<sub>3</sub>) and a Markush group (G). To the right of the structure editor is a search options panel titled "Search this structure as:". It includes radio buttons for "As drawn" (selected), "As substructure", and "Similar". Below these are checkboxes for "Tautomers", "Stereo", "Additional ring closures", "Related Markush", "Salts", "Mixtures", "Isotopes", "Charges", and "Radicals". A "+ More options" link is at the bottom of the panel. At the bottom of the interface, there are buttons for "Clear", "Cancel", and "Transfer to query".

除开‘G’官能团的剩下部分是‘确切结构’，索引实施例包含确切结构的专利

# Markush检索的基本模式-检索结果

Reaxys<sup>®</sup> Quick search Query builder Results Synthesis planner History Register > Sign in

1,341 Substances out of 6,429 Documents, containing 2,813 Reactions, 1,125 Targets

0 selected Limit To Exclude Export

Sort by No of References ↓ Grid Heatmap

Reaxys - 1,341

1 gefitinib  
C22H24N4ClFO3 446.909 8949523 184475-35-2

Identification Bioactivity (All) Spectra - 65 Preparations - 76 >  
Druglikeness Physical Data - 88 Other Data - 2,972 Reactions - 116 >  
Targets - 1,069 >  
Documents - 6,211 >

2

3

4

Spectra - 17

Preparations - 41 >  
Reactions - 254 >  
Targets - 7 >  
Documents - 72 >

Preparations - 3 >  
Reactions - 3 >  
Targets - 81 >  
Documents - 44 >

Preparations - 13 >  
Reactions - 109 >  
Documents - 28 >

Feedback

1.34 K Filters

Limit to > Exclude >

By Structure >  
Measurement pX >  
Highest Clinical Phases >  
Targets >  
Parameters >  
Substance Classes >  
Molecular Weight >  
Number of Fragments >  
Availability >  
Availability in other databases >  
Available Data >  
Document Type >  
Publication Year >  
Patent Assignee >  
LogP >  
H Bond Donors >  
H Bond Acceptors >  
Rotatable Bonds >  
TPSA >

在结果集中筛选‘无分子量’的‘Markush’

Molecular Weight

Clear selected x ↓ ↑ Sort by Occurrence v x

<input type="checkbox"/> >816 - 828	1
<input type="checkbox"/> >780 - 792	1
<input type="checkbox"/> >768 - 780	1
<input type="checkbox"/> >744 - 756	1
<input type="checkbox"/> >720 - 732	1
<input type="checkbox"/> >708 - 720	1
<input type="checkbox"/> >672 - 684	1
<input type="checkbox"/> >660 - 672	1
<input type="checkbox"/> >336 - 348	1
<input checked="" type="checkbox"/> (no entry given)	90

< 1 2 3 > Limit to > Exclude >

# Markush检索的基本模式-检索结果

Reaxys® Quick search Query builder **Results** Synthesis planner History Register Sign in

90 Substances out of 63 Documents, containing 16 Reactions, 1 Targets

90个 'Markush' 结构, 63篇专利

63 Documents with 90 Substances, 16 Reactions, 1 Targets

1 A benzo nitrogen hetero-aromatic ring compound and its preparation method and application (by machine translation)  
No author - CN107674059, 2018, A  
Patent Family Members: CN107674059 A  
Abstract Claims Front Page Info Substances 73 Reactions 107 Full Text  
Hit Substances 3

2 A model of the Buddhist compound  
Beijing University of Chemical Technology; Q  
Patent Family Members: CN108047209 A  
Abstract Claims Front Page Info  
Hit Substances 10

3 Lian xi amide-group-containing compound or protein labeling application in (b  
Peking University; Lei Xiaoguang; Li Qiang; L  
Patent Family Members: CN108148006 A  
Abstract Claims Front Page Info  
Hit Substances 5

Identification

Claims

1. The formula I shows the benzene and nitrogen hetero-aromatic ring compound or its pharmaceutically acceptable salts, stereoisomers, racemic modification, or a prodrug or solvate:  
R and R' in one of the substituted group is selected from The other substituted the base elects from the hydrogen, methoxy, methoxyethoxy,  
R'' is a substituted or unsubstituted phenyl, phenyl substituted group is selected from halogen, -NO<sub>2</sub>, -CN, -OH, R<sup>1</sup>R<sup>2</sup>N-, (3-fluorophenyl) methoxy, C<sub>1-6</sub> Alkyl, halogen substituted C<sub>1-6</sub> Alkyl, C<sub>2-6</sub> Alkenyl, C<sub>2-6</sub> Alkynyl, C<sub>3-6</sub> Cycloalkyl, C<sub>1-6</sub> Alkoxy, halogen-substituted C<sub>1-6</sub> Alkoxy, C<sub>3-6</sub> Naphthenic oxy; R<sup>1</sup>, R<sup>2</sup> Are respectively independently represent H, C<sub>1-6</sub> Alkyl;  
Wherein Q is selected from  
L<sup>1</sup> C selected from C<sub>2-8</sub> Alkyl, C<sub>2-6</sub> Alkenyl, C<sub>2-6</sub> Alkynyl, C<sub>3-6</sub> Cycloalkyl, and L<sup>1</sup> In S can then be<sup>1</sup> Substituted;  
A<sup>1</sup> Is selected from -O-, -NH-, S(=O)<sub>m</sub>, Amide linkage, ester bond (-COO-), (-COS-) thioester bond, disulfide bond, double bond [...], n-O or covalent bond, and A<sup>1</sup> In S can then be<sup>2</sup> Substituted;  
L<sup>2</sup> Said C<sub>2-8</sub> Alkyl, C<sub>2-6</sub> Alkenyl, C<sub>2-6</sub> Alkynyl, C<sub>3-6</sub> Cycloalkyl or covalent bond, and L<sup>2</sup> In S can then be<sup>3</sup> Substituted;  
A<sup>2</sup> Said -O-, -NH-, S(=O)<sub>m</sub>, C<sub>1-6</sub> Alkyl, C<sub>2-6</sub> Alkenyl, C<sub>2-6</sub> Alkynyl, C<sub>3-6</sub> Cycloalkyl, and A<sup>2</sup> In S can then be<sup>4</sup> Substituted;  
M=0, 1 or 2;  
S<sup>1</sup>, S<sup>2</sup>, S<sup>3</sup> And S<sup>4</sup> Are independently selected from -CN, -CF<sub>3</sub>, -CO<sub>2</sub>H, halogen, C<sub>1-6</sub> Alkyl, C<sub>3-6</sub> Cycloalkyl, C<sub>2-6</sub> Alkenyl, C<sub>2-6</sub> Alkynyl, R<sup>3</sup>O-, R<sup>3</sup>R<sup>4</sup>N-, R<sup>3</sup>S(=O)<sub>m</sub>-, R<sup>3</sup>R<sup>4</sup>NS(=O)<sub>m</sub>-, R<sup>3</sup>R<sup>4</sup>NC(=O)-, R<sup>3</sup>R<sup>4</sup>NC(=O)O-, R<sup>3</sup>OC(=O)-, R<sup>5</sup>C(=O)-, R<sup>5</sup>C(=O)NR<sup>3</sup>-, R<sup>3</sup>R<sup>4</sup>NC(=O)NR<sup>6</sup>-, R<sup>3</sup>OC(=O)NR<sup>6</sup>-, R<sup>3</sup>S(=O)<sub>m</sub>NR<sup>6</sup>-, R<sup>3</sup>R<sup>4</sup>NS(=O)<sub>m</sub>NR<sup>6</sup>-, R<sup>3</sup>R<sup>4</sup>NC(=NR<sup>7</sup>)NR<sup>6</sup>-, R<sup>3</sup>R<sup>4</sup>NC(=CHNO<sub>2</sub>)NR<sup>6</sup>-, R<sup>3</sup>R<sup>4</sup>NC(=N-CN)NR<sup>6</sup>-, R<sup>3</sup>R<sup>4</sup>NC(=NR<sup>7</sup>)-, R<sup>3</sup>S(=O)(=NR<sup>7</sup>)NR<sup>6</sup>- Or R<sup>3</sup>R<sup>4</sup>NS(=O)(=NR<sup>7</sup>)-;  
R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup> And R<sup>7</sup> Are respectively independently represent H, C<sub>1-6</sub> Alkyl, C<sub>3-6</sub> Cycloalkyl, C<sub>2-6</sub> Alkenyl, C<sub>2-6</sub> Alkynyl; when R<sup>3</sup> And R<sup>4</sup> Connected to the same nitrogen atom when on, together with the nitrogen atom can form a C<sub>3-12</sub> Heterolipid ring, this C<sub>3-12</sub> Heterolipid ring can include O, N, S(=O)<sub>m</sub> The hetero atom; and R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup> And R<sup>7</sup> Testing gas channel can be halogen, CN, C<sub>1-6</sub> C alkyl or C<sub>3-6</sub> Cycloalkyl substituted.

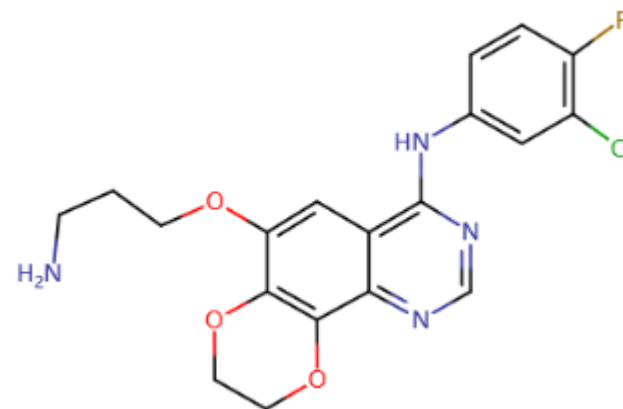
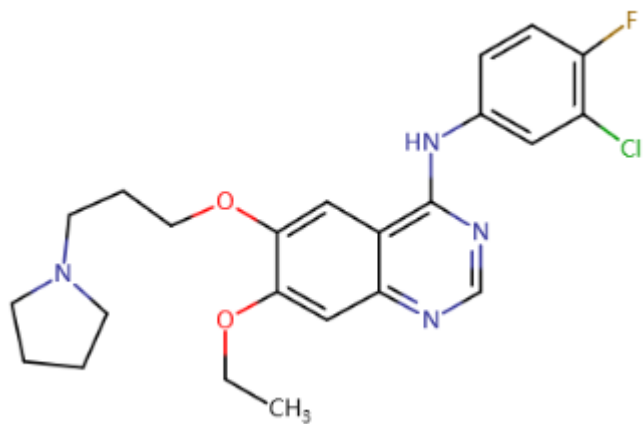
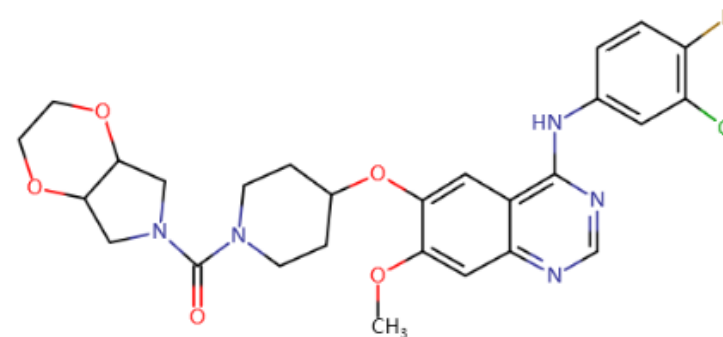
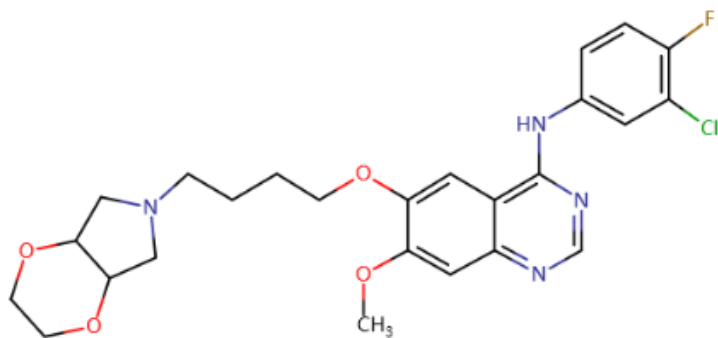
2. Benzo nitrogen hetero-aromatic ring compound according to Claim 1, characterized in that R and R' in one of the substituted group is selected from The other substituted the base elects from the hydrogen, methoxy, methoxyethoxy, R'' is a substituted or unsubstituted phenyl, phenyl substituted ethynyl group is selected from, F, Cl, Br, (3-fluorophenyl) methoxy, -NH<sub>2</sub>, -N(CH<sub>3</sub>)<sub>2</sub>;  
Wherein Q is selected from  
L<sup>1</sup> Is selected from -(CH<sub>2</sub>)<sub>t</sub>-, T is 2-8 integer;  
A<sup>1</sup> Is selected from -O-, -NH-, -NH- in C can then be C<sub>1-6</sub> Alkyl substituted, -S-, -SO-, -SO<sub>2</sub>- Or a covalent bond;  
L<sup>2</sup> Is selected from -(CH<sub>2</sub>)<sub>n</sub>-, N is 0-8 integer;  
A<sup>2</sup> Is selected from -O-, -NH-, -S-, -SO-, -SO<sub>2</sub>-.

3. Benzo nitrogen hetero-aromatic ring compound according to Claim 2, characterized in that R and R' in one of the substituted group is selected from The other substituted the base elects from the hydrogen, methoxy, R'' is a substituted or unsubstituted phenyl, phenyl substituted ethynyl group is selected from, F, Cl, Br, (3-fluorophenyl) methoxy, phenyl may be mono-substituted, can also be a multi-substituted;  
Wherein Q is selected from  
L<sup>1</sup> Is selected from -(CH<sub>2</sub>)<sub>t</sub>-, T is 2-7 of the integer;  
A<sup>1</sup> Is selected from -O-, -NH-, -NH- in C can then be C<sub>1-3</sub> Alkyl substituted or covalent bond;  
L<sup>2</sup> Is selected from -(CH<sub>2</sub>)<sub>n</sub>-, N is 0-2 integer;  
A<sup>2</sup> Is selected from -O-, -NH-, -S-, -SO<sub>2</sub>-.

专利的 'claim' 可以直接展开阅读

# CASE 5: 评估以下化合物的可专利性

➤ 当有多个分子需要同时评估时，可设计Markush结构



# Reaxys中的Markush检索

Reaxys<sup>®</sup> Quick search Query builder Results Synthesis planner History Sam Yu

Structure editor Create structure template from name >

R<sub>1</sub> R<sub>2</sub> R<sub>3</sub>

R1=

R2=

R3=

Search this structure as:

- As drawn
- As substructure
  - On all atoms
  - On heteroatoms
- Similar

Include

- Tautomers
- Stereo
- Additional ring closures
- Related Markush
- Salts
- Mixtures
- Isotopes
- Charges
- Radicals

+ More options

Clear Cancel Transfer to query Feedback



# 利用分子量筛选，筛出Markush结构

Reaxys<sup>®</sup> Quick search Query builder Results Synthesis planner History Sam Yu

37 Filters and Analysis

448

By Structure Measurement pX Highest Clinical Phases Targets Parameters Substance Classes Molecular Weight (no entry given) 37 Availability Availability in other databases Available Data Document Type Publication Year

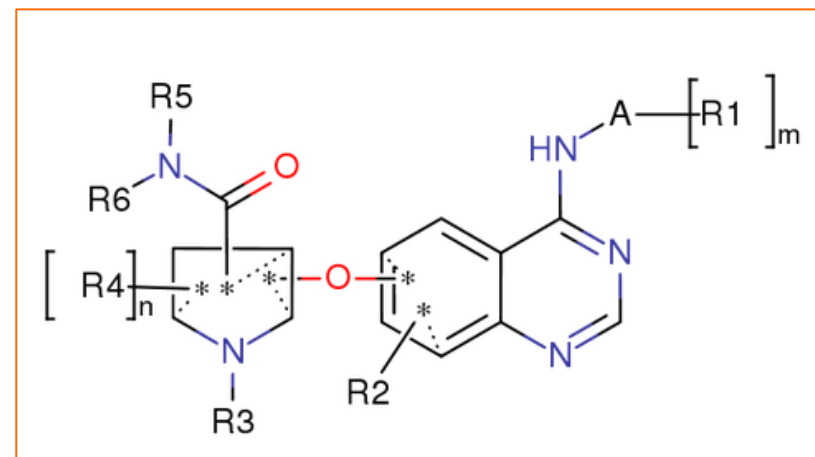
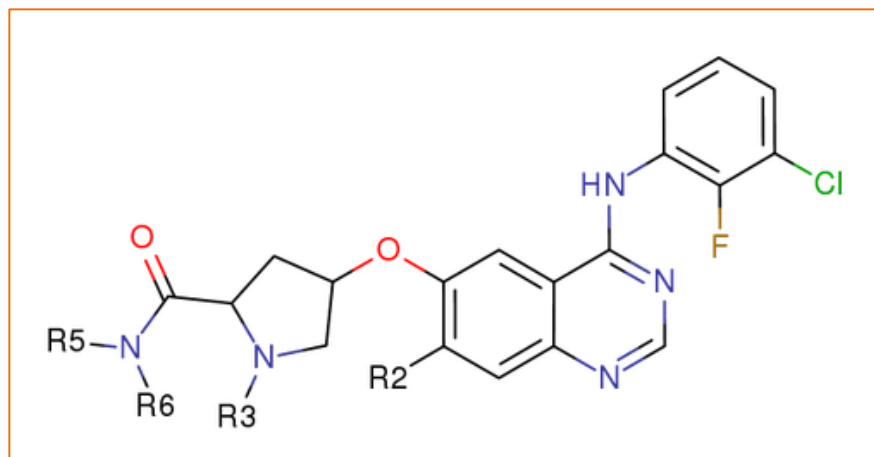
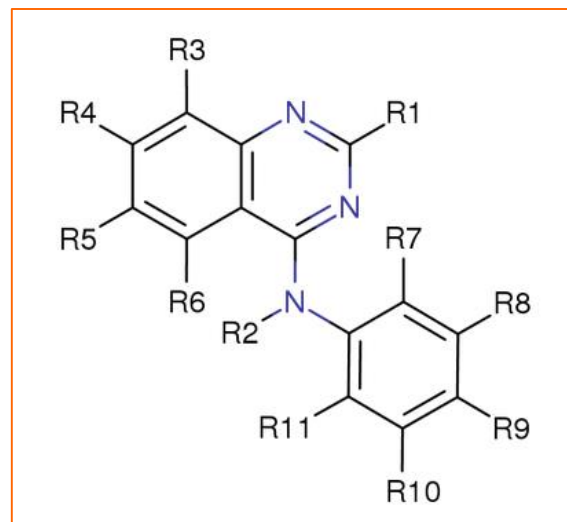
37 Substances out of 28 Documents, containing 11 Reactions, 0 Targets

0 selected Link To Exclude Export Sort by No of References Heatmap

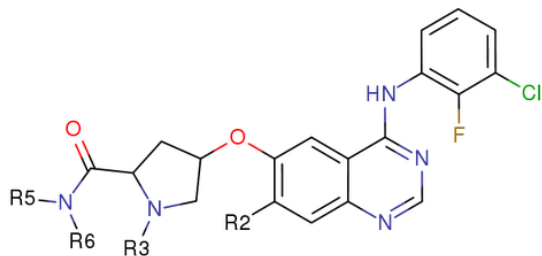
1 Reaxys ID: 11329531 11329531 Identification Other Data - 3 Documents - 1

2 Reaxys ID: 11334491 11334491 Identification Other Data - 4 Documents - 1

3 Reaxys ID: 12250782 12250782 Identification Documents - 1



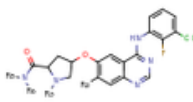
# Markush结构的解析



有时候，根据每篇专利的发明情况不同，可能会出现多个markush结构。Reaxys中的Markush标记出该结构在专利Claim中的位置

Reaxys ID: 12250782  
12250782

Identification Documents - 1 >



**Identification**

Reaxys ID: 12250782

Chemical Names:

CAS Registry Number(s):

Molecular Formula:

Molecular Weight:

InChIKey:

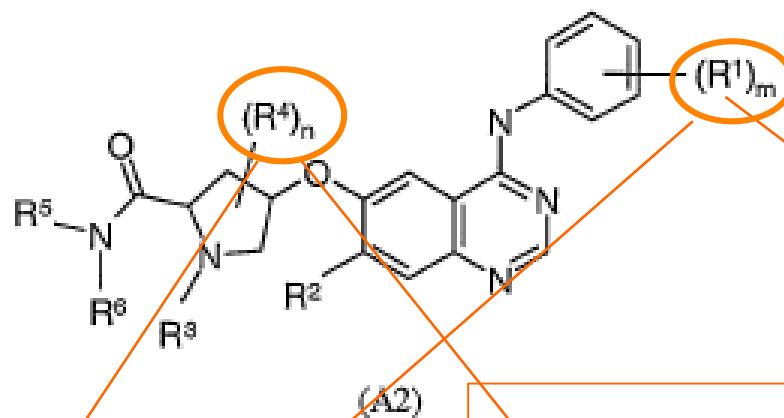
Location in Patent	Reference
Claim 24	ASTRAZENECA AB; ASTRAZENECA UK LIMITED - WO2005/30757, 2005, A1 <a href="#">Full Text ↗</a> <a href="#">Show details &gt;</a>

Substance Label - 1

Patent-Specific Data - 1

# Rx辅助专利中Markush结构的解读

24. A quinazoline derivative according to any one of the preceding claims having a structural sub-formula A2



wherein:

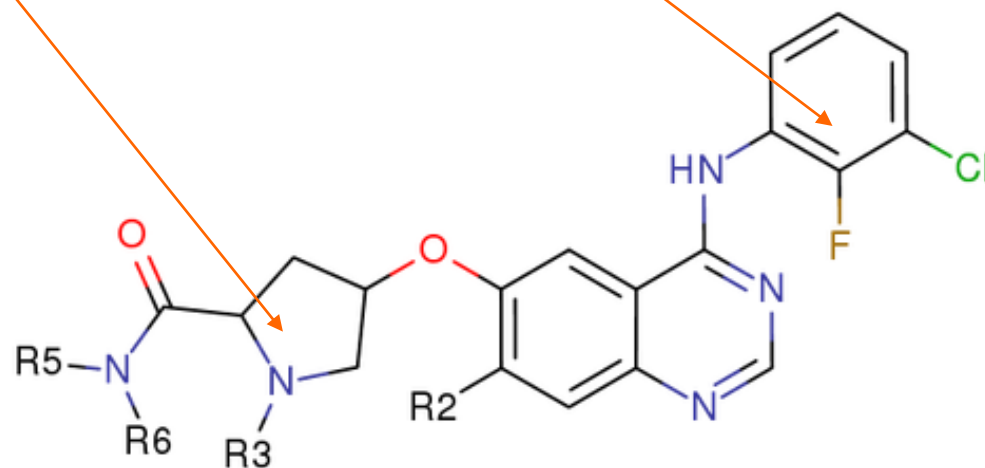
$m$  is 2 and  $R^1$  is 2-fluoro and 3-chloro;

$R^2$  is methoxy;

$R^3$  is methyl;

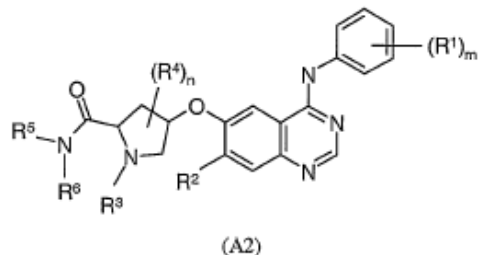
$n$  is 0;

Markush结构查新仅仅是起始，对于重要化合物保护专利，Markush结构的解读便于分析该专利排他性范围到底如何。



# 专利原文中对该结构的描述

24. A quinazoline derivative according to any one of the preceding claims having a structural sub-formula A2



wherein:

m is 2 and R<sup>1</sup> is 2-fluoro and 3-chloro;

R<sup>2</sup> is methoxy;

R<sup>3</sup> is methyl;

n is 0;

专利原文用文字进行结构的描述，  
较为复杂，不易阅读

WO 2005/030757

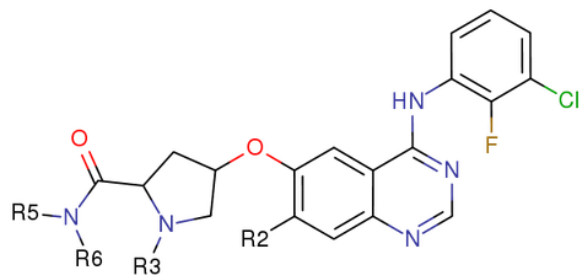
- 184 -

PCT/GB2004/004085

and R<sup>5</sup> is hydrogen or (1-6C)alkyl and R<sup>6</sup> is selected from substituted-(1-6C)alkyl (wherein substituted-(1-6C)alkyl is (1-6C)alkyl substituted by 1, 2 or 3 substituents independently selected from (1-6C)alkoxycarbonyl, carbamoyl, (2-6C)alkanoylamino, and oxo or a (1-6C)alkoxycarbonyl together with a hydroxy group), (1-6C)alkoxy, (1-6C)alkylsulfonyl, (3-7)heterocyclyl (wherein the heterocyclyl is carbon linked), heteroaryl, (3-7)heterocyclyl(1-6C)alkyl (wherein the heterocyclyl is carbon linked to the (1-6C)alkyl moiety) and heteroaryl(1-6C)alkyl, and wherein any heteroaryl or (3-7)heterocyclyl group within R<sup>6</sup> is optionally substituted (on any available carbon atoms) by 1, 2 or 3 substituents independently selected from halogeno, (1-6C)alkyl, hydroxy(1-6C)alkyl, (1-6C)alkoxycarbonyl, carbamoyl, (2-6C)alkanoylamino and hydroxy and/or optionally a substituent selected from oxo, cyano, nitro and (1-4C)alkoxy, and wherein any heteroaryl or heterocyclyl group within R<sup>5</sup> is optionally substituted on any available ring nitrogen (provided the ring is not thereby quaternised) by (1-4C)alkyl or (2-4C)alkanoyl, or R<sup>5</sup> and R<sup>6</sup> together with the nitrogen atom to which they are attached form a 4, 5 or 6 membered ring which contains one or two nitrogen atoms as the only heteroatoms present in the ring and which is optionally and which is substituted on an available ring carbon atom by 1 or 2 substituents independently selected from carbamoyl and (1-3C)alkylenedioxy.

25. A quinazoline derivative according to claim 24, wherein R<sup>6</sup> is selected from (3-7)heterocyclyl (wherein the heterocyclyl is carbon linked), heteroaryl, (3-7)heterocyclyl(1-6C)alkyl (wherein the heterocyclyl is carbon linked to the (1-6C)alkyl moiety) and heteroaryl(1-6C)alkyl, and wherein any heteroaryl or (3-7)heterocyclyl group within R<sup>6</sup> is optionally substituted (on

# Reaxys将结构翻译成图表



图表形式的解读更容易帮助理解结构保护的范

Label	Value	Size	Attributes	Substituted by	Frequency
R2	methoxy				
R3	methyl				
R5	hydrogen				
R6	alkyl	1-6C		<b>\$\$8</b>	0-3
	hydrogen				
	alkyl	1-6C			
	alkenyl	2-8C			
	alkynyl	2-8C			
	alkoxy	1-6C			
	cycloalkyl	3-7C			
	alkylsulfonyl	1-6C			
heterocyclyl				<b>\$\$9</b>	0-2
heteroaryl					
	<b>\$\$*cyclalk37\$*alk13</b>				
	<b>\$\$*hetar\$*alk13</b>				
	<b>\$\$*hets\$*alk13</b>				
<b>\$\$1</b>	alkyl	1-4C			

# 内容

## ➤ Elsevier 生命科学解决方案

1. Reaxys对信息的提炼介绍，以及信息检索基础技巧
2. Reaxys专利检索策略
3. RMC辅助药物分子设计研发决策
4. PharmaPendium辅助药物临床研究

## ➤ 总结

# RMC辅助药物分子设计研发决策

- 对文献数据的处理
- 特定信息检索功能
- 辅助药物分子改性

# 查看具体的生物数据

231 Substances out of 2,394 Documents, containing 1,199 Reactions, 65 Targets



0



Limit To



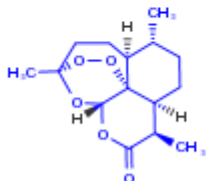
Exclude



Export



1



Reaxys ID: 4194670

C<sub>15</sub>H<sub>22</sub>O<sub>5</sub> 282.337 4194670 63968-64-9

Identification

Druglikeness

Bioactivity (All)

Physical Data - 375

Spectra - 102



## ^ Bioactivity (All)

- ✓ In vitro: Efficacy - 1,358
- ✓ In vivo: Animal Model - 135
- ✓ Metabolism - 160
- ✓ Pharmacokinetic - 98
- ✓ Toxicity/Safety Pharmacology - 343

pX	Parameter	Value (qual)	Value (quant)	Unit	Biological Species	Population	Route of administration	Dose	Dosing regimen	Reference
	metabolic stability	active			mouse		administration	mg/kg		<a href="#">Acquaah-Mensah, George K.; Rich, Stephen M. - Journal of Ethnopharmacology, 2014, vol. 153, # 3, p. 732 - 736</a> Full Text <a href="#">↗</a> Cited 15 times <a href="#">↗</a> Details <a href="#">&gt;</a> Abstract <a href="#">&gt;</a>
	Vd ss/F		1363	L	Human	Healthy	oral administration	500 mg	Single	<a href="#">Simonsson, Ulrika S. H.; Jansson, Britt; Hai, Trinh Ngoc; Huong, Dinh Xuan; Tybring, Gunnel; Ashton, Michael - Clinical Pharmacology and Therapeutics, 2003, vol. 74, # 1, p. 32 - 43</a> Full Text <a href="#">↗</a> Cited 68 times <a href="#">↗</a> Details <a href="#">&gt;</a> Abstract <a href="#">&gt;</a>
	Vd ss/F		967	L	Human	Healthy	oral administration	500 mg	Single	<a href="#">Simonsson, Ulrika S. H.; Jansson, Britt; Hai, Trinh Ngoc; Huong, Dinh Xuan; Tybring, Gunnel; Ashton, Michael - Clinical Pharmacology and Therapeutics, 2003, vol. 74, # 1, p. 32 - 43</a> Full Text <a href="#">↗</a> Cited 68 times <a href="#">↗</a> Details <a href="#">&gt;</a> Abstract <a href="#">&gt;</a>
	AUC		1696	ng.h/mL	Human	Healthy	oral administration	500 mg	Single	<a href="#">Simonsson, Ulrika S. H.; Jansson, Britt; Hai, Trinh Ngoc; Huong, Dinh Xuan; Tybring, Gunnel; Ashton, Michael - Clinical Pharmacology and Therapeutics, 2003, vol. 74, # 1, p. 32 - 43</a> Full Text <a href="#">↗</a> Cited 68 times <a href="#">↗</a> Details <a href="#">&gt;</a> Abstract <a href="#">&gt;</a>



# 单个化合物全部生物活性的导出

Reaxys

Quick search Query builder Results Synthesis planner History Register > Sign in

1 Substances out of 4,158 Documents, containing 0 selected

Export

1: 选择Excel

2: 选择

Export substances Reaxys

Choose a format: **Microsoft Excel**

Range: All results - 1

Export:

- All available data
- Identification data only
- Hit data only
- Choose specific data + Add datapoints

Additional options:  Include structures

Export substances

<input checked="" type="checkbox"/> Medicinal Chemistry		<input checked="" type="checkbox"/> Bioactivity	
<input type="checkbox"/> Other Data	1	<input type="checkbox"/> Druglikeness	1
<input type="checkbox"/> Physical Data	1		
<input type="checkbox"/> Spectra	1		

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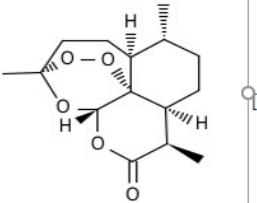
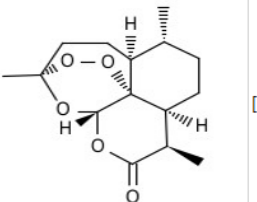
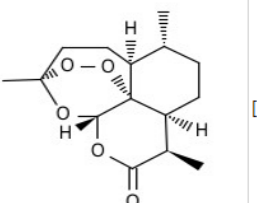
# 导出整理excel表格

The screenshot shows the Microsoft Excel interface with the following elements:

- Excel Ribbon:** The 'Find & Filter' button is highlighted with an orange box.
- Find and Replace Dialog:** A dialog box is open with 'Find what:' set to 'parameter'.
- Sort & Filter Menu:** A dropdown menu is open, showing various filter options. The 'Activity' checkbox is highlighted with an orange box.
- Spreadsheet Data:** The spreadsheet contains columns for chemical structures, SMILES, Substance Links, CAS, and various parameters. The 'Activity' column is highlighted in grey.

筛选各种需要数据

# 导出整理excel表格

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U	V	W	X
1	Structure: Image	SMILES	CAS Regist	Molecular	Molecular	Measure	Unit	Quantitativ	Deviation	Measur	References	Links to Reaxys												
70		[H][C@@]1	63968-64-	C15H22O5	282.337	EC50	muM	5.38	3.66000	5.27	Article; Per	<a href="https://www.reaxys.com/reaxys/secured/hopinto.do?context=C&amp;query=CNR.CNR=6601927&amp;database=RX&amp;origin=ReaxysOutput&amp;ln=">https://www.reaxys.com/reaxys/secured/hopinto.do?context=C&amp;query=CNR.CNR=6601927&amp;database=RX&amp;origin=ReaxysOutput&amp;ln=</a>												
233		[H][C@@]1	63968-64-	C15H22O5	282.337	AUC (0-10	ng.h/mL	1899			Article; Sim	<a href="https://www.reaxys.com/reaxys/secured/hopinto.do?context=C&amp;query=CNR.CNR=6540097&amp;database=RX&amp;origin=ReaxysOutput&amp;ln=">https://www.reaxys.com/reaxys/secured/hopinto.do?context=C&amp;query=CNR.CNR=6540097&amp;database=RX&amp;origin=ReaxysOutput&amp;ln=</a>												
234		[H][C@@]1	63968-64-	C15H22O5	282.337	AUC (0-inf	ng.h/mL	285			Article; Sim	<a href="https://www.reaxys.com/reaxys/secured/hopinto.do?context=C&amp;query=CNR.CNR=6540097&amp;database=RX&amp;origin=ReaxysOutput&amp;ln=">https://www.reaxys.com/reaxys/secured/hopinto.do?context=C&amp;query=CNR.CNR=6540097&amp;database=RX&amp;origin=ReaxysOutput&amp;ln=</a>												

快速删除不需要列  
之后得到的数据表  
格

# RMC-针对专利数据的快速导出

Reaxys® Quick search Query builder Results Synthesis planner History Register > Sign in ⓘ

Search in: Reactions > Targets > Substances > Documents >

Find search fields and forms  
patent

Import Save Reset form Delete all

Structure Molecular Formula CAS RN Doc. Index

Common Patent Number is WO2018/119266

Query Builder界面有针对专利检索的各种模块  
'common patent number' 通过专利号检索专利

WO2009/020825 (专利原文号需要处理成以下形式再检索)  
加工后的专利号: WO2009/20825  
WO2009\*20825

Feedback

# 快速摘取专利中的生物活性数据

1 Documents with 196 Substances, 397 Reactions, 1 Targets

0 selected Limit To Exclude Export

HETEROCYCLIC COMPOUNDS AS IMMUNOMODULATORS  
1 Incyte Corporation; Wu, Liangxing; Qian, Ding-Quan; Lu, Liang; Wenqing US2018/177784, 2018, A1  
Patent Family Members: TW2018/35073 A; US2018/177784 A1; U  
Abstract Claims Front Page Info Substance

Heatmap settings

Value of X-axis Parameter

Value of Y-axis Substances

Value of Cells Maximum of pX

Show substances  Names  Structure drawing

Display mode  Normal  Full Screen

Always show settings Apply

Heatmap

通过热图按钮，建立测量数据与化合物构效关系

# 导出该篇专利的信息

Limit To Exclude **Export** Settings Navigator Legend Documents Exit Full Screen

Export substances and bioactivities

Choose a format: Microsoft Excel

Range: All results - 196

Export:  All available data  Hit data only  Choose specific data

Additional options:  Include structures

Export >

Substances

(S)-1-((8-(2-  
N-(5-chloro...  
6-(2-methyl...  
2-((2-(2-me...  
N-(2-methyl...  
N,N-dimet...  
3-(2-methyl...  
2-(6-(2-met...  
2-((2-(2-me...  
3-(2-methyl...oacetate  
(4-(3-methyl...oacetate  
cis-4-((5-(3-...oacetate

ic50

7  
7  
7  
7  
7  
7  
7

Tab-delimited text

Microsoft Excel  
● Tab-delimited text  
XML  
SD/Molfile

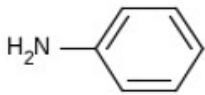
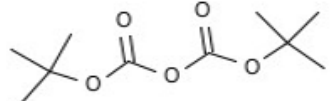
Navigator

Feedback

1. 导出时，选择 ‘hit data’
2. 导出 ‘excel’ 会包含结构式图片
3. 导出 ‘Tab’ 不会包含结构式图片

# 简单整理Excel表格即可规整数据

The screenshot shows an Excel spreadsheet with a table of chemical data. The table has columns for chemical structures, SMILES strings, and various identifiers. A 'Find and Replace' dialog box is open, with the 'Find' tab selected and 'parameter' entered in the 'Find what' field. The 'Find Next' button is highlighted.

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P
1	Structure: Image 	SMILES NC1=CC=C(C=C1)	Substance 605631	Links to ReData	Coun	CAS Regist	Chemical N	Linear Stru	Molecular	Molecular	Type of Su	Type and I	InChI Key	Compositi	Compositi	Compositi
2		CC(C)(C)OC(=O)OC(=O)C(C)(C)C	1911173	https://ww	(2 of 196)	24424-99-di-tert-bu	((C4H9)OC	C10H18O5	218.25	acyclic			DYHSDKLC			

打开表格后：  
1. 全选所有数据  
2. 点击查找  
3. 查找 'parameter'

# 简单整理Excel表格即可规整数据

Excel 2016 功能区：剪贴板、字体、对齐、数字、样式、单元格、公式、数据、窗口、帮助。

工作簿：Reaxys Export 20190407\_111908

	CH	CI	CJ	CK	CL	CM	CN	CO	CP	CO	CR	CS	CT	CU	CV	CW	CX	CY
1	Cell Fractic	Substance	Links to Re	Smiles	Substance	Substance	Substance	Substance	Qualitative	Measure	Unit	Measur	Medchem:	Quantitati	Deviation	Statistical	Statistical	Measurem
2																		

筛选的列表：  
 (Select All)  
 IC50  
 (Blanks)

查找找到 'parameter' 之后，建立 'filter'，并查看筛选需要数据即可

筛选的目的是排除掉 'blank' 中包含的没有数据的事实结构，当专利中有多种数据时，也可以快速选择

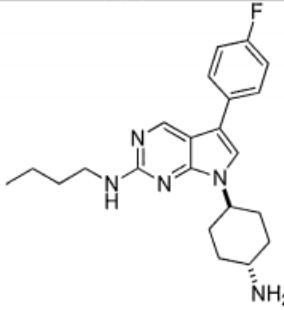


# 整理结果

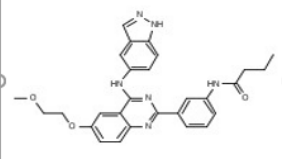
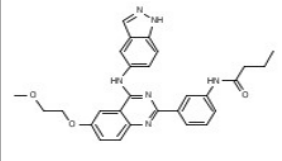
‘SMILES’(可转化为结构), 数据类型, 单位, 数值, 原文, 原文连接

	A	B	C	D	E	F	H	I	J	K	L	M	N	O	P
1	Structure	Bioassay Category	Measu	Unit	Medchem:	Quantitative	References	Links to Reaxys							
2	CN1CCN(CC2=CC=C	In Vitro (Efficacy)	IC50	nM	<	10	Patent, THE UNIVERSI	<a href="https://www.reaxys.com/reaxys/secured/hopinto.do?context=C&amp;query=CNR.CNR=35474696&amp;data">https://www.reaxys.com/reaxys/secured/hopinto.do?context=C&amp;query=CNR.CNR=35474696&amp;data</a>							
3	CCCCNC1=NC=C2C	In Vitro (Efficacy)	IC50	nM	<	10	Patent, THE UNIVERSI	<a href="https://www.reaxys.com/reaxys/secured/hopinto.do?context=C&amp;query=CNR.CNR=35474696&amp;data">https://www.reaxys.com/reaxys/secured/hopinto.do?context=C&amp;query=CNR.CNR=35474696&amp;data</a>							
4	CCCCNC1=NC=C2C	In Vitro (Efficacy)	IC50	nM	<	10	Patent, THE UNIVERSI	<a href="https://www.reaxys.com/reaxys/secured/hopinto.do?context=C&amp;query=CNR.CNR=35474696&amp;data">https://www.reaxys.com/reaxys/secured/hopinto.do?context=C&amp;query=CNR.CNR=35474696&amp;data</a>							
5	CCCCNC1=NC=C2C	In Vitro (Efficacy)	IC50	nM	<	10	Patent, THE UNIVERSI	<a href="https://www.reaxys.com/reaxys/secured/hopinto.do?context=C&amp;query=CNR.CNR=35474696&amp;data">https://www.reaxys.com/reaxys/secured/hopinto.do?context=C&amp;query=CNR.CNR=35474696&amp;data</a>							
6	CCCCNC1=NC=C2C	In Vitro (Efficacy)	IC50	nM	<	10	Patent, THE UNIVERSI	<a href="https://www.reaxys.com/reaxys/secured/hopinto.do?context=C&amp;query=CNR.CNR=35474696&amp;data">https://www.reaxys.com/reaxys/secured/hopinto.do?context=C&amp;query=CNR.CNR=35474696&amp;data</a>							
7	CCCCNC1=NC=C2C	In Vitro (Efficacy)	IC50	nM	<	10	Patent, THE UNIVERSI	<a href="https://www.reaxys.com/reaxys/secured/hopinto.do?context=C&amp;query=CNR.CNR=35474696&amp;data">https://www.reaxys.com/reaxys/secured/hopinto.do?context=C&amp;query=CNR.CNR=35474696&amp;data</a>							
8	N[C@H]1CC[C@H]	In Vitro (Efficacy)	IC50	nM	<	10	Patent, THE UNIVERSI	<a href="https://www.reaxys.com/reaxys/secured/hopinto.do?context=C&amp;query=CNR.CNR=35474696&amp;data">https://www.reaxys.com/reaxys/secured/hopinto.do?context=C&amp;query=CNR.CNR=35474696&amp;data</a>							
9	CCCCNC1=NC=C2C	In Vitro (Efficacy)	IC50	nM	<	10	Patent, THE UNIVERSI	<a href="https://www.reaxys.com/reaxys/secured/hopinto.do?context=C&amp;query=CNR.CNR=35474696&amp;data">https://www.reaxys.com/reaxys/secured/hopinto.do?context=C&amp;query=CNR.CNR=35474696&amp;data</a>							
10	CCCCNC1=NC=C2C	In Vitro (Efficacy)	IC50	nM	<	10	Patent, THE UNIVERSI	<a href="https://www.reaxys.com/reaxys/secured/hopinto.do?context=C&amp;query=CNR.CNR=35474696&amp;data">https://www.reaxys.com/reaxys/secured/hopinto.do?context=C&amp;query=CNR.CNR=35474696&amp;data</a>							
11	CCCC(C)C1=NC=C	In Vitro (Efficacy)	IC50	nM		100 - 1000	Patent, THE UNIVERSI	<a href="https://www.reaxys.com/reaxys/secured/hopinto.do?context=C&amp;query=CNR.CNR=35474696&amp;data">https://www.reaxys.com/reaxys/secured/hopinto.do?context=C&amp;query=CNR.CNR=35474696&amp;data</a>							
12	CCCCNC1=NC=C2C	In Vitro (Efficacy)	IC50	nM	<	10	Patent, THE UNIVERSI	<a href="https://www.reaxys.com/reaxys/secured/hopinto.do?context=C&amp;query=CNR.CNR=35474696&amp;data">https://www.reaxys.com/reaxys/secured/hopinto.do?context=C&amp;query=CNR.CNR=35474696&amp;data</a>							
13	CCCCNC1=NC=C2C	In Vitro (Efficacy)	IC50	nM	<	10	Patent, THE UNIVERSI	<a href="https://www.reaxys.com/reaxys/secured/hopinto.do?context=C&amp;query=CNR.CNR=35474696&amp;data">https://www.reaxys.com/reaxys/secured/hopinto.do?context=C&amp;query=CNR.CNR=35474696&amp;data</a>							
14	CCCCNC1=NC=C2C	In Vitro (Efficacy)	IC50	nM	<	10	Patent, THE UNIVERSI	<a href="https://www.reaxys.com/reaxys/secured/hopinto.do?context=C&amp;query=CNR.CNR=35474696&amp;data">https://www.reaxys.com/reaxys/secured/hopinto.do?context=C&amp;query=CNR.CNR=35474696&amp;data</a>							
15	O[C@H]1CC[C@H]	In Vitro (Efficacy)	IC50	nM	<	10	Patent, THE UNIVERSI	<a href="https://www.reaxys.com/reaxys/secured/hopinto.do?context=C&amp;query=CNR.CNR=35474696&amp;data">https://www.reaxys.com/reaxys/secured/hopinto.do?context=C&amp;query=CNR.CNR=35474696&amp;data</a>							

Table 2 describes compounds prepared following procedures described in Example 2 (General Procedure B), using appropriate reagents. (Note: Mer IC50: +++ means < 10 nM; +++ means between 10-100nM, ++ means between 100 nM-1 μM; + means between 1-30 μM; - means inactive.)

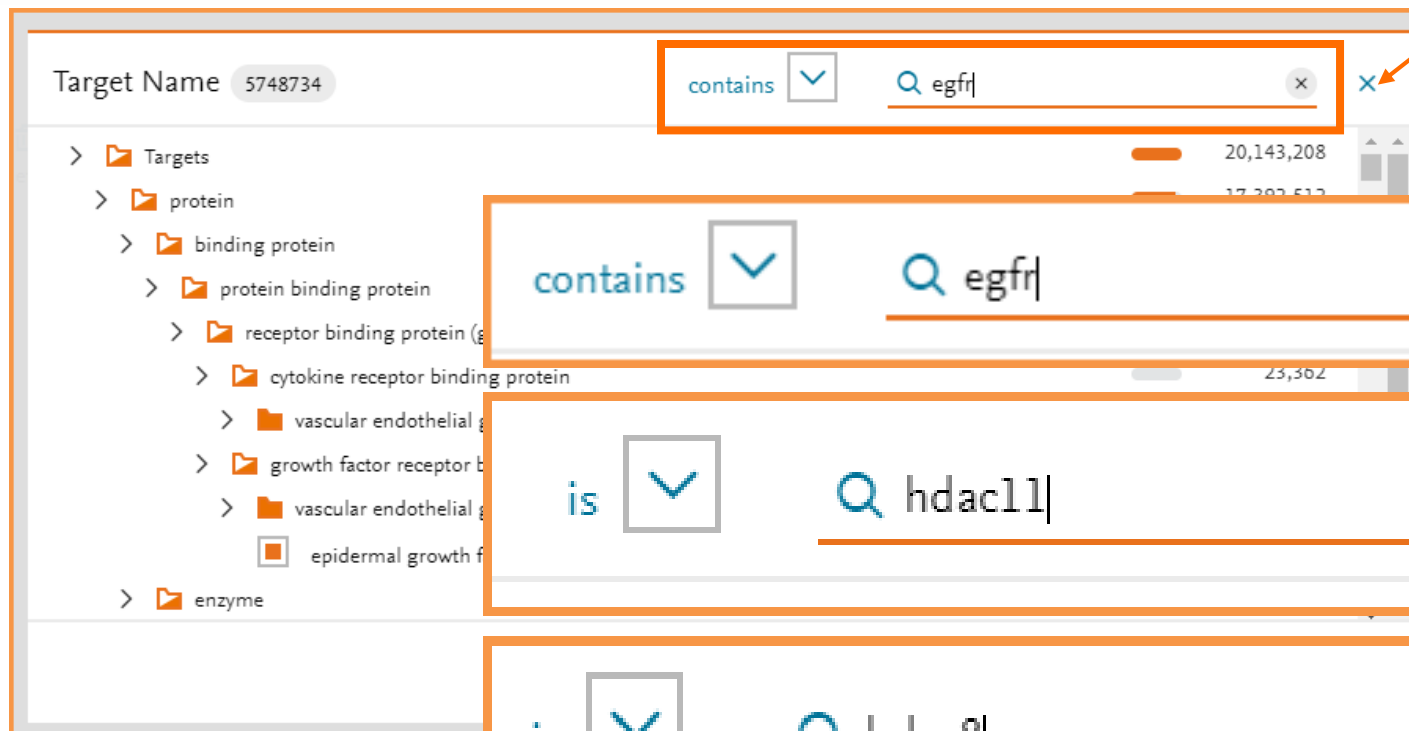
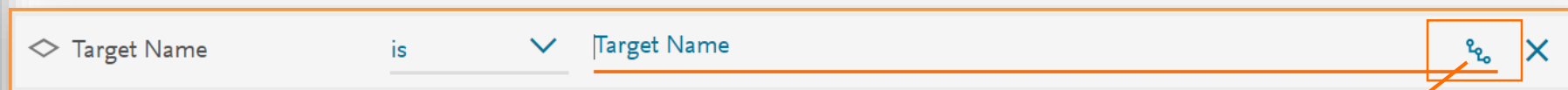
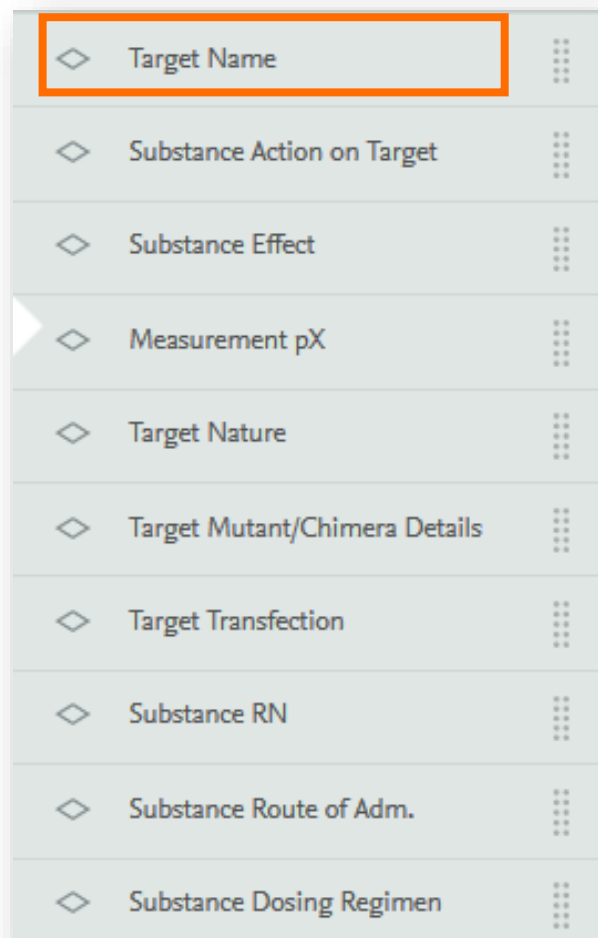
Structure	Compound_ID	Mer IC50	Physical Data MS m/z (M+1) or/and <sup>1</sup> H NMR (400 MHz, CD <sub>3</sub> OD)
	UNC1970A	++++	<sup>1</sup> H NMR (400 MHz, CD <sub>3</sub> OD) δ 8.75 (s, 1H), 7.81 (s, 1H), 7.71-7.62 (m, 2H), 7.25-7.16 (m, 2H), 4.72-4.60 (m, 1H), 3.55 (t, J = 7.1 Hz, 2H), 2.30-2.22 (m, 2H), 2.23-2.03 (m, 4H), 1.79-1.63 (m, 4H), 1.55-1.44 (m, 2H), 1.02 (t, J = 7.4 Hz, 3H); MS m/z 382.25 [M+H] <sup>+</sup> .

Reaxys把原文中的图形结果, 进行了数字化翻译

Structure: Image	SMILES	Molecular	Molecular	InChI Key	LogP	TPSA	Lipinski Nu	Veber Nun	Target Nar	Measur
	CCCC(=O)N	C28H28N6	496.569	TYDXNFSX	4.98	114.05	4	1	Rho-associ	IC50
	CCCC(=O)N	C28H28N6	496.569	TYDXNFSX	4.98	114.05	4	1	Rho-associ	IC50

# RMC-特定的信息检索方法

可以通过靶点，快速索引到，对应的化合物，文献等信息，且一定是原文中有该靶点实际内容的文献



# RMC-特定的信息检索方法

◇ Target Name	⋮
◇ Substance Action on Target	⋮
◇ Substance Effect	⋮
◇ Measurement pX	⋮
◇ Target Nature	⋮
◇ Target Mutant/Chimera Details	⋮
◇ Target Transfection	⋮
◇ Substance RN	⋮
◇ Substance Route of Adm.	⋮
◇ Substance Dosing Regimen	⋮

◇ Biological Material Name	⋮
◇ Biological Species	⋮
◇ (Clinical) findings / disease	⋮
◇ Organs/Tissues	⋮
◇ Cells/Cell Lines	⋮
◇ Cell Fraction	⋮
◇ Measurement Parameter	⋮
◇ Measurement Qualitative	⋮
◇ Measurement Unit	⋮

Substance Action on Target Search ×

<input type="checkbox"/> activator		75,140
<input type="checkbox"/> agonist	激动剂	,929
<input type="checkbox"/> allosteric modulator		,961
<input type="checkbox"/> antagonist		,683
<input type="checkbox"/> blocker	阻断剂	160,460
<input type="checkbox"/> inactivator		1,996
<input type="checkbox"/> inhibitor	抑制剂	10,470,915
<input type="checkbox"/> inverse agonist		13,321
<input type="checkbox"/> irreversible antagonist		3
<input type="checkbox"/> irreversible inhibitor		83
<input type="checkbox"/> modulator		313,006

1 of 2 Go to page Clear selected Transfer

检索对靶点作用机制的特点信息时的模块

Measurement Parameter is Enter search term ×

> cellular parameters	94,814
> epidemiological data	120,359
> in-vitro pharmacological parameters	20,175,771
> in-vivo pharmacological parameters	46,741
> mathematical parameters	148,038
> medical parameters	32,006
> metabolic parameters	54,026
> metabolism/transport parameters	110,315
> microbiological parameters	286,015
> pharmacokinetic parameters	835,343
> absorption parameters	59,818
> F (drug bioavailability)	56,062
> kabs	1,550
> MAT (mean absorption time)	7
> t1/2 abs	589
> tlag	1,582

Transfer

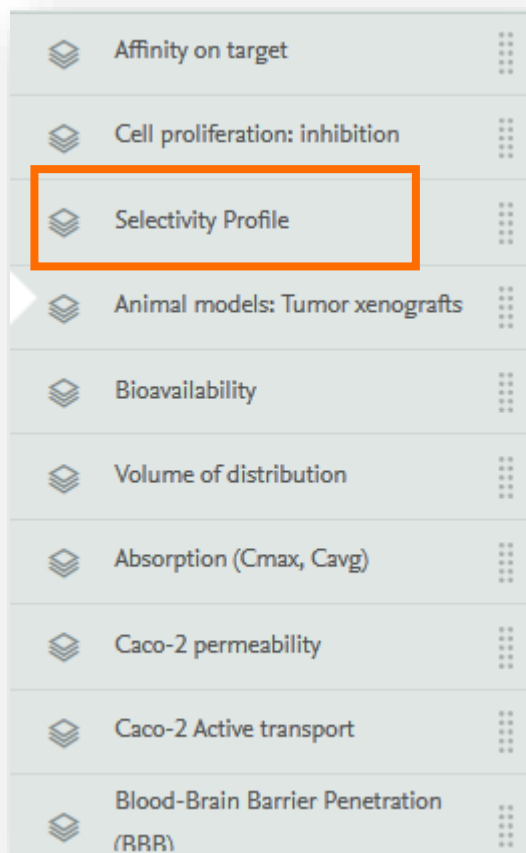
直接检索特定数据时的模块如PK的各种数据

各种分类细致的信息检索模块，快捷锁定对应结果



# RMC-组合信息便捷检索

预设的组合检索模块，便捷检索综合信息，如对于不同亚型的同类靶点，差异抑制性



**靶点选择性检索**

**靶点名称**

AND

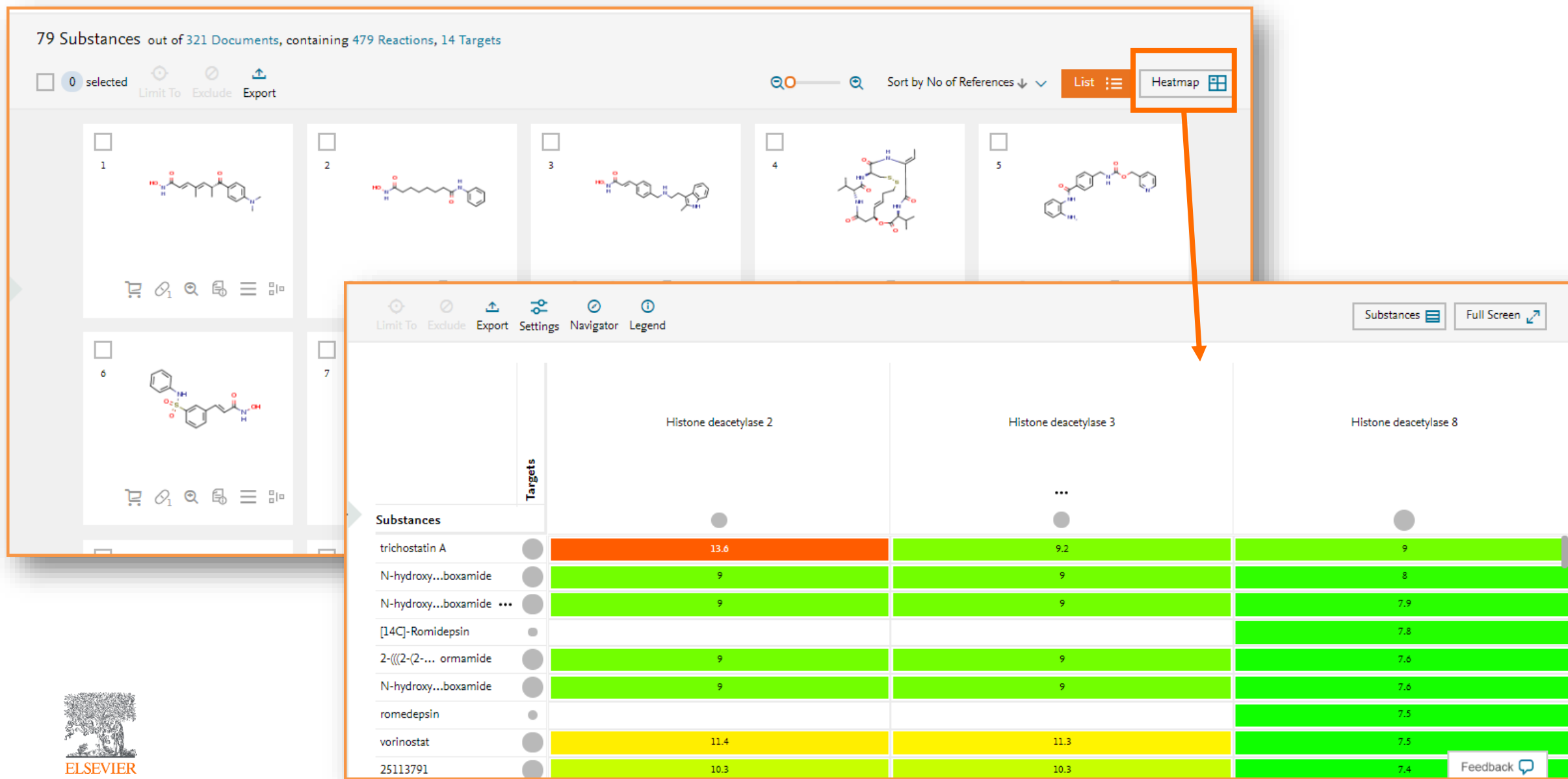
抑制‘数量级’以‘mol’为单位换算，9=10的负9次方

COMBI

AND

Target Name	Operator	Value
Histone deacetylase 2	is	9
Histone deacetylase 8; Histone deacetylase [Neovison vison]; Histone deacet...	is	8

# 选择性抑制结果-快速构建差异抑制构效关系图



# RMC-组合信息便捷检索

- Affinity on target
- Cell proliferation: inhibition
- Selectivity Profile
- Animal models: Tumor xenografts
- Bioavailability
- Volume of distribution
- Absorption (Cmax, Cavg)
- Caco-2 permeability
- Caco-2 Active transport
- Blood-Brain Barrier Penetration (BBB)

- Cytotoxicity
- hERG inhibition
- Cytochrome inhibition (CYP3A4)
- Metabolism by cytochrome (CYP2D6)
- Microsomal stability
- Protein binding (blood, plasma)
- Cardiotoxicity

### hERG inhibition

- Structure  
Create Structure / Reaction Drawing
- AND
- Target Name  
is Target Name 'Potassium voltage-gated channel subfamily H mem'
- AND
- Target Nature  
is Target Nature 'wild'
- AND
- Measurement Parameter  
is Measurement Parameter '%50';'K';'Kd';'kd'
- AND
- Measurement pX  
Measurement pX

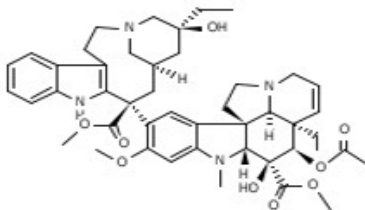
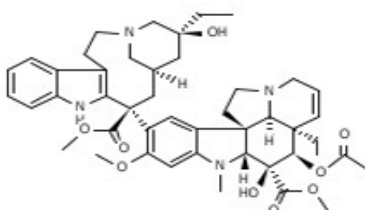
### Caco-2 permeability

- Structure  
Create Structure / Reaction Drawing
- AND
- Cells/Cell Lines  
is 'Caco-2 cell line';'Caco-2'
- AND
- Measurement Parameter  
is 'papp (a-b)';'papp (b-a)';'papp (transport)';'papp';'transport ratio';'transp'

只需要特定结构即可初步快速检索特殊信息

# RMC-组合信息便捷检索

快速整理 ‘特定结构’ Caco-2 数据

A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P
	[H][C@@]1	https://ww	(17 of 954)	363623-08	vinblastin	810.988	Caco-2 ce Papp (B-A cm/s			9.66E-06		Article; Act	https://www.reaxys.com/reaxys/se		
89															
	[H][C@@]1	https://ww	(17 of 954)	363623-08	vinblastin	810.988	Caco-2 ce Papp (A-B cm/s			1E-07		Article; Ca	https://www.reaxys.com/reaxys/se		

Reaxys Export 20190221\_163528

# RMC强大的组合式药物化学检索模块定义复杂问题

The screenshot displays the RMC search interface. At the top, there are navigation buttons for "Reactions", "Targets", "Substances", and "Documents". Below these are utility buttons: "Import", "Save", "Reset form", and "Delete all". On the right, there are search filters: "Structure", "Molecular Formula", "CAS RN", and "Doc. Index".

The central area shows a chemical structure of a molecule with a benzimidazole core. A 3,4-dichlorophenyl group is attached to the imidazole ring. The benzimidazole ring has a methyl group (-CH<sub>3</sub>) and a substituent 'G' at the 2-position. An orange circle highlights the 'G' substituent. Below the structure, the text "As drawn" is visible.

Below the structure, there are two search criteria defined in a list:

- Target Name is epidermal growth factor receptor binding protein;Epidermal growth factor receptor;epidermal growth factor-activated receptor;EGFR;EGFR (100)
- Measurement Parameter is ic50

Three orange boxes with Chinese text are overlaid on the image:

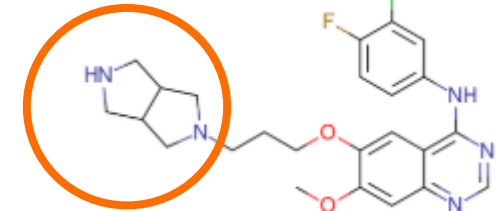
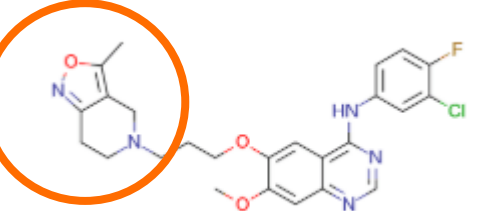
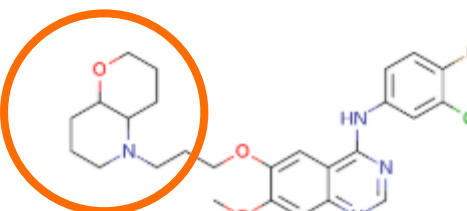
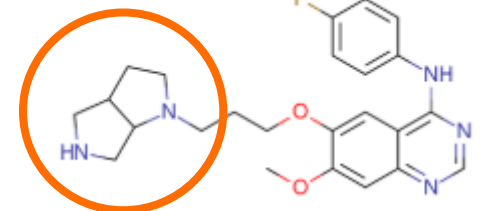
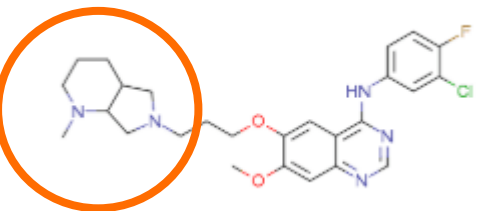
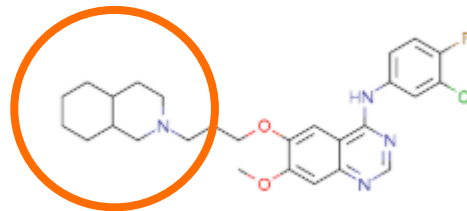
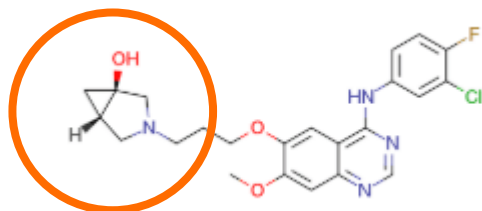
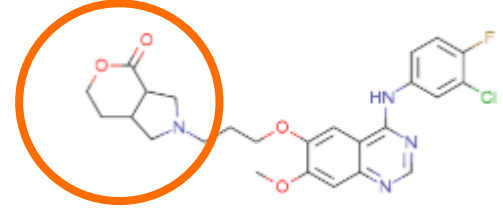
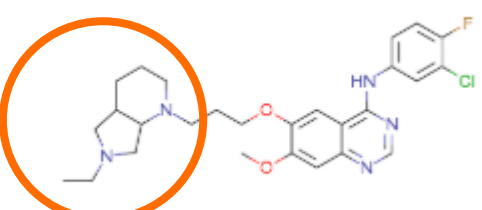
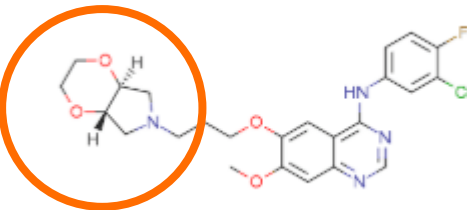
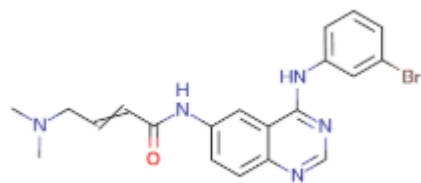
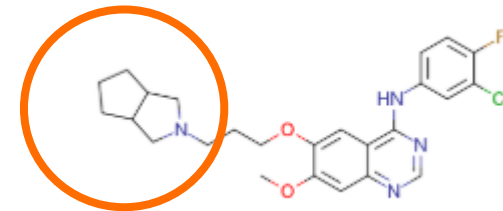
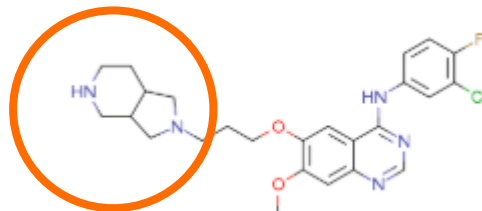
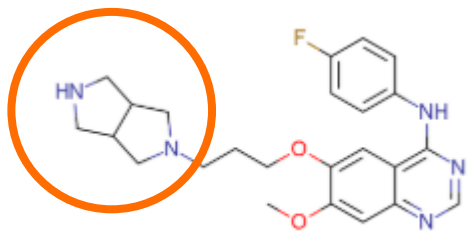
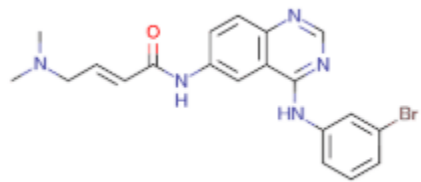
- A box around the 'G' substituent contains the text: "评估不同碎片结构，对药物分子IC50的影响" (Evaluate the influence of different fragment structures on the IC50 of drug molecules).
- A box around the search criteria list contains the text: "靶点" (Target).
- A box around the "ic50" parameter contains the text: "参数" (Parameter).



# 同位置侧链，生物活性影响度评估



# 筛选出高活性化合物，获取设计灵感



# 以结构为基础，多种数据组合评估

7 8 9 10 11 12

13 14 15 16 17 18

19 20

33,096 Substances out of 3,529 Documents containing 53,980 Reactions, 1,863 Targets

Reaxys - 33,096

Substances Full Screen

Limit To Exclude Export Settings Navigator Legend

Parameter	auc	clint (intrinsic clearance)	emax	ed50	emax	gi50	k50	t1/2 el
Substances	*	*	*	*	*	*	●	*
(S)-N-(4-(3-... boxamide							9.4	
(4S,5R)-N-(4... boxamide							9.4	
N-(2-chloro-... fonamide							9.4	
N-(5-(3,5-di... -4-amine							9.4	
N-(5-(3,5-di... -4-amine							9.4	
6-(1-acryloyl... -4-amine							9.4	
(S)-N <sup>6</sup> -(1-acr... -diamine							9.4	
28395477							9.4	
27951527							9.4	
N-(3-bromo... -4-amine							9.4	
N-(3-bromo... -4-amine							9.4	
N-(3-chloro-... -4-amine							9.4	

# 内容

## ➤ Elsevier 生命科学解决方案

1. Reaxys对信息的提炼介绍，以及信息检索基础技巧
2. Reaxys专利检索策略
3. RMC辅助药物分子设计研发决策
4. PharmaPendium辅助药物临床研究

## ➤ 总结

# PharmaPendium数据库涵盖的内容

**PharmaPendium**是唯一提供上市药物，临床前与临床，药效，药物安全与药代动力学、药物代谢与转运酶，药物不良反应报告等数据的一站式平台；同时还收录此领域的权威期刊书籍内容，如Meyler副反应大全和Mosby用药参考等，助力药物筛选和研发进程。

FDA & EMA所有的approval package (FDA: 1938年至今，EMA: 1995年至今)

2.29M+

FDA 审评文件

200K+

EMA 审评文件

9.45M+

FDA 药物不良  
反应报告

673K+

FDA 咨询委员  
会会议档案

Extracted Data: PK Module

MET Module

FDA AERS

Efficacy Module

DDI Risk

4450

种药物的可  
检索信息

1.6M+

药代动力学信息

305K+

药物代谢与转运  
酶信息

1.66M+

药物安全信息

2.45M+

药效信息

115K+

生物活性信息

# Pharmapendium辅助解决临床前，临床，以及上市后信息检索的需求/挑战



<p><b>药物安全与毒理 (Safety, Toxicity)</b></p> <ul style="list-style-type: none"><li>➢ 支持临床前动物毒理数据分析</li><li>➢ 支持临床人体毒理研究</li><li>➢ 辅助临床试验方案决策</li><li>➢ 更好地预测候选药物的潜在毒性</li></ul>	<p><b>药物代谢，转运酶及药物相互作用 (MET&amp;DDI)</b></p> <ul style="list-style-type: none"><li>➢ 查找获批药物的代谢酶、转运体的相关数据，辅助在研项目的决策</li><li>➢ 基于已有的代谢数据，判断在研药物发生药物相互作用的可能性</li><li>➢ 根据获批药物的真实数据，构建药物的相互作用模型</li></ul>
<p><b>药代动力学与药效 (PK&amp;Efficacy)</b></p> <ul style="list-style-type: none"><li>➢ 更详细地评价候选药物的药物动力学参数和性质</li><li>➢ 为候选药物的筛选，评估与优先性等提供参考</li><li>➢ 辅助临床前动物模型选择与药效研究</li><li>➢ 为药物临床试验方案设计提供信息参考</li><li>➢ 辅助选择更合理的给药方式，并类推到整个药物类型研究中</li><li>➢ 通过药效数据综合分析，增加候选药物申报的成功机率</li></ul>	<p><b>药物不良反应追踪与药物注册 (Registration, AERS)</b></p> <ul style="list-style-type: none"><li>➢ 直观的大数据药物不良反应分析，辅助药物安全评估</li><li>➢ 分析FDA和EMA审批过程中的差异，为药物审批占得先机。</li><li>➢ 通过分析药物各阶级详细数据，增加候选药物申报的成功机率</li></ul>



# PharmaPendium深度提取FDA,EMA官方文档中的数据

Study type	Study pts.	Sample Size (N)	Design	1 <sup>st</sup> endpoint	2 <sup>nd</sup> endpoint	Completion date
Adjuvant	Stage IB, II, III Resected	1160	Double-blind Placebo control	OS	DFS	10/07
Maintenance	Stage III Inoperable	840	Double-blind Placebo control	OS & PFS	-	5/06
First-line	Stage III/IV PS 2-3 LCS <=20 Medical conditions	207	Double-blind BSC control	Symptom improvement	OS TTP	9/06
Refractory	Stage III/IV PS 0-3	624	Double-blind BSC control	OS	PFS Symptoms	9/06
Refractory	Stage III/IV PS 0-2 LCS <=20	207	Double-blind BSC control	Symptom improvement	OS TTP	9/06

BSC=best supportive care; DFS=disease free survival; LCS= Lung cancer subscale; PFS=progression free survival; PS=performance status; OS=overall survival

# PharmaPendium深度提取FDA,EMA官方文档中的数据

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Metabolizing Enz. & Trans. Data  
Drug Safety Data  
FAERS Data NEW  
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数千条PK数据规范整理

Pharmacokinetic data search results

21381 records from PK Data: [Sofosbuvir; Velpatasvir (696) OR Interferon Alfacon-1 (8) OR Interferon Alfa-2b, Recombinant (205) OR Sofosbuvir; Velpatasvir; Voxilaprevir (553) OR Peginterferon Alfa-2b; Ribavirin (50) OR Ritonavir (0) OR Ledipasvir; Sofosbuvir (823) OR Telaprevir (1691) OR Simeprevir Sodium (122) OR Elbasvir; Grazoprevir (569) OR Dasabuvir Sodium (27) OR Ribavirin (2818) OR Glecaprevir; Pibrentasvir (465) OR ...

Export date: 10-09-2018

Efficacy Data Search Results For: Drugs: [Gefitinib (684)] AND Phase: [III (684)]

Total results: 684

Sort order: Drug (Ascending); Indication Type (Ascending); Endpoint Type (Ascending);

Preclinical Data Clinical Data All Data

ID	Drug	Species	Study Group	Dose
1	Boceprevir	Human	healthy, Caucasian	400 mg
2	Boceprevir	Rat		3 mg/kg
3	Boceprevir	Human	healthy, Caucasian	1200 mg
4	Boceprevir	Cynomolgus monkey		25 mg/kg

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规范化数据导出

Drug	Study Number	Phase/Combination	Study Design	Species	Sex	Route	Dose Regimen	Dose Frequency	Endpoint Type	Endpoint Subtype	Endpoint Tested	Value
Gefitinib	IPASS	III	Monotherapy	Human	Both	Oral	250 mg per day		Survival	Progression free survival	Treatment difference in progression-free survival	0.74
Gefitinib	IPASS (D791AC000)	III	Monotherapy	Human	Both	Oral	0		Clinical response	Objective response	Objective response rate in EGFR mutation positive patients	47.3
Gefitinib	IPASS (D791AC000)	III	Monotherapy	Human	Both	Oral	250 mg once daily	Once a day	Clinical response	Complete response	Percentage of patients with complete response	0.8
Gefitinib	IPASS (D791AC000)	III	Monotherapy	Human	Both	Oral	0		Clinical response	Objective response	Objective response rate in mutation unknown group of patients	29.2
Gefitinib	IPASS (D791AC000)	III	Monotherapy	Human	Both	Oral	0		Clinical response	Disease control	Number of patients with disease control	482
Gefitinib	ISEL (D7913C00709)	III	Monotherapy	Human	Both	Oral	250 mg once daily	Once a day	Clinical response	Objective response	Objective response rate in EGFR mutation negative patients	2.6
Gefitinib	ISEL (D7913C00709)	III	Monotherapy	Human	Both	Oral	250 mg once daily	Once a day	Clinical response	Objective response	Objective response rate	10.1
Gefitinib	ISEL	III	Monotherapy	Human	Both	Oral	0		Clinical response	Objective response	Objective response rate	1.6
Gefitinib	IPASS (D791AC000)	III	Monotherapy	Human	Both	Oral	0		Clinical response	Objective response	Objective response rate in EGFR mutation positive patients	47.3
Gefitinib	IPASS (D791AC000)	III	Monotherapy	Human	Both	Oral	0		Clinical response	Response	Number of EGFR mutation negative patients with objective response	20
Gefitinib	IPASS	III	Monotherapy	Human	Both	Oral	250 mg once daily	Once a day	Clinical response	Objective response	Objective response rate	43.0
Gefitinib	ISEL	III	Monotherapy	Human	Both	Oral	250 mg once daily	Once a day	Clinical response	Objective response	Objective response rate	2.6
Gefitinib	ISEL	III	Monotherapy	Human	Both	Oral	0		Clinical response	Objective response	Objective response rate	2.1
Gefitinib	Study 17	III	Combination	Human	Both	Oral	500 mg once daily	Once a day	Clinical response	Objective response	Objective response rate	32.1
Gefitinib	Study 17	III	Combination	Human	Both	Oral	250 mg once daily	Once a day	Clinical response	Objective response	Objective response rate	35.0
Gefitinib	INTEREST;ISEL;IN	III	Monotherapy	Human	Both	Oral	250 mg once daily	Once a day	Clinical response	Response	Number of patients with objective response in patients with EGFR FISH+ tumours	5
Gefitinib	Study 14	III	Combination	Human	Both	Oral	500 mg once daily	Once a day	Clinical response	Objective response	Objective response rate	49.7
Gefitinib	IPASS (D791AC000)	III	Monotherapy	Human	Both	Oral	0		Clinical response	Objective response	Objective response rate in mutation known group of patients	37.9
Gefitinib	IPASS (D791AC000)	III	Monotherapy	Human	Both	Oral	0		Clinical response	Stable disease	Number of patients with stable disease	286
Gefitinib	IPASS	III	Monotherapy	Human	Both	Oral	250 mg once daily	Once a day	Clinical response	Objective response	Objective response rate	43.3





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FDA Approval Package - Gefitinib > Medical/Clinical Review

Medical/Clinical Review 021399/S-000 Part 01

clinical review 28/198 Go

2015-06-04 PDF(1305k)  
Other Important Information from FDA > Cross Discipline Team Leader Review  
206995/S-000 Part 01  
... Pharmaceuticals LP September 17, 2014 July 17, 2015 Iressa (Gefitinib)  
**Clinical Review** Primary/ Secondary Reviewer ...

2003-01-31 PDF(2024k)  
**Medical/Clinical Review > Medical/Clinical Review 021399/S-000 Part 01**  
... Review(s) **CLINICAL REVIEW** Clinical Review NDA 21-399 Drug Name Medical Reviewer Martin H. Cohen, M.D. ...

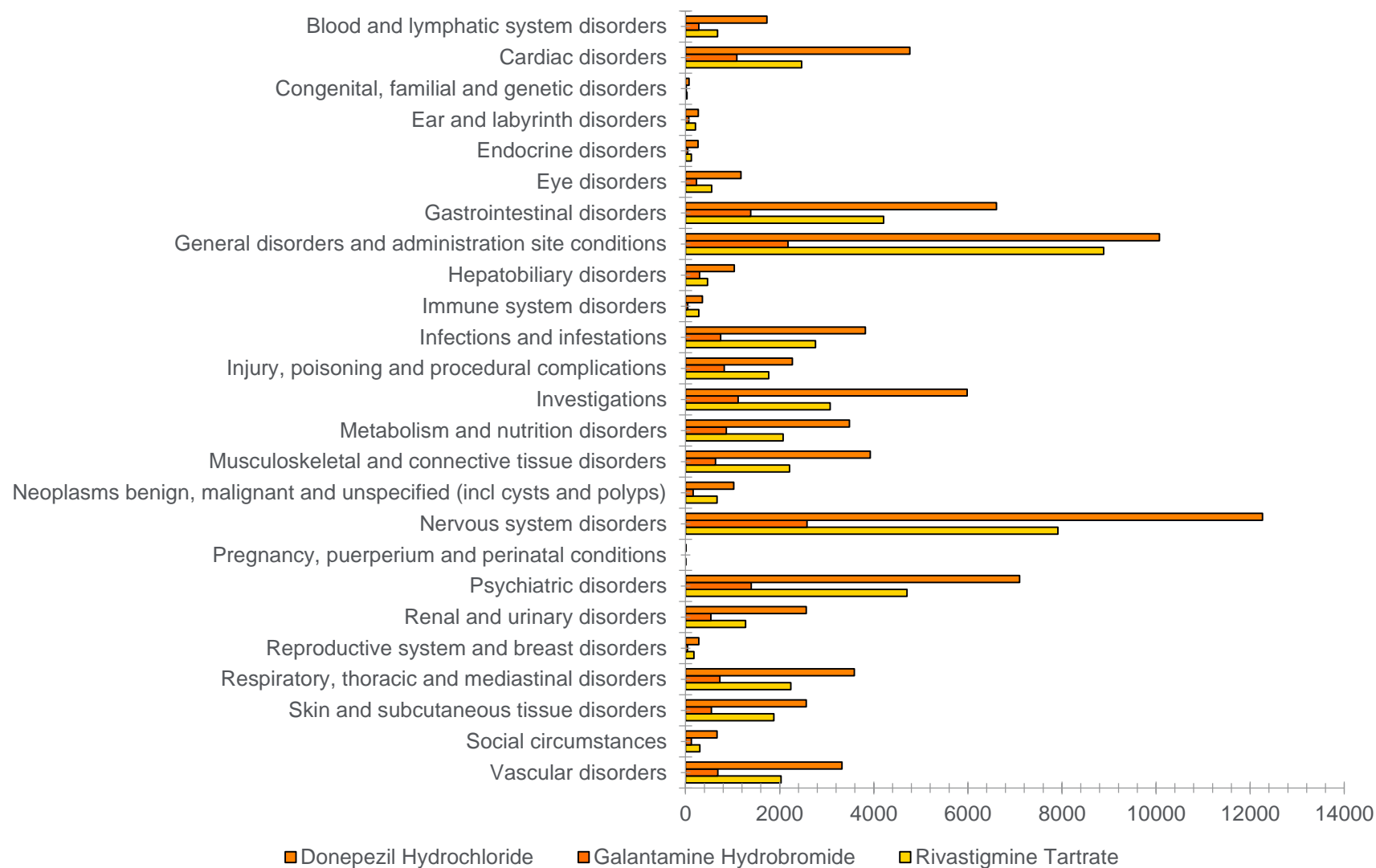
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Other Important Information from FDA > Cross Discipline Team

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# 直方图总览，展示副作用分布，辅助决策

## 多奈哌齐，加兰他敏，卡巴拉汀直方图



PharmaPendium在全球超过100家用户，其中包括FDA，全球前20的制药企业，日本前10的制药企业等



Thank you

