Elsevier
Life Science Solution
获取药物研发信息系列主题培训

Jul 2020

Agenda

- 7月8日
  - 15：00-15：10：Elsevier Life Science整体解决方案介绍
  - 15：10-16：30：物质结构/合成信息的获取与精炼
- 7月15日
  - 15：00-16：00：生物活性数据与文献的获取与提炼
- 7月22日
  - 15：00-16：00：化合物毒理药理学文献的获取
- 7月29日
  - 15：00-16：00： Elsevier Life Science整体解决方案数据库使用答疑
- 8月5日
  - 15：00-16：00：如何将Elsevier Life Science整体解决方案贯穿药物研发的全流程

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生物活性数据与文献的获取与提炼

涉及：RMC， PharmaPendium

Agenda

- 化合物活性数据的获取
- 文献与专利中活性数据的获取与提炼
- FDA/EMA审评文档中活性数据的获取与提炼

RMC（Reaxys Medicinal Chemistry）

- RMC是建立在Reaxys平台上的，和药物化学数据有关的数据库。
  - 包含真实的，实验确证的，小分子化合物在不同生物体系中的相关实验数据
  - 是市场上最全的，最广泛的小分子生物活性数据库
  - 实验数据源自对学术全文，专利中的相关数据的摘取，以及来自GOSTAR数据库的相关数据，并将二者在底层数据上进行整合。
  - RMC中所提供的文献，包含所有摘录的相关信息和数据，可靠，可信

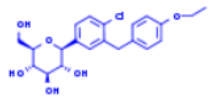
Patents Origin and starting date
• **>126 600 Patents** • US : 1971-present • EP : 1979-present • WO : 1978-present (English only) • Patents are coming from the A61K class mainly but not only.

Articles and Journals
• **>5000 Journals Covered** • **>353 400 Articles** • From 1980 to Present

Drugable Targets
• **>12 700 Drugable Targets**

Case 1：单一化合物生物活性数据的获取

1



dapagliflozin

$C_{21}H_{25}ClO_6$ 408.879 11966426 461432-26-8

Identification

Druglikeness

Bioactivity (All)

Physical Data - 52

Spectra - 54

Other Data - 351

Preparations - 81

Reactions - 398

Targets - 24

Documents - 217

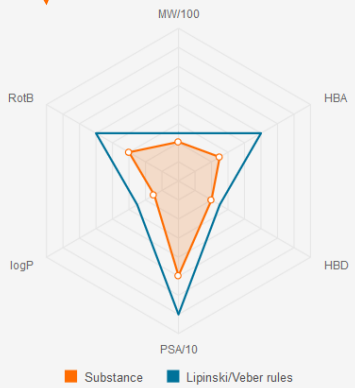
Druglikeness

Lipinski rules component

Molecular Weight	408.879
logP	2.937
HBA	5
HBD	4
Matching Lipinski Rules	4

Veber rules component

Polar Surface Area (PSA)	99.38
Rotatable Bond (RotB)	6
Matching Veber Rules	2



Bioactivity (All)

- In vitro: Efficacy - 261
- In vivo: Animal Model - 208
- Metabolism - 67
- Pharmacokinetic - 229
- Toxicity/Safety Pharmacology - 114

具体化合物的生物活性数据

- Bioactivity (All)
  - In vitro: Efficacy - 261
  - In vivo: Animal Model - 208
  - Metabolism - 67
  - Pharmacokinetic - 229
  - Toxicity/Safety Pharmacology - 114

RMC将全文中的数据全部提炼出来，同时对于用Mol为单位的数据进行标准化处理: pX=-lg(~mol)

In vitro: Efficacy - 261

Quantitative Results

Show/Hide columns

pX	Parameter	Value (qual)	Value (quant)	Unit	Biological Species	Action on target	Target	Tissue/Organ	Cell	Dose	Effect	Concomitants	Reference
9.91	amount (Glycogen)		50 - 175	pg/ml	Sprague Dawley rat			pancreas		20 µmol/l	antidiabetic agent		Wang, May-Yun; Yu, Xinxin; Lee, Young; McCorkle, Sara Kay; Chen, Shiuhwei; Li, Jianping; Wang, Zhao V.; (...) Unger, Roger H.; Roth, Michael G.[**Proceedings of the National Academy of Sciences of the United States of America**, **2017**, vol. 114, # 25, p. 6611 - 6616] Full Text Cited 10 times Details Abstract
9.84	pIC50 ([14c]Methyl-Alpha-D-Glucopyranoside Uptake)		9.84		human		Sodium/glucose cotransporter 2 [human]:Wild		COS-7 cell line			Radioligand: [14C]AMG	Ho, Low-Tone; Kulkarni, Suvarn S.; Lee, Jinq-Chyi[**Current Topics in Medicinal Chemistry**, **2011**, vol. 11, # 12, p. 1476 - 1512] Full Text Cited 9 times Details Abstract
9.84	pIC50		9.84		human		Sodium/glucose cotransporter 2 [human]:Wild		COS-7 cell line			Radioligand: ALPHA-D-(U-14C)-GLUCOPYRANOSIDE; Other compound: NACL;	Zhou, Huiqiang; Danger, Dana P.; Dock, Steven T.; Hawley, Lora; Roller, Shane G.; Smith, Chari D.; Handlon, Anthony L.[**ACS Medicinal Chemistry Letters**, **2010**, vol. 1, # 1, p. 19 - 23] Full Text Cited 35 times Details Abstract
9.31	IC50	=	0.49	nM	human	Inhibitor	Sodium/glucose cotransporter 2 [human]:Wild		CHO cell line				Lee, Suk Ho; Song, Kwang-Seop; Kim, Jong Yup; Kang, Misuk; Lee, Jun Sung; Cho, Seung-Hwan; Park, Hyun-Ju; Kim, Jeongmin; Lee, Jinhwa[**Bioorganic and Medicinal Chemistry**, **2011**, vol. 19, # 19, p. 5813 - 5832] Full Text Cited 17 times Details Abstract
9.31	IC50	=	0.49	nM	human	Inhibitor	Sodium/glucose cotransporter 2 [human]:Wild					Radioligand: [14C]Methyl-alpha-D-glucopyranoside	Lee, Jinhwa; Kang, Suk Youn; Song, Kwang-Seop; Lee, Junwon; Lee, Sung-Han[**Bioorganic and Medicinal Chemistry**, **2010**, vol. 18, # 16, p. 6069 - 6079] Full Text Cited 30 times Details Abstract
9.31	IC50 ([14c]Methyl-Alpha-D-Glucopyranoside Uptake)	=	0.49	nM	human		Sodium/glucose cotransporter 2 [human]:Wild		CHO cell line			Radioligand: [14C]AMG	Ho, Low-Tone; Kulkarni, Suvarn S.; Lee, Jinq-Chyi[**Current Topics in Medicinal Chemistry**, **2011**, vol. 11, # 12, p. 1476 - 1512] Full Text Cited 9 times Details Abstract
9.31	IC50	=	0.49	nM	human		Sodium/glucose cotransporter 2 [human]:Wild		CHO cell line			Substrate: [14C]AMG	Park, Eun-Jung; Kong, Younggyu; Lee, Jun Sung; Lee, Sung-Han; Lee, Jinhwa[**Bioorganic and Medicinal Chemistry Letters**, **2011**, vol. 21, # 2, p. 742 - 746] Full Text Cited 10 times Details Abstract

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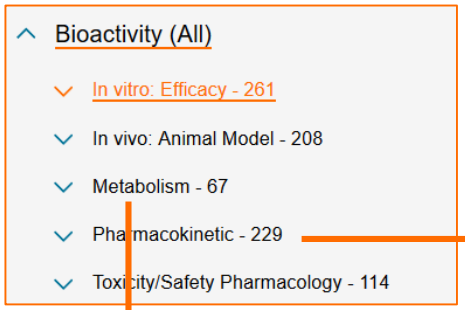
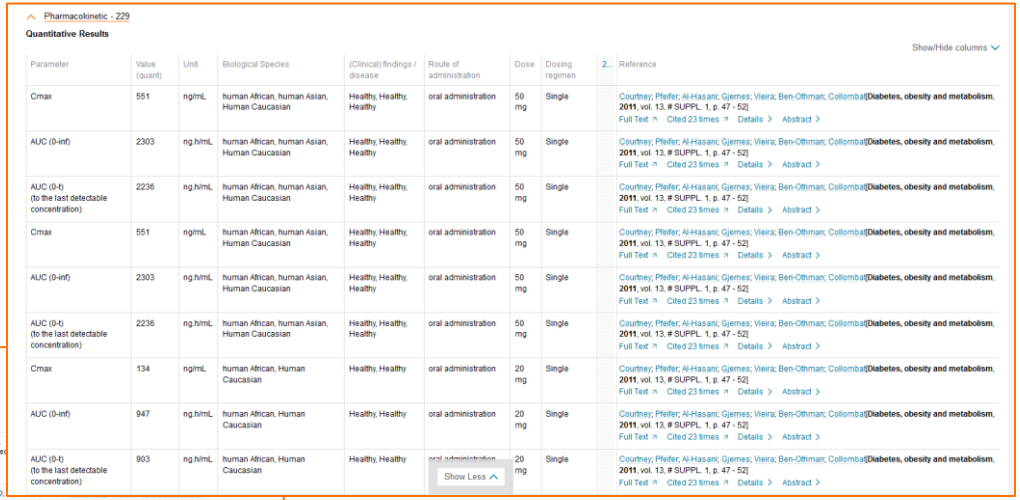
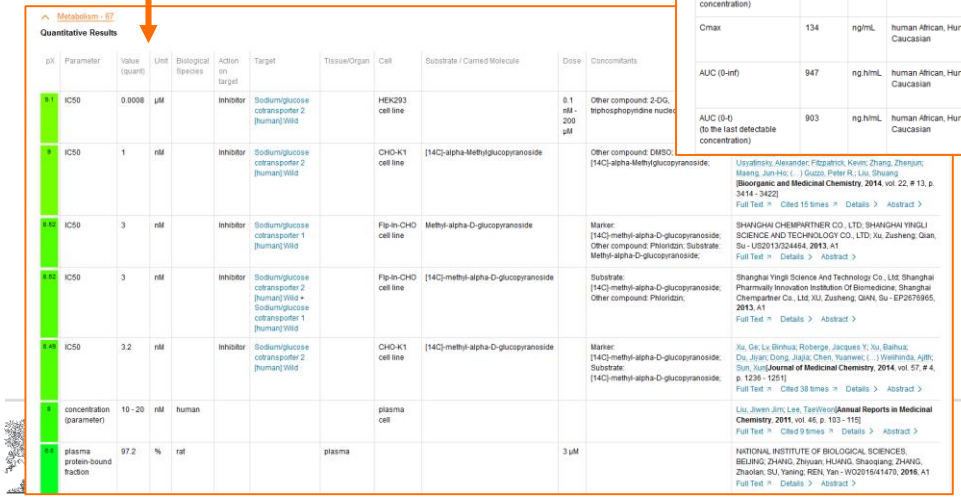
具体化合物的生物活性数据







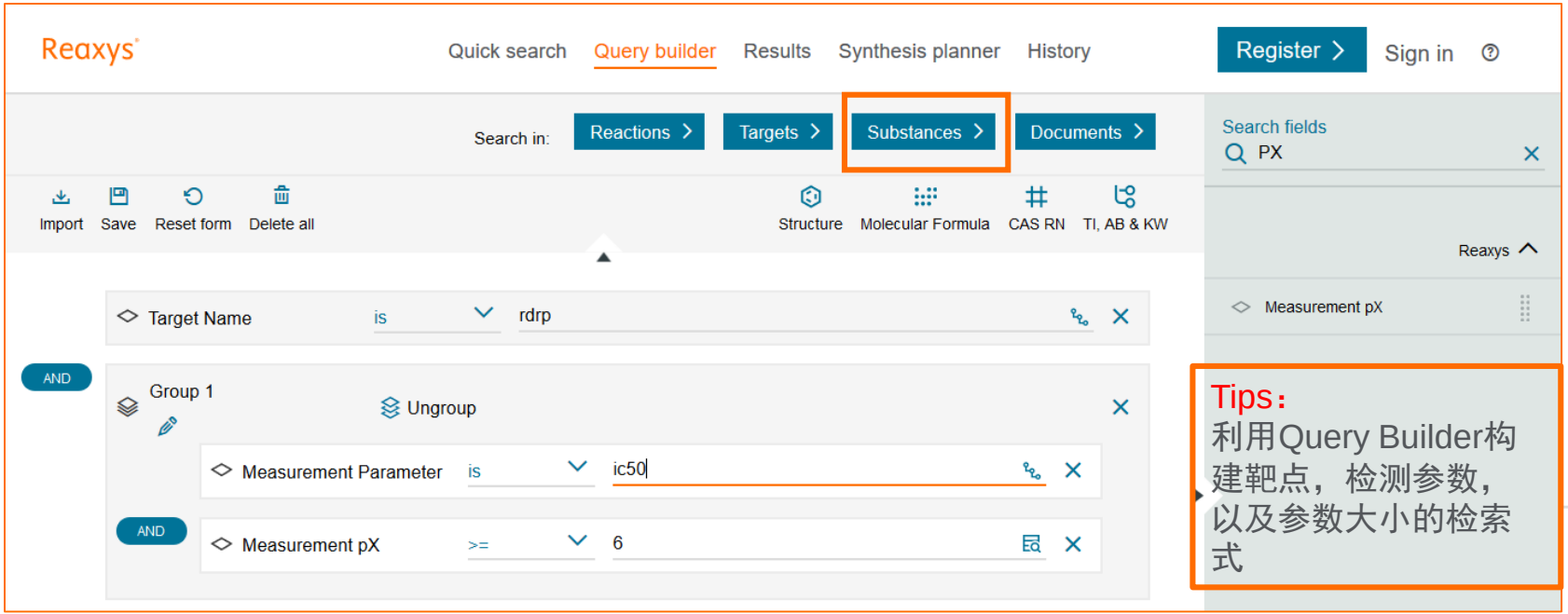
所有数据都提供原文链接，以保证数据的真实性。

Agenda

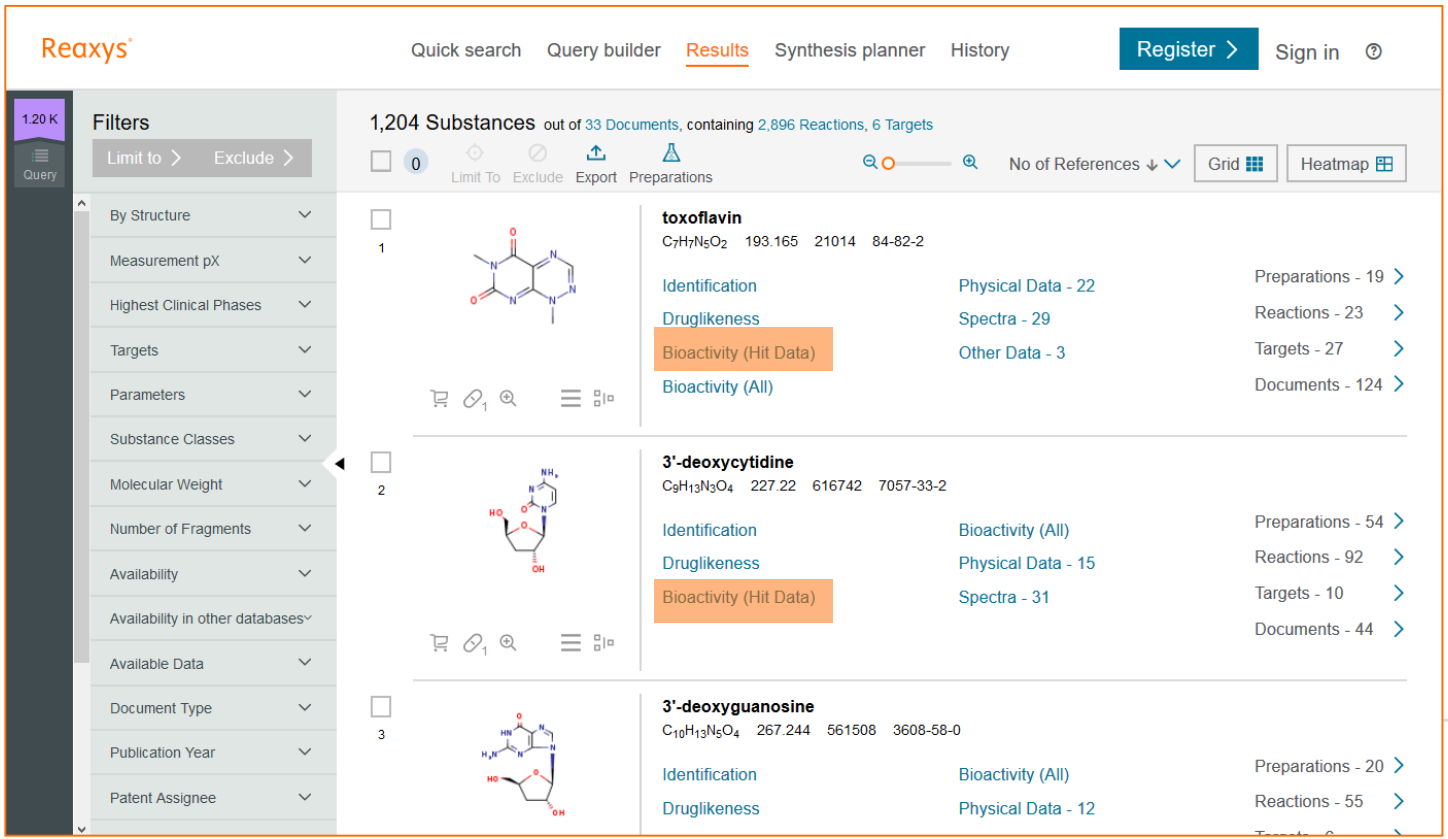
- 化合物活性数据的获取
- 文献与专利中活性数据的获取与提炼
- FDA/EMA审评文档中活性数据的获取与提炼

Case 2：如何用Reaxys快速筛选对“冠状病毒”有活性的化合物

- 获取文献中报道的对“RNA依赖的RNA聚合酶（RdRp）”有活性报道的化合物
- 希望这些化合物的IC50在um级别

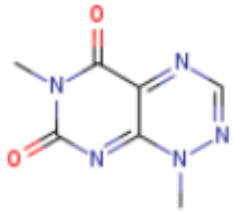


Reaxys中的结果



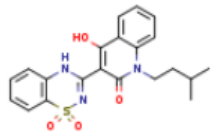
Reaxys直接给出符合条件的化合物，大量节省了科研人员阅读文献，并查找数据的时间，可以通过各自的Hit Data查看具体数据

Reaxys中的结果



pX	Parameter	Value (qual)	Value (quant)	Unit	Biological Species	Action on target	Target	Concomitants	Reference
6.22	IC50	=	0.6	μM	Hepatitis C virus	Inhibitor	RNA-dependent RNA polymerase [Hepatitis C virus]:Wild	Other compound: ATP; Radioligand: [3H]UTP;	Middleton; Lim; Montgomery; Rockway; Liu; Klein; Qin; Harlan; Kati; Molla[**Letters in drug design and discovery**, **2007**, vol. 4, # 1, p. 1 - 8] Full Text ↗ Cited 3 times ↗ Details › Abstract ›

pX	Parameter	Value (qual)	Value (quant)	Unit	Biological Species	Action on target	Target	Concomitants	Reference
7.1	IC50		0.08 - 1.2	μM	Hepatitis C virus		RNA-dependent RNA polymerase [Hepatitis C virus]:Wild		Mayhoub, Abdelrahman S.[**Bioorganic and Medicinal Chemistry**, **2012**, vol. 20, # 10, p. 3150 - 3161] Full Text ↗ Cited 35 times ↗ Details › Abstract ›



pX	Parameter	Value (qual)	Value (quant)	Unit	Biological Species	Action on target	Target	Concomitants	Reference
7.1	IC50	=	0.08	μM	Hepatitis C virus (strain DELTA 21)	Inhibitor	RNA-dependent RNA polymerase [Hepatitis C virus]:Wild		Dhanak, Dashyant; Duffy, Kevin J.; Johnston, Victor K.; Lin-Goerke, Juili; Darcy, Michael; Shaw, Antony N.; Gu, Baohua; (…) Keenan, Richard M.; Sarisky, Robert T. [**Journal of Biological Chemistry**, **2002**, vol. 277, # 41 p. 38322 - 38327] Full Text ↗ Cited 172 times ↗ Details › Abstract

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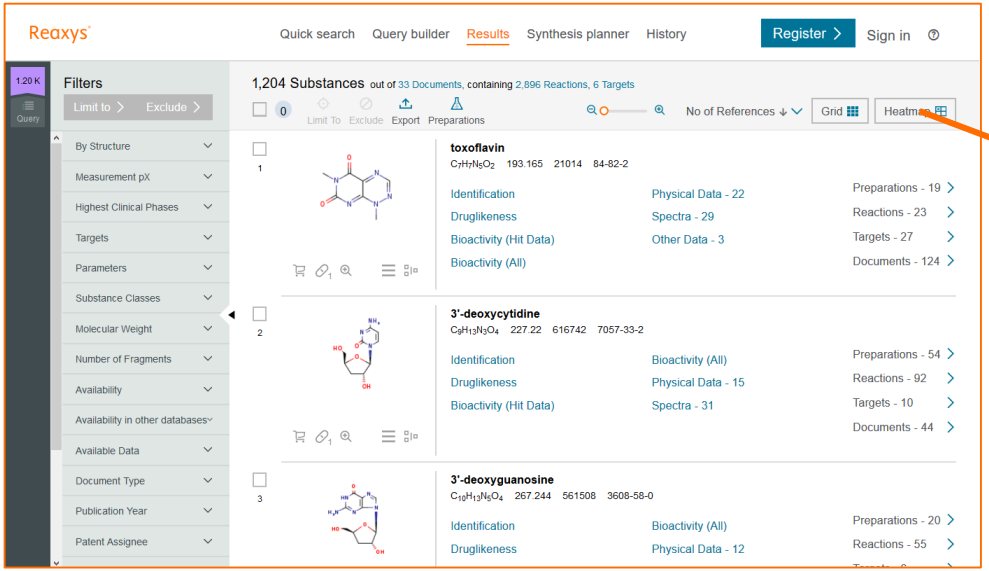
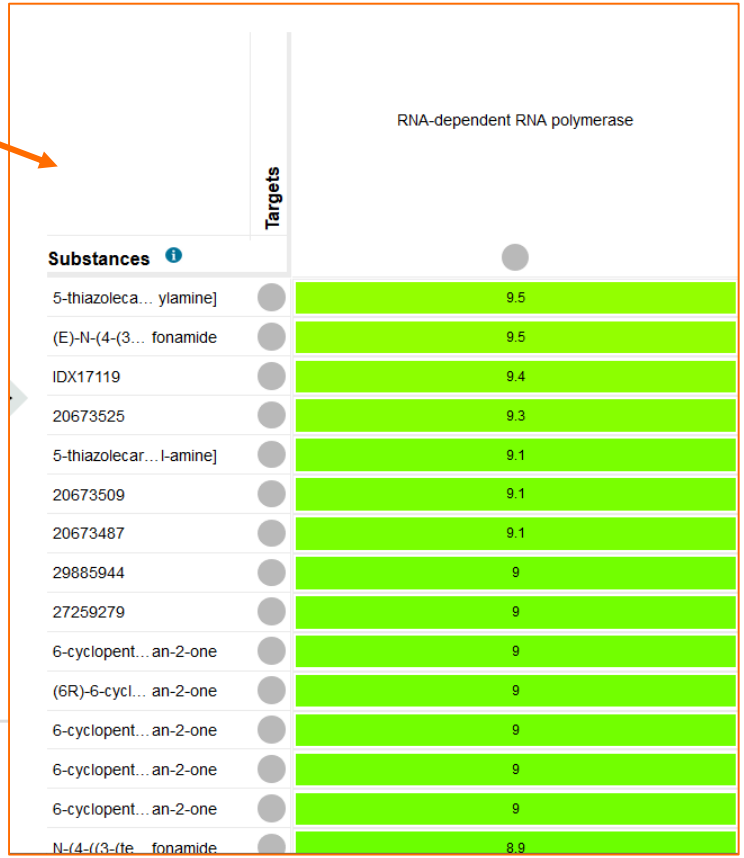
利用HeatMap看结构与靶点关系





利用Reaxys中的Heat Map，直接进行查看，靶点，结构，活性数据之间的关系，并可将活性从高到低进行排序。

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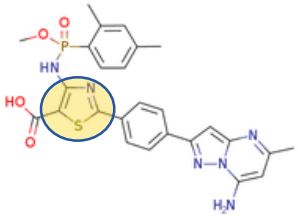
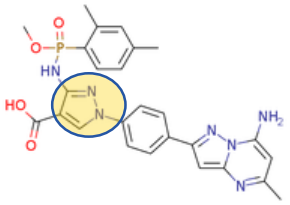
一些非常有意思的结构

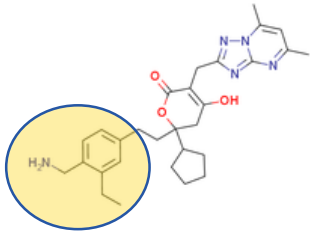
Substances	Targets: RNA-dependent RNA polymerase
5-thiazolec… ylamine]	9.5
(E)-N-(4-(… fonamide	9.5
IDX17119	9.4
20673525	9.3
5-thiazolec… l-amine]	9.1
20673509	9.1
20673487	9.1
29885944	9
27259279	9
6-cyclope… an-2-one	9
(6R)-6-cy… an-2-one	9
6-cyclope… an-2-one	9
6-cyclope… an-2-one	9
6-cyclope… an-2-one	9
N-(4-((3-(t… fonamide	8.9
5-[2-(4-flu…boxamide	8.7
(1aR,12b… boxamide	8.7
20673500	8.7
N-[4-(2-[2-…cetamide	8.7
6-cyclope… an-2-one	8.7
6-cyclope… an-2-one	8.7
N-[2-[4-(2-…cetamide	8.7
6-cyclope… an-2-one	8.7



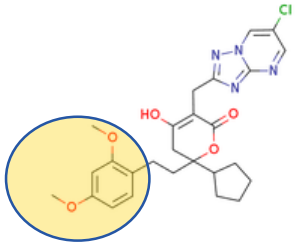
PX=9.5



PX=9.4



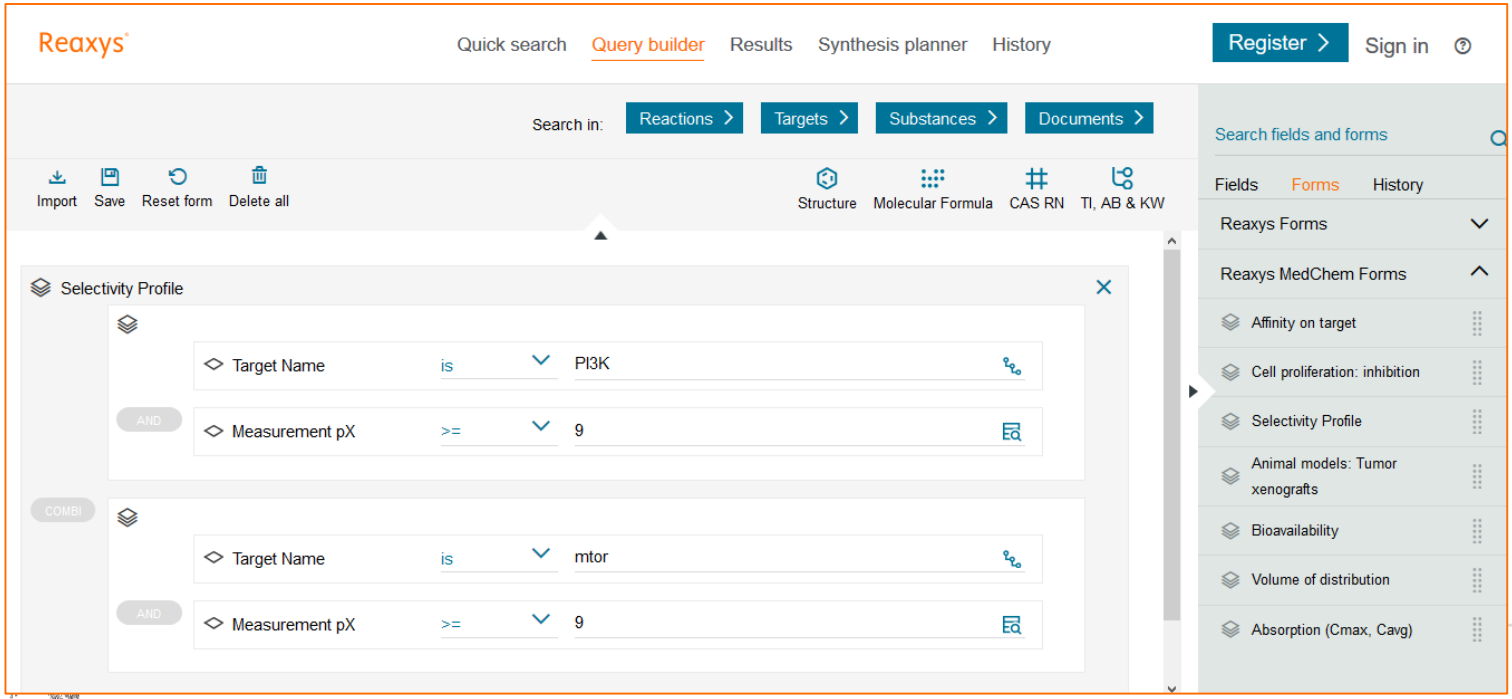
PX=8.0



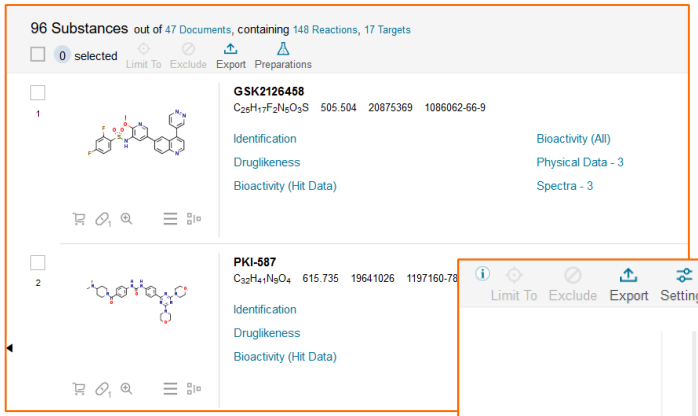
PX=7.7

Case 3：双靶点活性化合物的获取

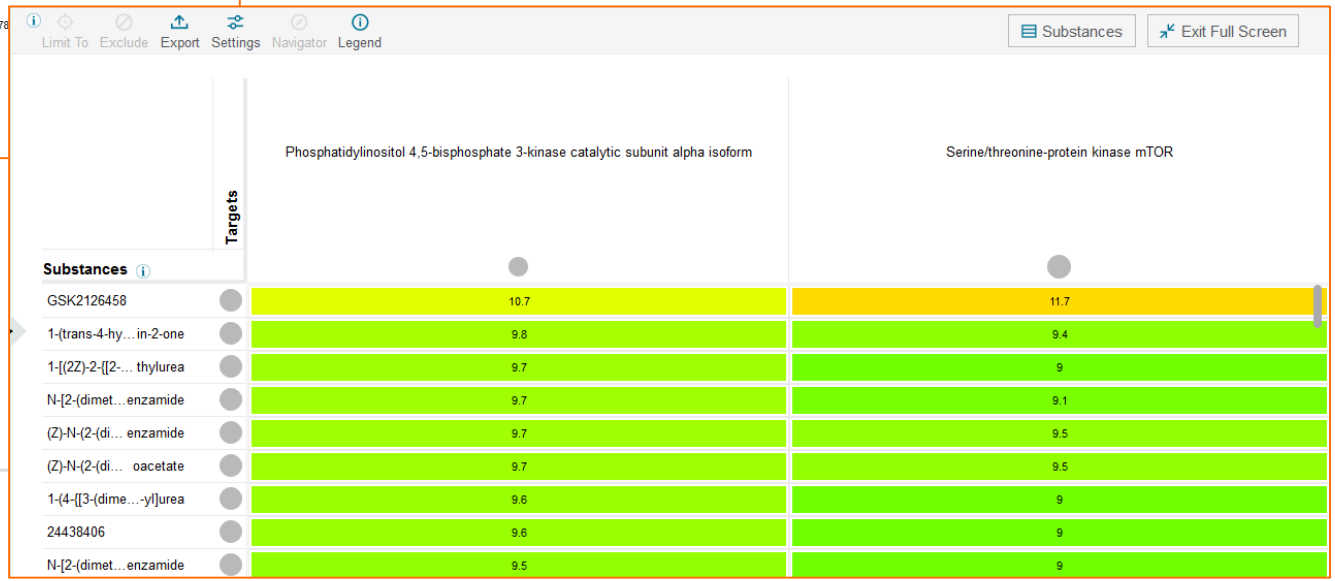
- PI3K和mTOR双抑制剂，且活性都在nM级别化合物



双靶点活性化合物



利用Heat Map查看活性数据



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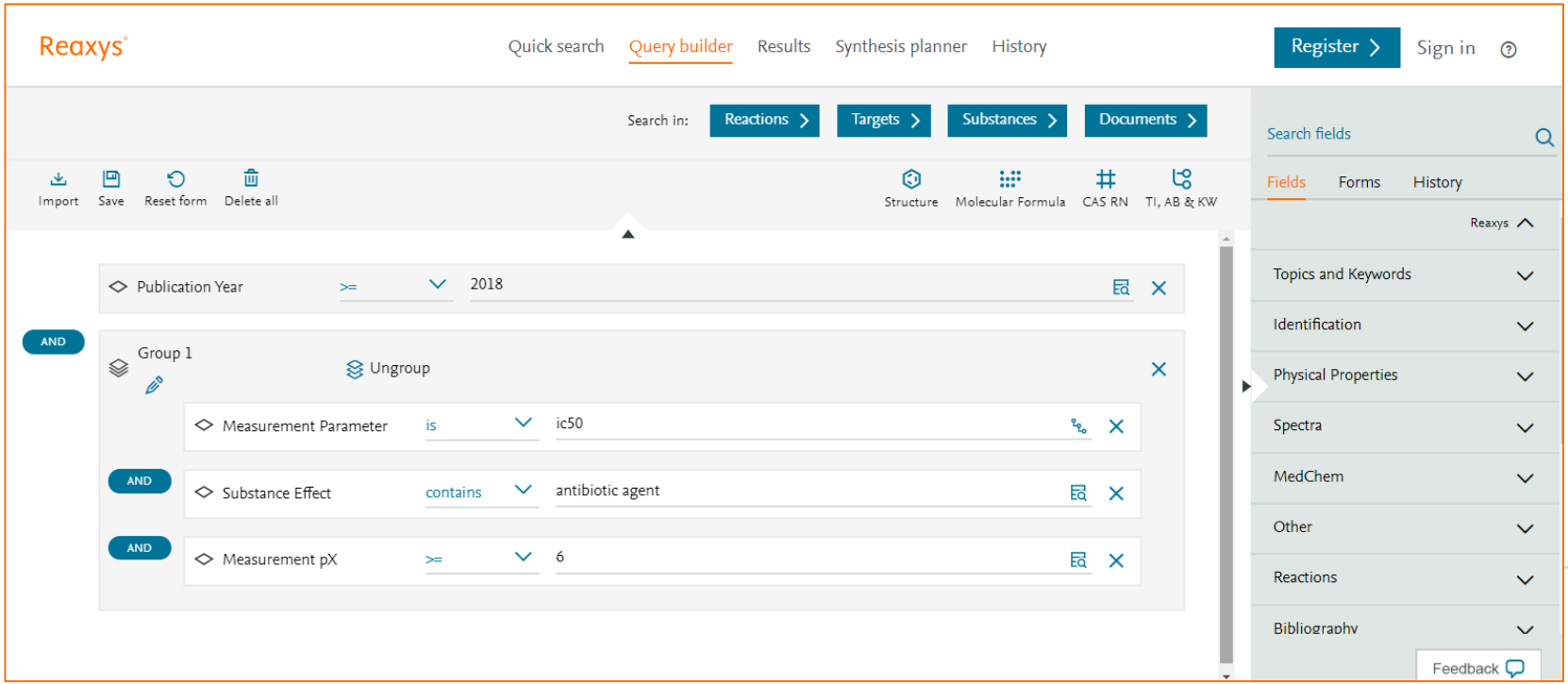
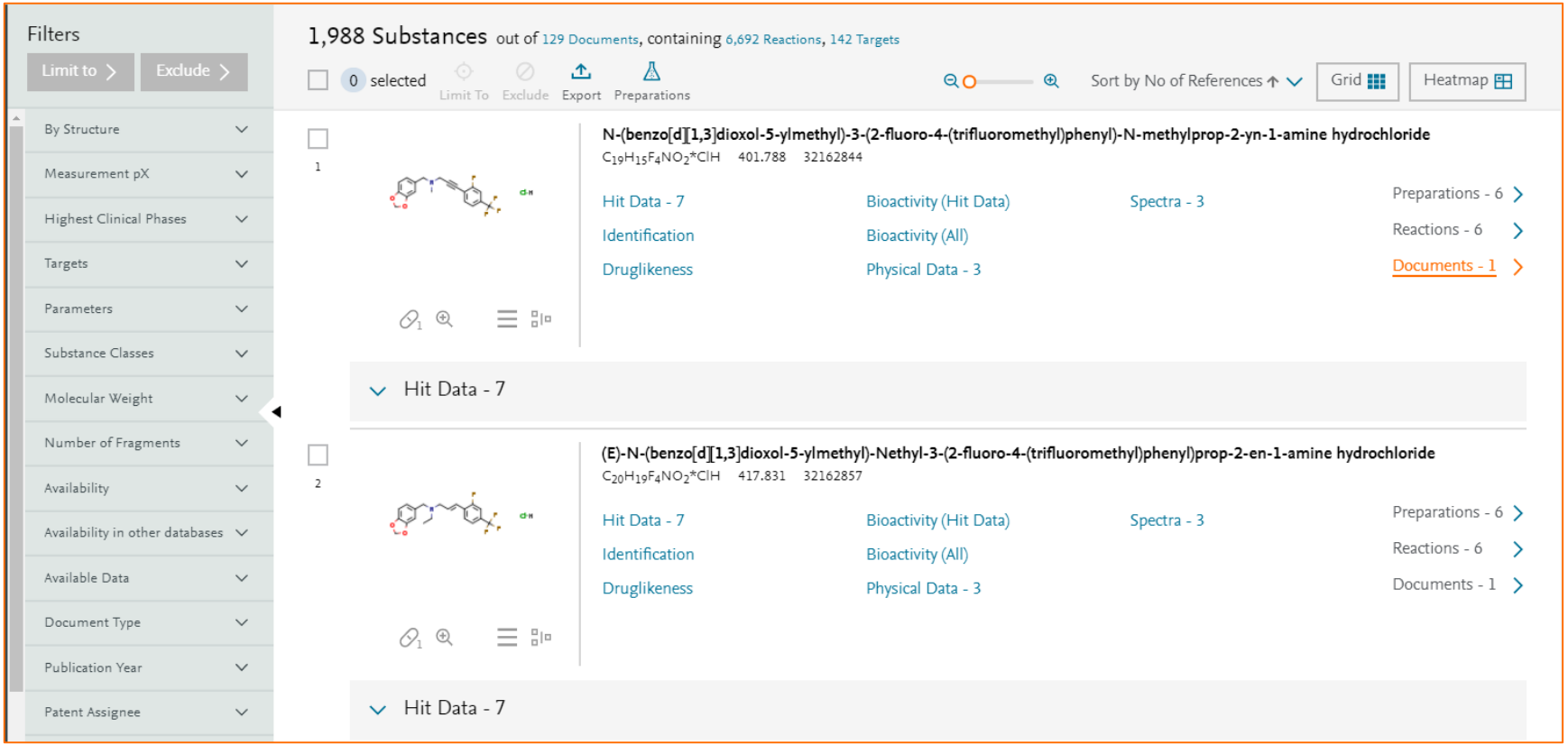
Case 4：通过效用找化合物

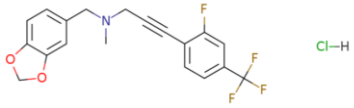
- 看一下近3年内文献/专利中报道过的，有抗生素效用的化合物，且IC50在uM级别的化合物



最后的结果


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
1,988 Substances out of 129 Documents, containing 6,692 Reactions, 142 Targets
0 selected
Limit To
Exclude
Export
Preparations
Sort by No of References
Grid
Heatmap
1
N-(benzo[d][1,3]dioxol-5-ylmethyl)-3-(2-fluoro-4-(trifluoromethyl)phenyl)-N-methylprop-2-yn-1-amine hydrochloride
C19H15F4NO2*ClH 401.788 32162844
Hit Data - 7
Bioactivity (Hit Data)
Spectra - 3
Identification
Bioactivity (All)
Druglikeness
Physical Data - 3
Preparations - 6
Reactions - 6
Documents - 1
Hit Data - 7
2
(E)-N-(benzo[d][1,3]dioxol-5-ylmethyl)-Nethyl-3-(2-fluoro-4-(trifluoromethyl)phenyl)prop-2-en-1-amine hydrochloride
C20H19F4NO2*ClH 417.831 32162857
Hit Data - 7
Bioactivity (Hit Data)
Spectra - 3
Identification
Bioactivity (All)
Druglikeness
Physical Data - 3
Preparations - 6
Reactions - 6
Documents - 1
Hit Data - 7

一些比较有意思的数据

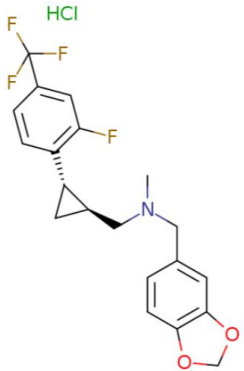


In vitro: Efficacy - 1

Quantitative Results

Show/Hide columns

pX	Parameter	Value (quant)	Unit	Biological Species	Effect	Reference
7.75	IC50	17.9	nM	Staphylococcus aureus Newman	antibiotic agent	Wei, Hanwen; Mao, Fei; Ni, Shuaishuai; Chen, Feifei; Li, Baoli; Qiu, Xiaoxia; Hu, Linghao; (...) Lan, Lefu; Li, Jian[**European Journal of Medicinal Chemistry**, **2018**, vol. 145, p. 235 - 251] Full Text ↗ Cited 4 times ↗ Details › Abstract ›



In vitro: Efficacy - 1

Quantitative Results

Show/Hide columns

pX	Parameter	Value (qual)	Value (quant)	Unit	Biological Species	Effect	Reference
6	IC50	>	1000	nM	Staphylococcus aureus Newman	antibiotic agent	Wei, Hanwen; Mao, Fei; Ni, Shuaishuai; Chen, Feifei; Li, Baoli; Qiu, Xiaoxia; Hu, Linghao; (...) Lan, Lefu; Li, Jian[**European Journal of Medicinal Chemistry**, **2018**, vol. 145, p. 235 - 251] Full Text ↗ Cited 4 times ↗ Details › Abstract ›

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Agenda

- 化合物活性数据的获取
- 文献与专利中活性数据的获取与提炼
- FDA/EMA审评文档中活性数据的获取与提炼

PharmaPendium(www.pharmapendium.com)

- 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- 今， EMA: 1995年— 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

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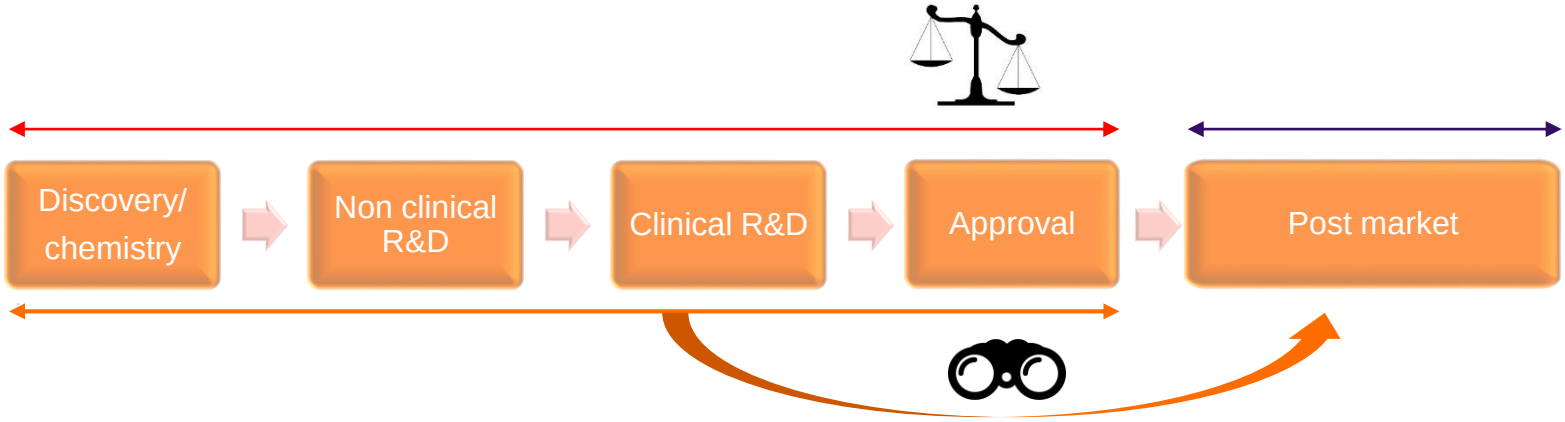
PharmaPendium的主要用途

报批：监管机构将安全性、有效性和可交付性与已上市药品进行比较（风险/效益分析）

只有当药物的性能优于市场上已经上市的药物时，才会批准使用



因此，在开发和批准过程中，您需要充分了解已上市药品的监管数据！！

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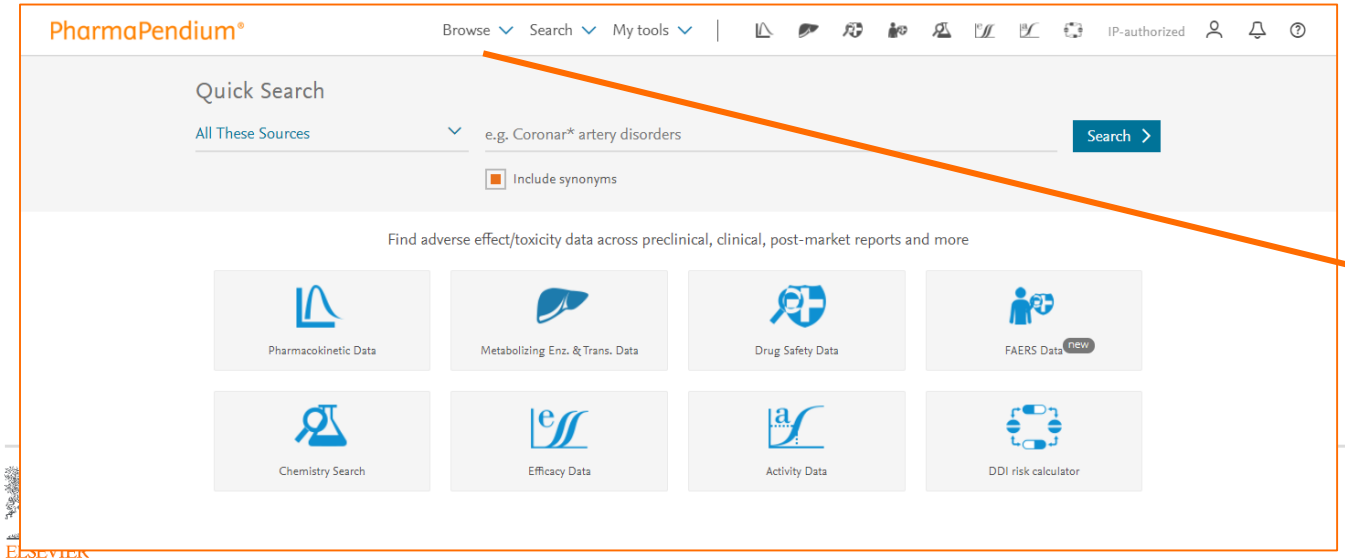
Case 5：FDA/EMA中获批药物活性数据的获取

- 案例要求与背景：
  - 正在开发一个用于治疗克罗恩病的单抗
  - 竞争产品的Cmax数据有哪些？什么情况下做出来的这个数据？
  - 数据影响：评估竞争定位并优化实验设计



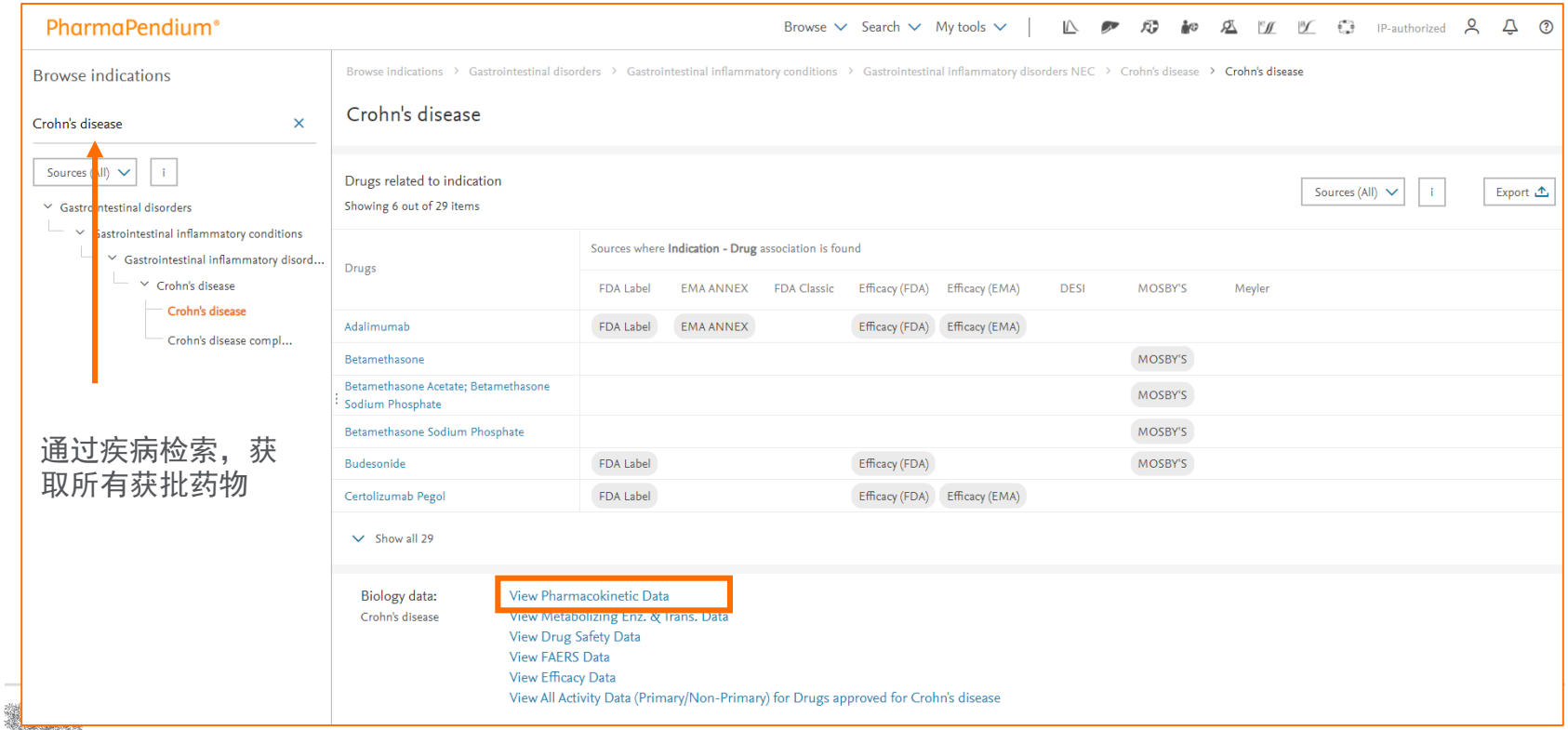
Drugs

Adverse Effects/Toxicity

Targets

Indications

获取所有FDA/EMA中用于治疗克罗恩疾病的药物



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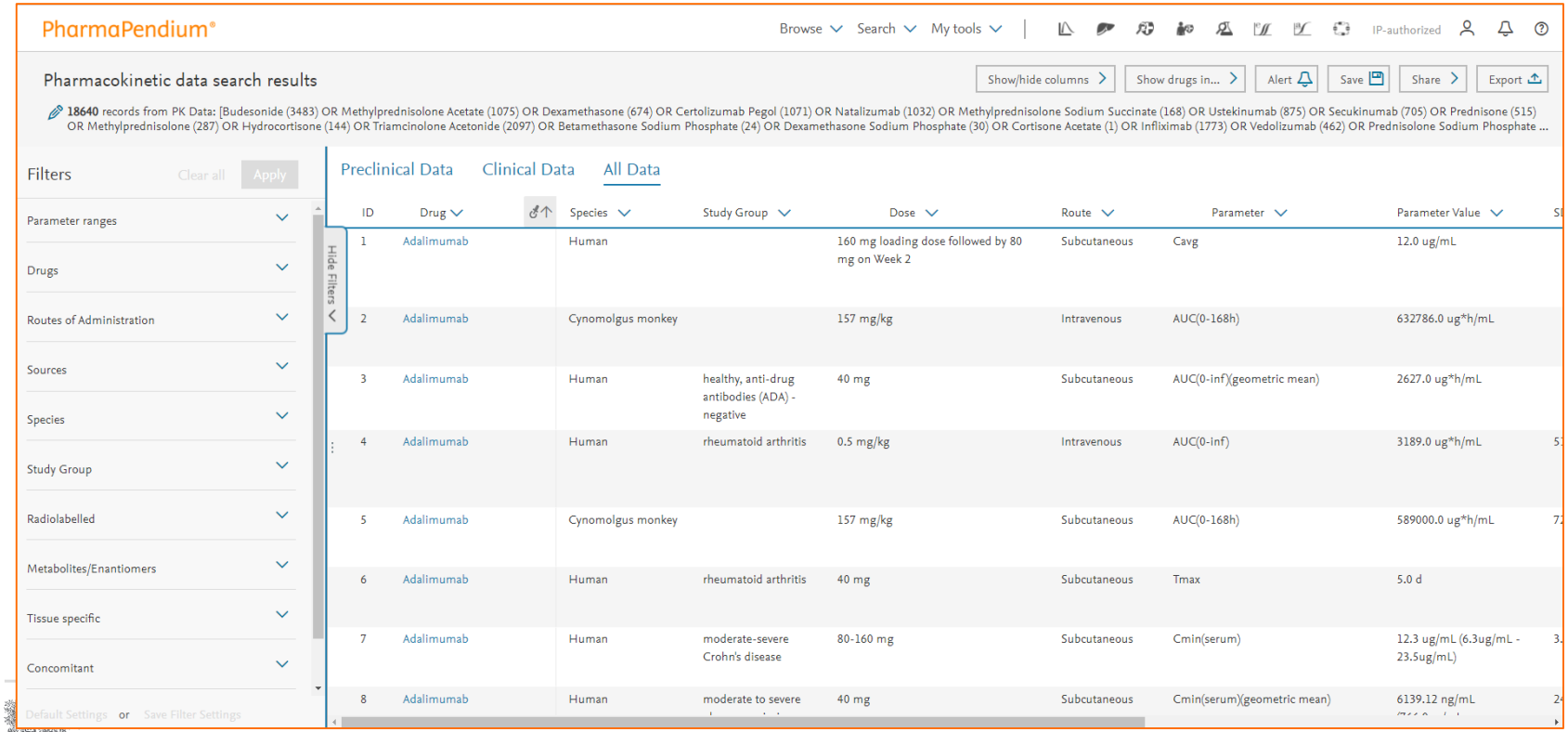
其中所有的PK数据



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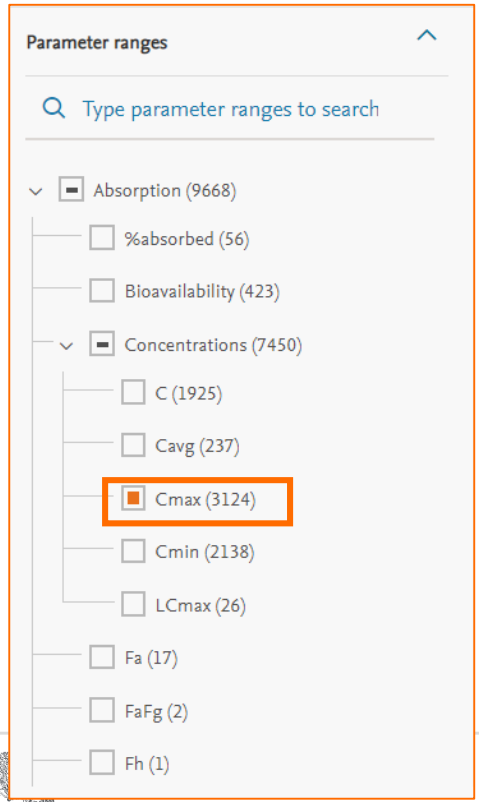
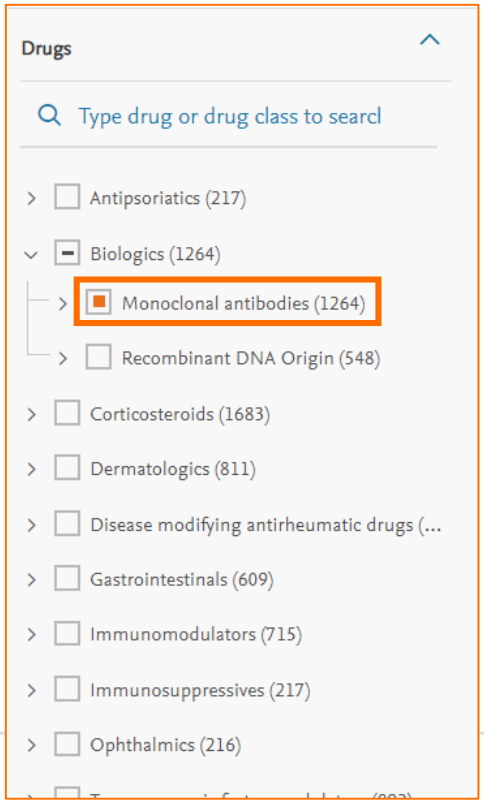
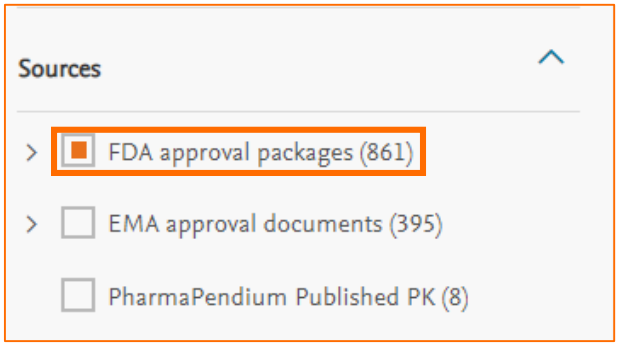
利用筛选工具进行筛选

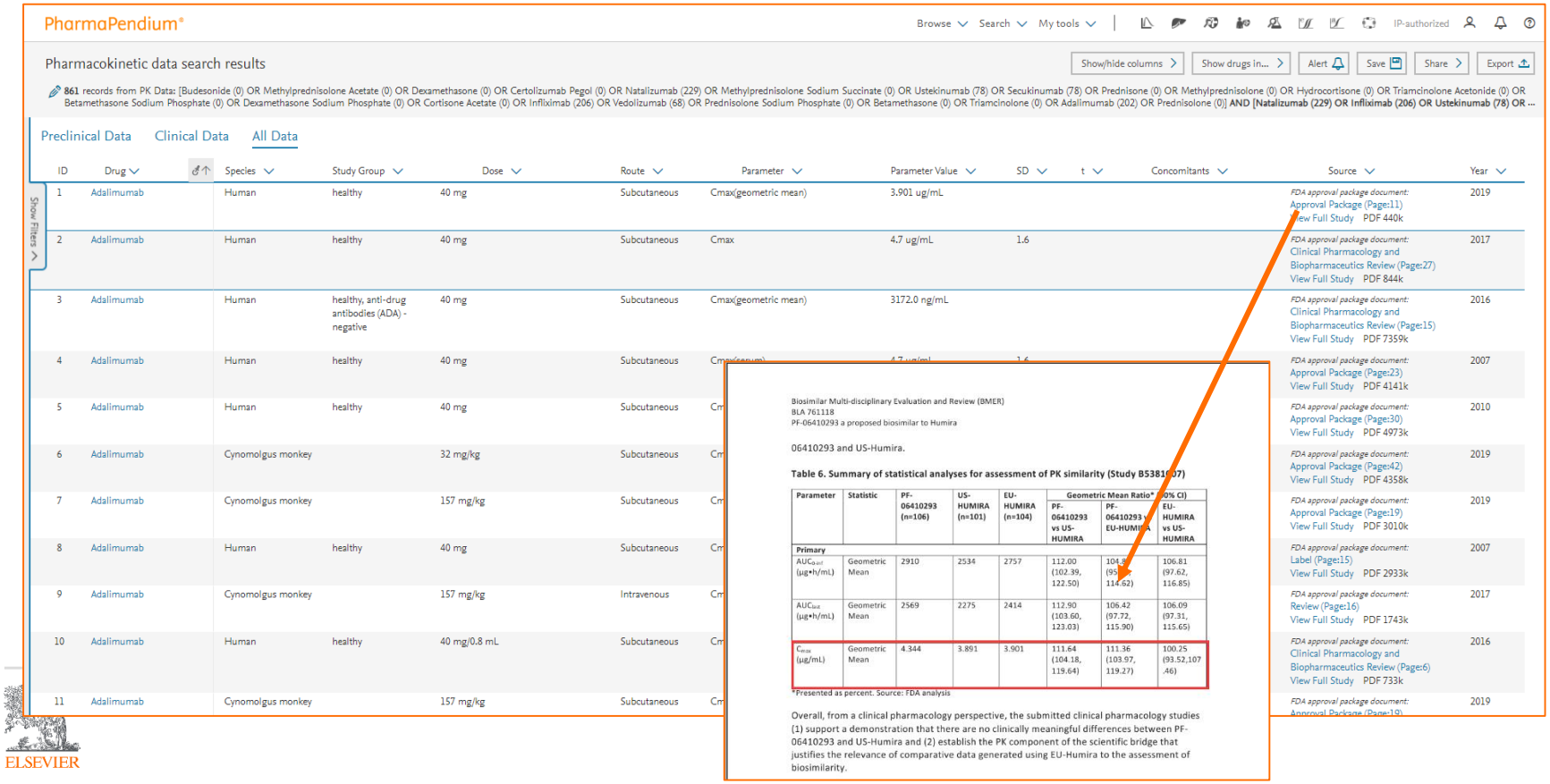






多种筛选工具，进行筛选，Cmax，单抗，FDA

最后的结果



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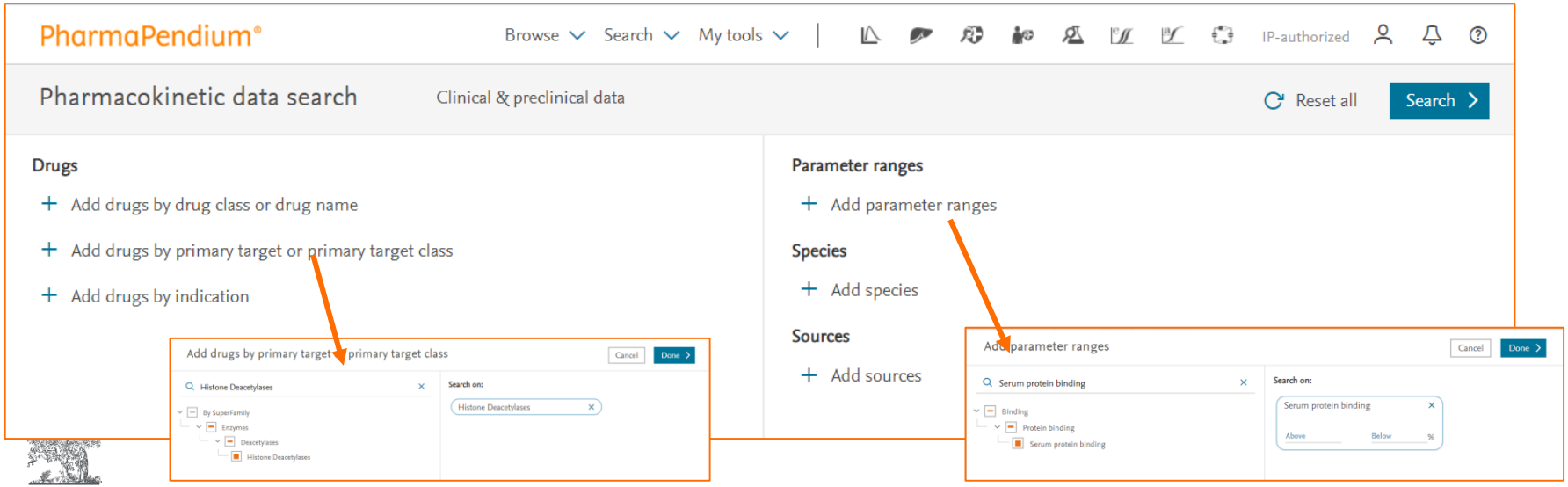
Case 6：如何利用FDA/EMA中的数据评估竞争地位

- 案例要求与背景：
  - 想评估我的新药对Histone deacetylases（HDAC）的血清蛋白结合率
  - 其他药物的血清蛋白结合值有哪些？
  - 数据影响：评估竞争定位和优化实验设计，避免监管问题



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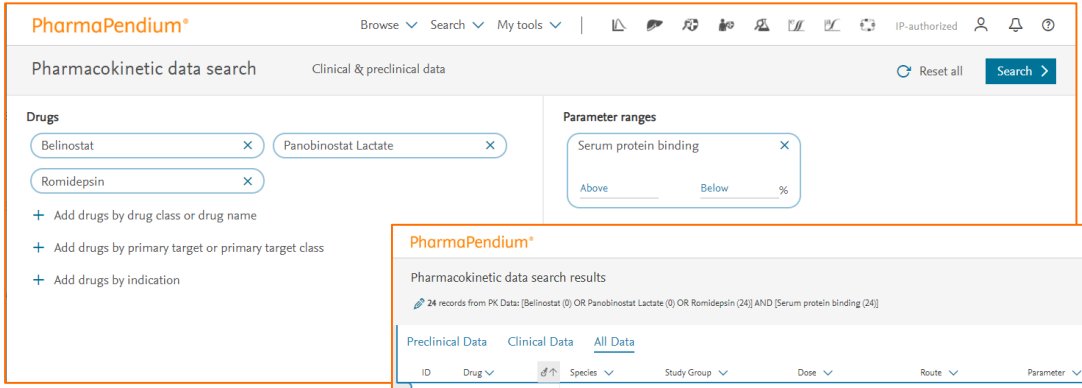
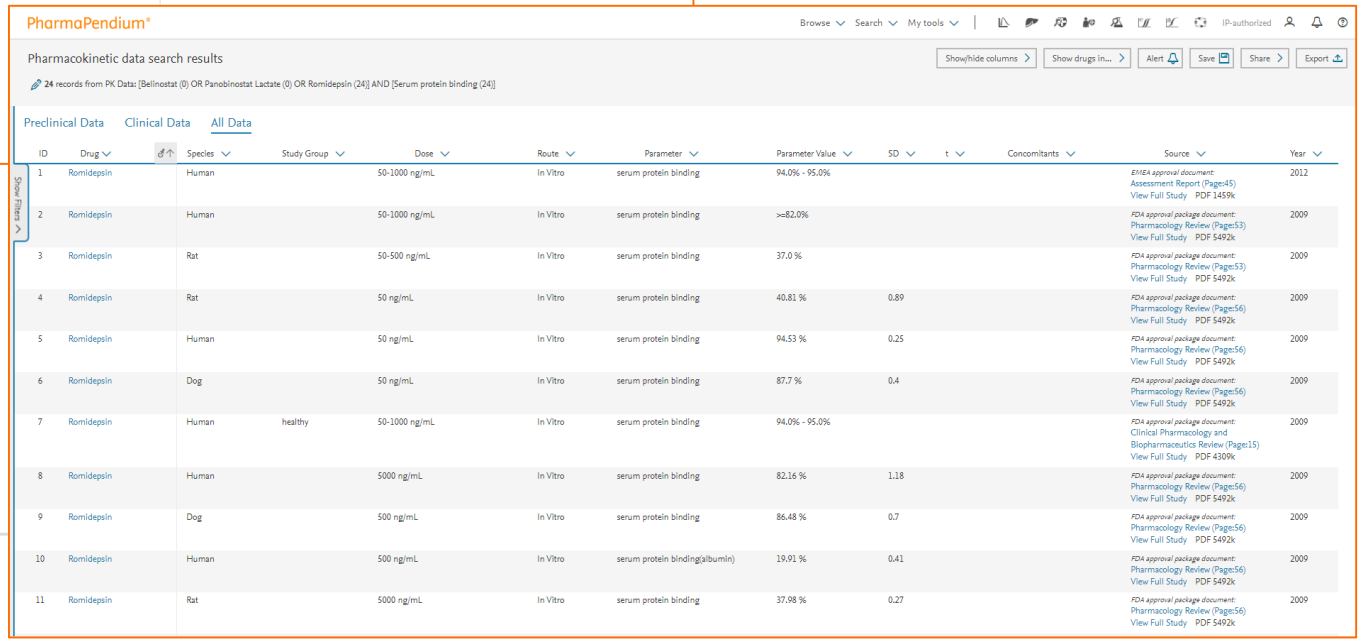
最后的检索策略





Pharmapendium将FDA/EMA中的数据全部提炼，并做了结构化处理

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导出后的结果

Export date: 14-07-2020
Pharmacokinetic Data Search Results For: Drugs: [Belinostat (0) OR Panobinostat Lactate (0) OR Romidepsin (24)] AND Parameters
Total results: 24
Sort order: Drug (Ascending);

Drug	Species	Study Group	Dose	Route	Parameter	Value	Units	ormalized Value (only standard units are	nly s	SD	t	Concomitants	Source	Source Link
Romidepsin	Human		50-1000 ng/mL	In Vitro	serum protein binding	94 to 95	%	94 to 95	%				EMA approval document: Assessment Re	https://www.pharmapendium.com/b
Romidepsin	Human		50-1000 ng/mL	In Vitro	serum protein binding	>=82	%	>=82	%				FDA approval package document: Pharma	https://www.pharmapendium.com/b
Romidepsin	Rat		50-500 ng/mL	In Vitro	serum protein binding	37	%	37 (37 to 37)	%				FDA approval package document: Pharma	https://www.pharmapendium.com/b
Romidepsin	Rat		50 ng/mL	In Vitro	serum protein binding	40.81	%	40.81 (39.92 to 41.7)	%	0.89			FDA approval package document: Pharma	https://www.pharmapendium.com/b
Romidepsin	Human		50 ng/mL	In Vitro	serum protein binding	94.53	%	94.53 (94.28 to 94.78)	%	0.25			FDA approval package document: Pharma	https://www.pharmapendium.com/b
Romidepsin	Dog		50 ng/mL	In Vitro	serum protein binding	87.7	%	87.7 (87.3 to 88.10000000000001)	%	0.4			FDA approval package document: Pharma	https://www.pharmapendium.com/b
Romidepsin	Human	healthy	50-1000 ng/mL	In Vitro	serum protein binding	94 to 95	%	94 to 95	%				FDA approval package document: Clinical	https://www.pharmapendium.com/b
Romidepsin	Human		5000 ng/mL	In Vitro	serum protein binding	82.16	%	82.16 (80.97999999999999 to 83.34)	%	1.18			FDA approval package document: Pharma	https://www.pharmapendium.com/b
Romidepsin	Dog		500 ng/mL	In Vitro	serum protein binding	86.48	%	86.48 (85.78 to 87.18)	%	0.7			FDA approval package document: Pharma	https://www.pharmapendium.com/b
Romidepsin	Human		500 ng/mL	In Vitro	serum protein binding(albumin)	19.91	%	19.91 (19.5 to 20.32)	%	0.41			FDA approval package document: Pharma	https://www.pharmapendium.com/b
Romidepsin	Rat		5000 ng/mL	In Vitro	serum protein binding	37.98	%	37.98 (37.709999999999994 to 38.25)	%	0.27			FDA approval package document: Pharma	https://www.pharmapendium.com/b
Romidepsin	Rat		500 ng/mL	In Vitro	serum protein binding	37	%	37 (37 to 37)	%				FDA approval package document: Pharma	https://www.pharmapendium.com/b
Romidepsin	Human	healthy	5000 ng/mL	In Vitro	serum protein binding	82	%	82 (82 to 82)	%				FDA approval package document: Clinical	https://www.pharmapendium.com/b
Romidepsin	Dog		500 ng/mL	In Vitro	serum protein binding	86	%	86 (86 to 86)	%				FDA approval package document: Pharma	https://www.pharmapendium.com/b
Romidepsin	Human		500 ng/mL	In Vitro	serum protein binding(alpha1-acid glycoprotein)	93.51	%	93.51 (93 to 94.02000000000001)	%	0.51			FDA approval package document: Pharma	https://www.pharmapendium.com/b
Romidepsin	Dog		500 ng/mL	In Vitro	serum protein binding	86	%	86 (86 to 86)	%				FDA approval package document: Pharma	https://www.pharmapendium.com/b
Romidepsin	Rat		500 ng/mL	In Vitro	serum protein binding	37.75	%	37.75 (37.47 to 38.03)	%	0.28			FDA approval package document: Pharma	https://www.pharmapendium.com/b
Romidepsin	Human		500 ng/mL	In Vitro	serum protein binding	94	%	94 (94 to 94)	%				FDA approval package document: Pharma	https://www.pharmapendium.com/b
Romidepsin	Human		500 ng/mL	In Vitro	serum protein binding	94.18	%	94.18 (93.81 to 94.55000000000001)	%	0.37			FDA approval package document: Pharma	https://www.pharmapendium.com/b
Romidepsin	Human		500 ng/mL	In Vitro	serum protein binding	94	%	94 (94 to 94)	%				FDA approval package document: Pharma	https://www.pharmapendium.com/b
Romidepsin	Human		1000 ng/mL	In Vitro	serum protein binding	93.55	%	93.55 (93.42999999999999 to 93.67)	%	0.12			FDA approval package document: Pharma	https://www.pharmapendium.com/b
Romidepsin	Dog		5000 ng/mL	In Vitro	serum protein binding	73.14	%	73.14 (73.02 to 73.26)	%	0.12			FDA approval package document: Pharma	https://www.pharmapendium.com/b
Romidepsin	Rat		500 ng/mL	In Vitro	serum protein binding	37	%	37 (37 to 37)	%				FDA approval package document: Pharma	https://www.pharmapendium.com/b
Romidepsin	Dog												FDA approval package document: Pharma	https://www.pharmapendium.com/b

2.6.4.4 Distribution

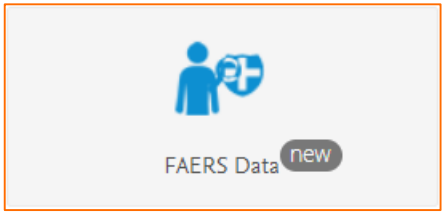
Study title: Non-clinical pharmacokinetics: *in vitro* protein binding of FR901228 in rats, dogs, humans, and human serum proteins

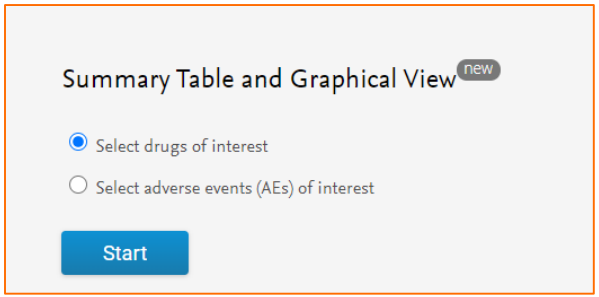
Key study findings:

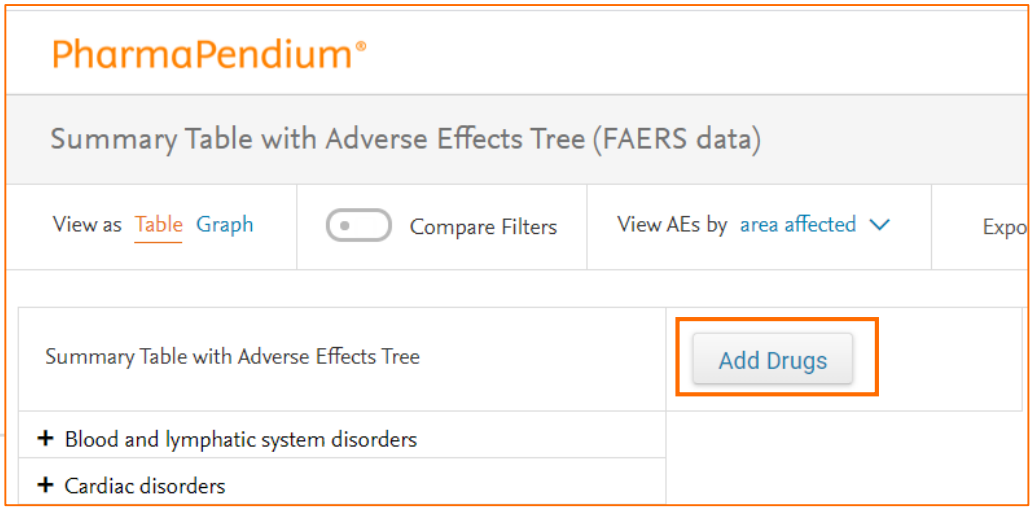
- Protein binding was independent of romidepsin concentration from 50 ng/mL – 500 ng/mL in rat and dog serum and from 50 ng/mL – 1000 ng/mL in human serum.
- Protein binding decreased at 5000 ng/mL romidepsin in human and dog serum.
- Protein binding was higher in serum from dogs (86%) and humans (94%) than in rats (37%) at 500 ng/mL romidepsin.
- Romidepsin bound better to α_1-AGP (93%) than to albumin (20%).

Case 7：如何利用FDA/EMA中的数据进行安全基线评估

- 案例要求与背景：
  - 开发PD-1/PD-L1药物
  - 作用于这些靶点的药物的上市后常见效应是什么？
  - 数据影响：竞争定位和安全基准的获取







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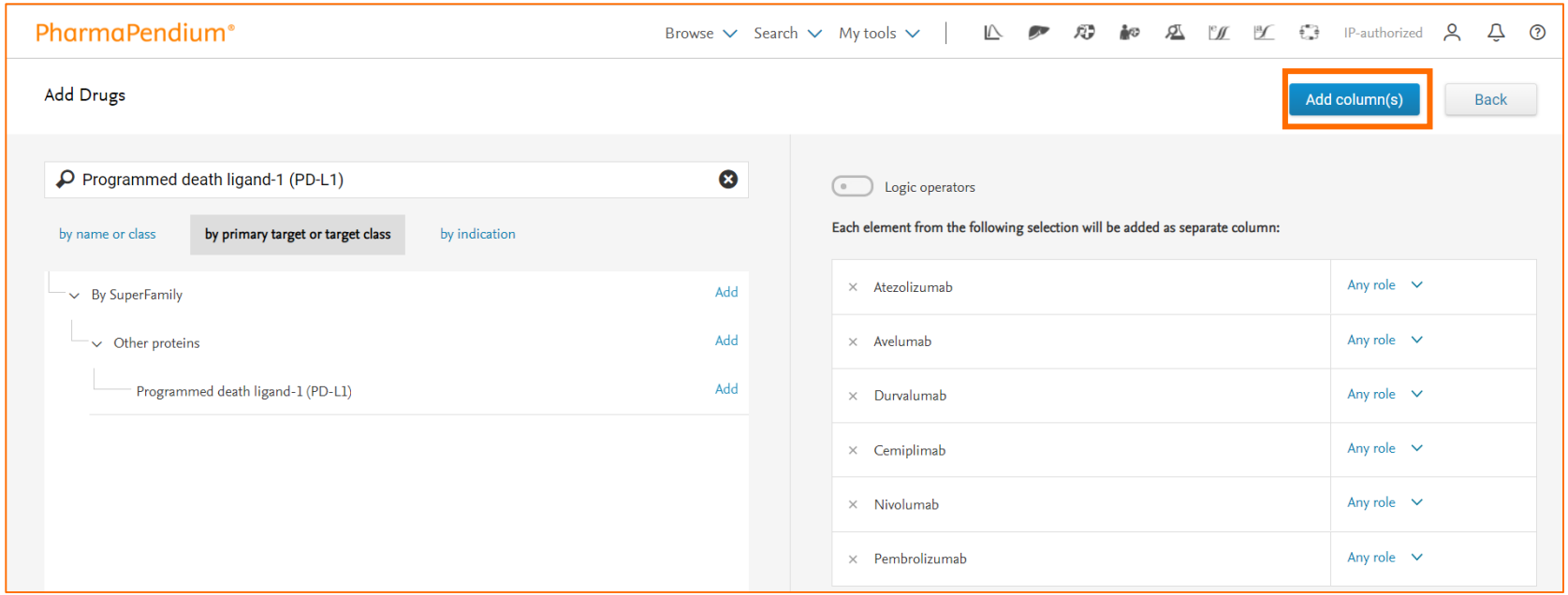
添加所有的PD-1/PD-L1药物



通过靶点添加PD-1，PD-L1药物

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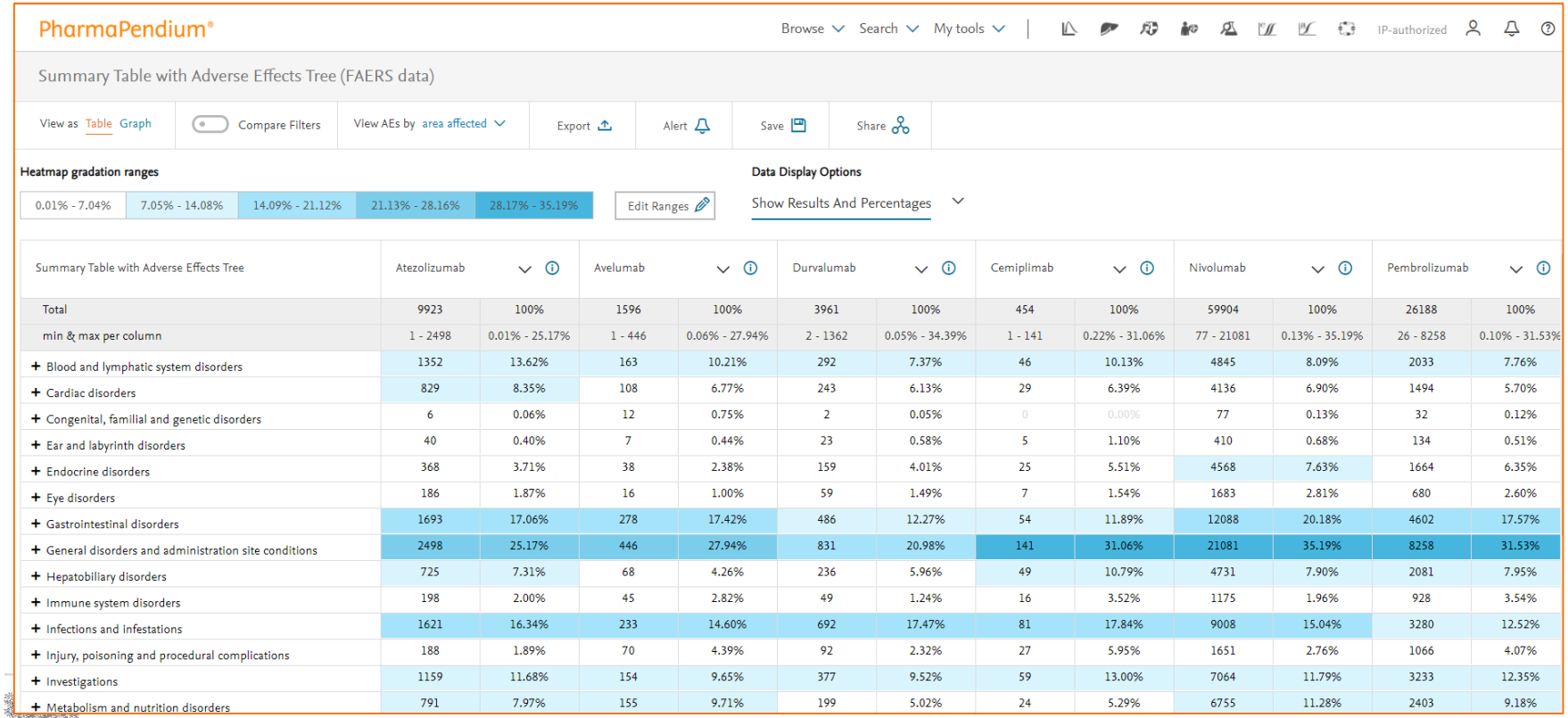
一键生成数据热图



PharmaPendium®

Browse Search My tools IP-authorized

Summary Table with Adverse Effects Tree (FAERS data)

View as Table Graph | Compare Filters | View AEs by area affected | Export | Alert | Save | Share

Heatmap gradation ranges

0.01% - 7.04% | 7.05% - 14.08% | 14.09% - 21.12% | 21.13% - 28.16% | 28.17% - 35.19% | Edit Ranges

Data Display Options

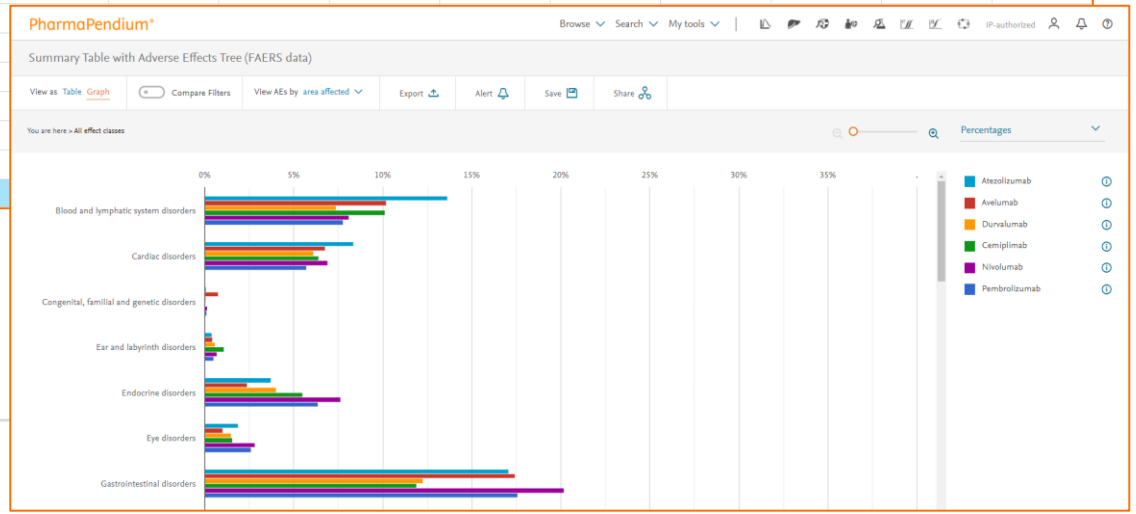
Show Results And Percentages

Summary Table with Adverse Effects Tree	Atezolizumab		Avelumab		Durvalumab		Cemiplimab		Nivolumab		Pembrolizumab	
Total	9923	100%	1596	100%	3961	100%	454	100%	59904	100%	26188	100%
min & max per column	1 - 2498	0.01% - 25.17%	1 - 446	0.06% - 27.94%	2 - 1362	0.05% - 34.39%	1 - 141	0.22% - 31.06%	77 - 21081	0.13% - 35.19%	26 - 8258	0.10% - 31.53%
+ Blood and lymphatic system disorders	1352	13.62%	163	10.21%	292	7.37%	46	10.13%	4845	8.09%	2033	7.76%
+ Cardiac disorders	829	8.35%	108	6.77%	243	6.13%	29	6.39%	4136	6.90%	1494	5.70%
+ Congenital, familial and genetic disorders	6	0.06%	12	0.75%	2	0.05%	0	0.00%	77	0.13%	32	0.12%
+ Ear and labyrinth disorders	40	0.40%	7	0.44%	23	0.58%	5	1.10%	410	0.68%	134	0.51%
+ Endocrine disorders	368	3.71%	38	2.38%	159	4.01%	25	5.51%	4568	7.63%	1664	6.35%
+ Eye disorders	186	1.87%	16	1.00%	59	1.49%	7	1.54%	1683	2.81%	680	2.60%
+ Gastrointestinal disorders	1693	17.06%	278	17.42%	486	12.27%	54	11.89%	12088	20.18%	4602	17.57%
+ General disorders and administration site conditions	2498	25.17%	446	27.94%	831	20.98%	141	31.06%	21081	35.19%	8258	31.53%
+ Hepatobiliary disorders	725	7.31%	68	4.26%	236	5.96%	49	10.79%	4731	7.90%	2081	7.95%
+ Immune system disorders	198	2.00%	45	2.82%	49	1.24%	16	3.52%	1175	1.96%	928	3.54%
+ Infections and infestations	1621	16.34%	233	14.60%	692	17.47%	81	17.84%	9008	15.04%	3280	12.52%
+ Injury, poisoning and procedural complications	188	1.89%	70	4.39%	92	2.32%	27	5.95%	1651	2.76%	1066	4.07%
+ Investigations	1159	11.68%	154	9.65%	377	9.52%	59	13.00%	7064	11.79%	3233	12.35%
+ Metabolism and nutrition disorders	791	7.97%	155	9.71%	199	5.02%	24	5.29%	6755	11.28%	2403	9.18%

更多具体细节信息

Summary Table with Adverse Effects Tree	Atezolizumab		Avelumab		Durvalumab		Cemiplimab		Nivolumab		Pembrolizumab	
- General disorders and administration site conditions	2498	25.17%	446	27.94%	831	20.98%	141	31.06%	21081	35.19%	8258	31.53%
+ Administration site reactions	6	0.06%	2	0.13%	19	0.48%	6	1.32%	88	0.15%	118	0.45%
+ Body temperature conditions	589	5.94%	81	5.08%	199	5.02%	30	6.61%	3120	5.21%	1321	5.04%
+ Complications associated with device	3	0.03%	0	0.00%	5	0.13%	0	0.00%	43	0.07%	10	0.04%
- Fatal outcomes	609	6.14%	95	5.95%	233	5.88%	22	4.85%	8468	14.14%	2085	7.96%
- Death and sudden death	609	6.14%	95	5.95%	233	5.88%	22	4.85%	8468	14.14%	2085	7.96%
Accidental death	0	0.00%	0	0.00%	0	0.00%	0	0.00%	2	0.00%	0	0.00%
Brain death	2	0.02%	0	0.00%	0	0.00%	0	0.00%	2	0.00%	3	0.01%
Cardiac death	2	0.02%	0	0.00%	1	0.03%	0	0.00%	2	0.00%	3	0.01%
Death	587	5.92%										
Death neonatal	0	0.00%										
Drowning	0	0.00%										
Euthanasia	0	0.00%										
Sudden cardiac death	0	0.00%										
Sudden death	18	0.18%										
+ General system disorders NEC	1442	14.53%										

查看不同领域的效应



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生物活性数据与文献的获取与提炼

- RMC从大量文献和专利中摘取和物质生物活性相关的数据，帮助科研人员获得标准化，规范化，格式化的数据列表及参考文献
- PharmaPendium帮助全面获取上市药物的监管数据，可以为实验方案的设计，产品定位提供全方位的数据支持
- Elsevier Life Science培训中心
  - https://www.elsevier.com/zh-cn/rd-solutions/pharma-and-life-sciences-solutions/life-sciences-online-training-center

扫码进群，获取视频，PPT以及最新资料。

Thank you