
Application of N-(bromoacetyl)-3, 3-dinitroazetidine (ABDNAZ)

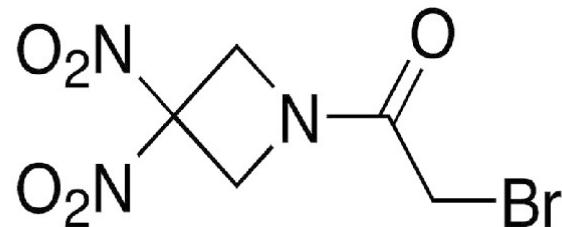
Production: Methods of synthesizing and isolating N-(bromoacetyl)-3,3-dinitroazetidine and a composition including the same

Inventors: Nicholas A. Straessler, Louis F. Cannizzo, Ping Li, Michael P. Kramer, David M. Rosenberg

Patent Number: US 8471,041 B2

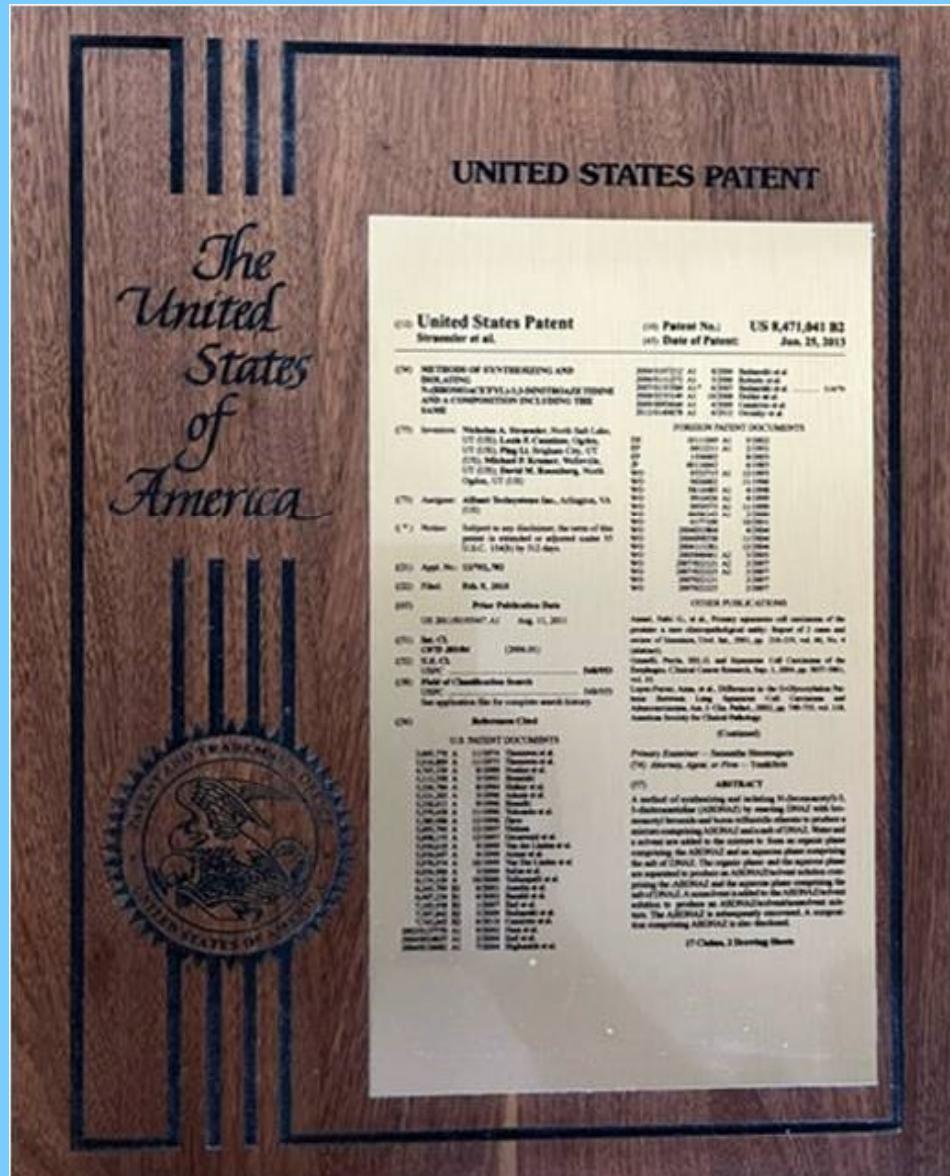
Date: June 25, 2013

Orbital ATK developed and patented the process to manufacture N-(Bromoacetyl)-3,3-Dinitroazetidine (ABDNAZ). This anticancer active ingredient was made, analyzed and characterized following FDA regulations and GLP and GMP regulated procedures.



Chemical Formula: C₅H₆BrN₃O₅

Molecular Weight: 268.02



Methods of synthesizing and isolating N-(bromoacetyl)-3,3-dinitroazetidine and a composition including the same

ChatGPT said: Here are the key points from the paper:

Focus:

The patent outlines the methods for synthesizing and isolating N-(bromoacetyl)-3,3-dinitroazetidine, a chemical compound with potential applications in various industries.

Key Points:

Synthesis Method: Describes the specific chemical processes and reactions required to synthesize N-(bromoacetyl)-3,3-dinitroazetidine, ensuring a **high yield and purity**.

Isolation Techniques: Details the methods used to isolate the compound from reaction mixtures, including purification steps to obtain the desired product in its pure form.

Composition: The patent also includes information on compositions that incorporate N-(bromoacetyl)-3,3-dinitroazetidine, suggesting its potential use in various applications, possibly in pharmaceuticals or materials science.

Industrial Applications: While the specific applications might not be fully detailed in the summary, the compound is likely intended for use in specialized industrial processes or as a precursor in the synthesis of other compounds.

Significance:

This patent is valuable for industries seeking new synthetic routes and applications for novel chemical compounds, particularly those involving azetidine derivatives.

The methods provided could be important for researchers and manufacturers looking to produce this compound efficiently and at scale.

This summary captures the essential aspects of the patent.

Methods of synthesizing and isolating N-(bromoacetyl)-3,3-dinitroazetidine and a composition including the same

ChatGPT 说：以下是论文的要点：

重点：该专利概述了合成和分离 N-(溴乙酰基)-3,3-二硝基氮杂环丁烷的方法，这是一种具有潜在应用的化合物，可能用于多个行业。

要点：

合成方法：描述了合成 N-(溴乙酰基)-3,3-二硝基氮杂环丁烷所需的特定化学工艺和反应，以确保高产率和纯度。

分离技术：详细说明了从反应混合物中分离该化合物的方法，包括纯化步骤，以获得纯净的目标产物。

成分：专利还包括了含有 N-(溴乙酰基)-3,3-二硝基氮杂环丁烷的组合物信息，表明其可能用于制药或材料科学中的潜在应用。

工业应用：尽管在摘要中没有详述具体应用，但该化合物可能用于专门的工业工艺，或作为合成其他化合物的前体。

意义：对于寻求新型化合物合成途径和应用的行业来说，这项专利具有重要价值，特别是在涉及氮杂环丁烷衍生物的领域。这些方法对研究人员和制造商而言，可能在高效、规模化生产此化合物方面至关重要。此摘要概括了该专利的主要内容。

Medication Application of ANDNAZ

Title: Treatment with a Novel Dinitroazetidine (Abdnaz) Improves Nitrite Reductase Activity of Sickle Red Blood Cells

Authors: Marcel H.A.M. Fens, PhD; Sandra K. Larkin, MS; William L. Fitch, PhD; Jan Scicinski, PhD; Bryan Oronsky, MD; Frans A. Kuypers, PhD

Presented at: Hemoglobinopathies, excluding Thalassemia: Poster III | November 16, 2012

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For **Frans A. Kuypers, PhD**, I couldn't find specific contact details.

Treatment with a Novel Dinitroazetidine, Abdnaz, Improves Nitrite Reductase Activity of Sickle Red Blood Cells

From Copilot:

The study investigates the effects of a novel compound, Abdnaz, which is a dinitroazetidine, on the nitrite reductase activity of sickle red blood cells.

Key Points:

Novel Compound (Abdnaz): Abdnaz is identified as a dinitroazetidine compound. Its specific structure or the mechanism of action might be connected to its effects on sickle cell pathology.

Nitrite Reductase Activity: The research focuses on how Abdnaz affects the nitrite reductase activity in sickle red blood cells. Nitrite reductase activity is crucial because it can influence nitric oxide (NO) production, which has vasodilatory effects and can help alleviate the vaso-occlusive crises characteristic of sickle cell disease.

Sickle Red Blood Cells: The study likely addresses the pathological characteristics of sickle red blood cells, including their impaired functionality and how Abdnaz might mitigate these issues.

Significance:

Potential Therapeutic Implications: The findings suggest that Abdnaz could have therapeutic potential for improving the function of sickle red blood cells, possibly offering a new avenue for treating sickle cell disease.

Further Research: This study likely serves as a foundation for further investigations into Abdnaz and similar compounds in the context of hemoglobinopathies and other blood-related disorders.

Medication Application of ANDNAZ

From Copilot: 以下是这项研究的中文摘要：

标题: 使用一种新型的二硝基氮杂环丁烷（Abdnaz）改善镰状红细胞的亚硝酸还原酶活性

作者: Marcel H.A.M. Fens博士, Sandra K. Larkin硕士, William L. Fitch博士, Jan Scicinski博士, Bryan Oronskey医生, Frans A. Kuypers博士

会议: 血红蛋白病（不包括地中海贫血）：海报III | 2012年11月16日

研究重点:

该研究探讨了一种新型化合物Abdnaz（二硝基氮杂环丁烷）对镰状红细胞亚硝酸还原酶活性的影响。

关键点:

新型化合物（Abdnaz）: Abdnaz被确定为一种二硝基氮杂环丁烷化合物。其特定结构或作用机制可能与其对镰状细胞病理的影响有关。

亚硝酸还原酶活性: 研究的重点是Abdnaz如何影响镰状红细胞的亚硝酸还原酶活性。亚硝酸还原酶活性对一氧化氮（NO）的生成具有重要作用，而一氧化氮具有血管扩张作用，可以帮助缓解镰状细胞病的血管阻塞危机。

镰状红细胞: 该研究可能还涉及镰状红细胞的病理特征，包括其功能障碍，以及Abdnaz如何减轻这些问题。

研究意义:

潜在的治疗意义: 研究结果表明，Abdnaz可能在改善镰状红细胞功能方面具有治疗潜力，可能为治疗镰状细胞病提供新的途径。

进一步研究: 这项研究可能为进一步研究Abdnaz及类似化合物在血红蛋白病和其他血液相关疾病中的应用奠定基础。

这份摘要突出了该研究的核心内容

Medication Application of ANDNAZ

ARTICLES [Volume 16, Issue 9](#), P1133-1142, September 2015

Safety and activity of RRx-001 in patients with advanced cancer: a first-in-human, open-label, dose-escalation phase 1 study

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Affiliations

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Medication Application of ANDNAZ

From Copilot:

The significant conclusions from the study “**Safety and activity of RRx-001 in patients with advanced cancer: a first-in-human, open-label, dose-escalation phase 1 study**”:

Safety and Tolerability: RRx-001 was well-tolerated by patients, with manageable side effects. This indicates that the drug can be safely administered at various dose levels.

Pharmacokinetics: The study provided valuable data on the pharmacokinetics of RRx-001, helping to understand how the drug is absorbed, distributed, metabolized, and excreted in the body.

Anti-Tumor Activity: Promising signs of anti-tumor activity were observed, suggesting that RRx-001 has potential efficacy in treating advanced solid tumors.

Further Research: The findings support the need for further clinical trials to explore the efficacy and safety of RRx-001 in a larger patient population and in combination with other treatments.

These conclusions highlight the potential of RRx-001 as a novel therapeutic option for patients with advanced cancer, warranting additional studies to confirm its benefits.

Medication Application of ANDNAZ

From ChatGPT:

The study on RRx-001, a novel anticancer compound, aimed to assess its safety, tolerability, and early activity in patients with advanced cancer. The results showed that RRx-001 was generally well tolerated, with mild side effects like injection site pain and vein hardening. No dose-limiting toxicities were observed. While only one patient had a partial response, 67% had stable disease. Importantly, four patients became responsive again to treatments they were previously resistant to, indicating potential for resensitization. The recommended dose for future trials was 16.7 mg/m^2 .

The key contributions of the RRx-001 phase 1 study include:

Safety Profile: RRx-001 was well tolerated with mild side effects, demonstrating no dose-limiting toxicities.

Preliminary Efficacy: Although one patient had a partial response, the majority (67%) achieved stable disease.

Resensitization: RRx-001 showed promise in resensitizing cancer patients to therapies they had become resistant to, offering a potential breakthrough in treatment.

Phase 2 Dose Recommendation: A dose of 16.7 mg/m^2 was recommended for further trials.

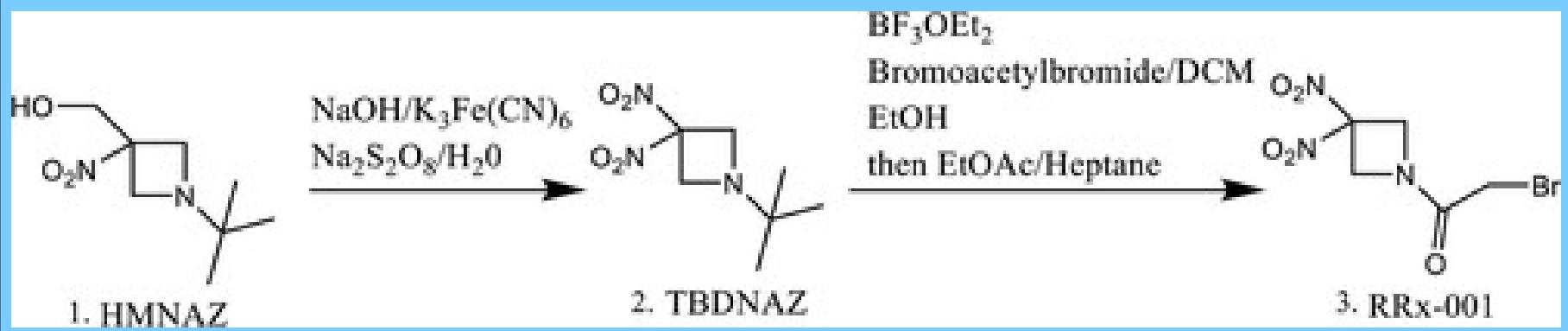
Per-clinical trial of ABDNAZ

Title: Discovery of RRx-001, a Myc and CD47 Downregulating Small Molecule with Tumor Targeted Cytotoxicity and Healthy Tissue Cytoprotective Properties in Clinical Development

Authors: Bryan Oronsky, XiaoNing Guo, XiaoHui Wang, Pedro Cabrales, David Sher, Lou Cannizzo, Bob Wardle, Nacer Abrouk, Michelle Lybeck, Scott Caroen, Arnold Oronsky, Tony R. Reid

Publication Date: May 27, 2021

Journal: Journal of Medicinal Chemistry, Vol 64, Issue 11



Per-clinical trial of ABDNAZ

Focus of the Study:

The discovery and development of RRx-001, a small molecule drug that down regulates Myc and CD47.

Myc: A well-known oncogene involved in cell proliferation, making it a target for cancer therapy.

CD47: A protein that acts as a "don't eat me" signal to the immune system, often over expressed in cancer cells to evade immune detection.

Key Properties of RRx-001:

Tumor-Targeted Cytotoxicity: RRx-001 specifically targets and kills tumor cells while sparing healthy tissue.

Cytoprotective Properties: In addition to its anti-tumor effects, RRx-001 has properties that protect healthy tissues from damage, potentially reducing side effects.

Clinical Development: The molecule is currently under clinical development, suggesting it has shown promise in preclinical and early clinical trials.

This summary encapsulates the essence of the research, highlighting the dual function of RRx-001 as both a cancer therapy and a protective agent for healthy tissues.

Per-clinical trial of ABDNAZ

以下是这项研究的中文摘要：

文章标题: 发现RRx-001，一种可下调Myc和CD47的小分子，具有肿瘤靶向细胞毒性和健康组织细胞保护特性的临床开发药物

作者: Bryan Oronsky, 郭晓宁, 王晓辉, Pedro Cabrales, David Sher, Lou Cannizzo, Bob Wardle, Nacer Abrouk, Michelle Lybeck, Scott Caroen, Arnold Oronsky, Tony R. Reid

出版日期: 2021年5月27日

期刊: 《药物化学杂志》 (Journal of Medicinal Chemistry)，第64卷，第11期

研究重点:

发现并开发了RRx-001，这是一种能够下调Myc和CD47的小分子药物。

Myc: 一种众所周知的癌基因，参与细胞增殖，是癌症治疗的一个靶点。

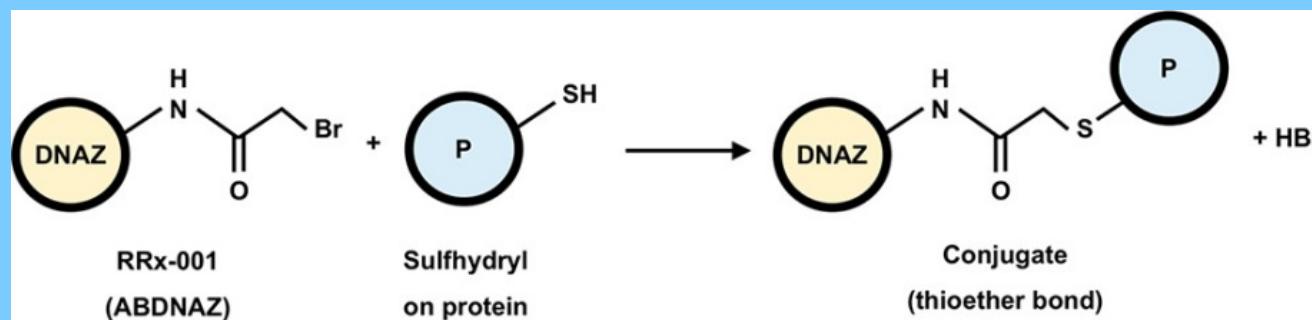
CD47: 一种蛋白质，作为免疫系统的“别吃我”信号，癌细胞常常通过过度表达CD47来逃避免疫检测。

RRx-001的关键特性:

肿瘤靶向细胞毒性: RRx-001能够特异地靶向并杀死肿瘤细胞，同时保护健康组织不受损害。

细胞保护特性: 除了抗肿瘤作用外，RRx-001还具有保护健康组织免受损伤的特性，可能有助于减少副作用。

临床开发: 该分子目前正处于临床开发阶段，表明其在临床前和早期临床试验中表现出良好的前景。



Per-clinical trial of ABDNAZ

RRx-001, a tumor-activated small molecule, is currently being investigated in a **global Phase 3 clinical trial called REPLATINUM (NCT05566041) in China and the United States.**

Here are the key details:

Purpose: The trial aims to evaluate the efficacy of RRx-001 in third-line or beyond extensive stage small cell lung cancer (SCLC) patients who previously received a platinum doublet and a checkpoint inhibitor.

Mechanism: RRx-001 inhibits the NLRP3 inflamma some and repolarizes tumor-associated macrophages (TAMs), restoring sensitivity to chemotherapy.

Endpoints: The study focuses on progression-free survival (PFS) and overall survival (OS) in SCLC patients.

Challenges: SCLC is highly aggressive and resistant, making RRx-001's potential impact crucial.

Licensing Agreement: EpicentRx and SciClone Pharmaceuticals established a licensing agreement for RRx-001 in Greater China¹.

Per-clinical trial of ABDNAZ

RRx-001 是一种肿瘤激活的小分子，目前正在中国和美国进行全球性的 III 期临床试验（REPLATINUM，临床试验编号 NCT05566041）。以下是关键信息：

目的：该试验旨在评估 RRx-001 对之前接受过铂双联药物和 PD-1/PD-L1 抑制剂治疗的晚期小细胞肺癌（SCLC）患者的疗效。

作用机制：RRx-001 抑制 NLRP3 炎症小体并重新极化肿瘤相关巨噬细胞（TAMs），从而恢复对化疗的敏感性。

终点指标：该研究关注 SCLC 患者的无进展生存期（PFS）和总生存期（OS）。

挑战：SCLC 具有高度侵袭性和耐药性，因此 RRx-001 的潜在影响至关重要。

许可协议：EpicentRx 和 SciClone Pharmaceuticals 在大中华区建立了 RRx-001 的许可协议。

EpicentRx Announces First Patient Dosed in China for the Phase 3 REPLATINUM Global Study with RRx-001 in Third Line and Beyond Extensive Stage Small Cell Lung Cancer (SCLC), Oct 6, 2022

Per-clinical trial of ABDNAZ

The clinical trial progress for RRx-001, a direct NLRP3 inflamma some inhibitor, is as follows:

REPLATINUM Trial (Phase 3):

Indication: Third-line and beyond small cell lung cancer (SCLC).

Treatment: RRx-001 combined with reintroduced chemotherapy (carboplatin/cisplatin and etoposide).

ClinicalTrials.gov Identifier: NCT03699956¹.

Status: Ongoing.

KEVLARx Trial (Phase 2b):

Indication: Newly diagnosed head and neck cancer.

Treatment: RRx-001.

Status: Ongoing².

G-FORCE-1 Trial (Phase 1):

Indication: First-line glioblastoma (GBM).

Treatment: RRx-001 as an add-on therapy to temozolomide and radiotherapy.

Status: Completed (determined recommended Phase 2 dose)³.

RRx-001 has shown safety and tolerability in humans and holds promise for various diseases where immune and inflamasome activation plays a role.

Per-clinical trial of ABDNAZ

EpicentRx Announces First Patient Dosed in China for the Phase 3 REPLATINUM Global Study with RRx-001 in Third Line and Beyond Extensive Stage Small Cell Lung Cancer (SCLC)

October 6, 2022 |

On October 6, 2022, EpicentRx announced that the first patient in China was dosed for the Phase 3 REPLATINUM global study with RRx-001. This trial, conducted in collaboration with SciClone Pharmaceuticals, aims to evaluate the efficacy of RRx-001 combined with a platinum doublet versus a platinum doublet alone in approximately 300 patients with third-line or beyond extensive stage small cell lung cancer (SCLC) who have previously received a platinum doublet and a checkpoint inhibitor¹². RRx-001 is a tumor-activated small molecule that inhibits the NLRP3 inflammasome and repolarizes tumor-associated macrophages (TAMs), helping to restore sensitivity to chemotherapy¹. The primary endpoints of the study are progression-free survival (PFS) and overall survival (OS)¹.

2022年10月6日，EpicentRx宣布中国首位患者在全球Ⅲ期REPLATINUM研究中接受了RRx-001的治疗。该试验与SciClone Pharmaceuticals合作进行，旨在评估RRx-001联合铂类双药与单独铂类双药在约300名接受过铂类双药和检查点抑制剂治疗的三线或以上广泛期小细胞肺癌(SCLC)患者中的疗效。

RRx-001是一种肿瘤激活的小分子，能够抑制NLRP3炎症小体并重新极化肿瘤相关巨噬细胞(TAMs)，帮助恢复对化疗的敏感性。该研究的主要终点是无进展生存期(PFS)和总生存期(OS)。

Per-clinical trial of ABDNAZ

RRx-001 是一种直接的 NLRP3 炎症小体抑制剂，目前正在以下进行临床试验：

REPLATINUM 试验（III 期）：

适应症：晚期小细胞肺癌（SCLC）的第三线及以后治疗。

治疗方案：RRx-001 与重新引入的化疗联合使用（卡铂/顺铂和依托泊苷）。

临床试验编号：NCT03699956¹。

状态：正在进行中。

KEVLARx 试验（IIb 期）：

适应症：新诊断的头颈部肿瘤。

治疗方案：RRx-001。

状态：正在进行中²。

G-FORCE-1 试验（I 期）：

适应症：一线胶质母细胞瘤（GBM）。

治疗方案：RRx-001 作为替莫唑胺和放疗的附加治疗。

状态：已完成（确定了推荐的 II 期剂量）³。

RRx-001 在人体中已经显示出安全性和耐受性，并在免疫和炎症激活驱动疾病病理学的多种疾病中具有潜在疗效。

Per-clinical trial of ABDNAZ

截至目前，RRx-001 在中国的全球 III 期临床试验（REPLATINUM，临床试验编号 NCT05566041）已经开始。该试验由合作伙伴 SciClone Pharmaceuticals 监管，共有超过 50 个位于美国和中国的临床试验中心。试验旨在比较 RRx-001 与一线铂双联药物相比，对之前接受过铂双联药物和 PD-1/PD-L1 抑制剂治疗的约 300 名晚期小细胞肺癌（SCLC）患者的疗效。RRx-001 是一种肿瘤激活的小分子，通过抑制 NLRP3 炎症小体并重新极化肿瘤相关巨噬细胞（TAMs），恢复对已尝试过的化疗的敏感性。该研究的主要终点是晚期 SCLC 患者的无进展生存期（PFS）和总生存期（OS）。RRx-001 有望帮助全球范围内的 SCLC 患者，这是一种顽固耐药且几乎百分之百致命的高度侵袭性癌症。¹ ☈ [EpicentRx Announces First Patient Dosed in China for the Phase 3 REPLATINUM Global Study with RRx-001 in Third Line and Beyond Extensive Stage Small Cell Lung Cancer \(SCLC\)](#)

Per-clinical trial of ABDNAZ

A Review of RRx-001: A Late-Stage Multi-Indication Inhibitor of NLRP3 Activation and Chronic Inflammation

Review Article

[Open access](#), Published: 15 March 2023, Volume 83, pages 389–402, (2023)

A multicenter, phase 1, dose escalation clinical trial (G-FORCE-1) of XRT, RRx-001 and temozolomide followed by temozolomide +/- RRx-001 in newly diagnosed glioblastoma

Howard Fine¹Tony Reid²[Scott Caroen](#)³[Bryan Oronsky](#)^{3*}Nacer Abrouk³[Nicholas Butowski](#)⁴

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³Department of Drug Development, Clinical Trial Innovations, Mountain View, CA, United States

⁴Department of Neuro-oncology, UCSF Brain Tumor Center, San Francisco, CA, United States

RRx-001: a chimeric triple action NLRP3 inhibitor, Nrf2 inducer, and nitric oxide superagonist

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³Department of Bioengineering, University of California at San Diego, La Jolla, CA, United States

Per-clinical trial of ABDNAZ

A Review of RRx-001: A Late-Stage Multi-Indication Inhibitor of NLRP3 Activation and Chronic Inflammation

Review Article

[Open access](#), Published: 15 March 2023, Volume 83, pages 389–402, (2023)

The conclusion of the review article on RRx-001 likely summarizes the drug's potential as a multi-indication inhibitor of NLRP3 activation and chronic inflammation. It would emphasize the promising results from preclinical and clinical studies, highlighting RRx-001's ability to inhibit the NLRP3 inflammasome and repolarize tumor-associated macrophages (TAMs). The conclusion might also discuss the ongoing clinical trials, such as the REPLATINUM study, and the potential future applications of RRx-001 in treating various inflammatory and cancerous conditions.

这篇关于 RRx-001 的综述文章的结论可能总结了该药物作为多适应症 NLRP3 激活和慢性炎症抑制剂的潜力。结论会强调临床前和临床研究的有希望的结果，突出 RRx-001 抑制 NLRP3 炎症小体和重新极化肿瘤相关巨噬细胞（TAMs）的能力。结论还可能讨论正在进行的临床试验，如 REPLATINUM 研究，以及 RRx-001 在治疗各种炎症和癌症中的潜在未来应用。