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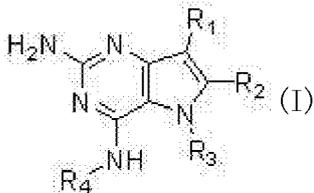
(54)发明名称

用于治疗病毒感染及其他疾病的吡咯并[3,2-d]嘧啶衍生物

(57)摘要

本发明涉及吡咯并[3,2-d]嘧啶衍生物、用于制备它们的方法、药物组合物、以及它们在疾病的治疗和/或疗法中的用途。

1. 一种具有化学式 (I) 的化合物



以及其药学上可接受的盐,其中

R<sub>1</sub>是H、氟或甲基;

R<sub>2</sub>是H、卤素或C<sub>1-3</sub>烷基;

R<sub>3</sub>是任选地被芳基取代的C<sub>1-6</sub>烷基,该芳基任选地进一步被一个或多个取代基取代,该一个或多个取代基独立地选自芳氧基、卤素、芳基、C<sub>1-6</sub>烷基、羧酸酰胺基、氰基或C<sub>1-6</sub>烷氧基;或

R<sub>3</sub>是任选地被C<sub>1-6</sub>烯烃、C<sub>3-7</sub>环烷基或C<sub>3-7</sub>杂环烷基取代的C<sub>1-6</sub>烷基;或

R<sub>3</sub>是任选地被C<sub>1-6</sub>烷氧基取代的C<sub>1-6</sub>烷基,该C<sub>1-6</sub>烷氧基任选地进一步被芳基取代;

R<sub>4</sub>是任选地被一个或多个取代基取代的C<sub>1-8</sub>烷基,该一个或多个取代基独立地选自羟基、C<sub>1-6</sub>烷氧基、C<sub>1-6</sub>烷基、C<sub>3-7</sub>环烷基、C<sub>2-6</sub>烯基、芳基、任选地进一步被C<sub>1-6</sub>烷基取代的杂芳基、以及任选地进一步被C<sub>1-6</sub>烷基取代的C<sub>3-7</sub>环烷基;

其中所述芳基是具有5、6或7个环原子的芳香族环结构,任选地包括一个或两个选自N、O和S的杂原子,任选地与另一芳基环稠合,提供二环结构;所述杂环选自四氢呋喃、二噁烷、氮杂环丁烷、吗啉、哌啶、哌嗪、吡咯烷、硫代吗啉以及环砜;

其条件是不包括2-氨基,4-(N-丁基氨基)-5-( $\alpha$ 甲基苄基)吡咯并[3,2-d]嘧啶。

2. 根据权利要求1所述的具有化学式 (I) 的化合物,其中R<sub>3</sub>是被芳基取代的甲基,该芳基任选地进一步被一个或多个取代基取代,该一个或多个取代基独立地选自芳氧基、卤素、芳基、C<sub>1-6</sub>烷基、羧酸酰胺基、氰基或C<sub>1-6</sub>烷氧基,并且R<sub>1</sub>、R<sub>2</sub>和R<sub>4</sub>按在权利要求1中所述。

3. 根据权利要求1所述的具有化学式 (I) 的化合物,其中R<sub>3</sub>和R<sub>4</sub>是被芳基取代的C<sub>1-3</sub>烷基,该芳基按在权利要求1中所述任选地进一步被取代。

4. 根据权利要求1所述的具有化学式 (I) 的化合物,其中R<sub>1</sub>是氟,R<sub>2</sub>是氢,并且R<sub>3</sub>和R<sub>4</sub>按在权利要求1中所述。

5. 一种药物组合物,包括根据权利要求1所述的具有化学式 (I) 的化合物或其药学上可接受的盐,连同一种或多种药学上可接受的赋形剂、稀释剂或载体。

6. 根据权利要求1所述的具有化学式 (I) 的化合物或其药学上可接受的盐,或者根据权利要求5所述的包括所述具有化学式 (I) 的化合物或其药学上可接受的盐的药物组合物,用作药剂。

7. 根据权利要求1所述的具有化学式 (I) 的化合物或其药学上可接受的盐或者根据权利要求5所述的包括所述具有化学式 (I) 的化合物或其药学上可接受的盐的药物组合物,用于在治疗涉及TLR7和/或TLR8调节的障碍中使用。

## 用于治疗病毒感染及其他疾病的吡咯并[3,2-d]嘧啶衍生物

[0001] 本发明涉及吡咯并[3,2-d]嘧啶衍生物、用于制备它们的方法、药物组合物、以及它们在疾病的治疗和/或疗法中的用途。

[0002] 本发明涉及吡咯并-嘧啶衍生物的用途,更确切地说,涉及吡咯并[3,2-d]嘧啶衍生物在治疗病毒感染、免疫或炎症疾病中的用途,由此涉及Toll样受体(TLR)的调节或激动作用。Toll样受体是主要的跨膜蛋白质,其特征在于一种细胞外富含亮氨酸的结构域以及包含一个保守区域的细胞质延伸。先天免疫系统可以经由在某些类型的免疫细胞的细胞表面上表达的这些TLR来识别病原体相关分子模式。外来病原体的识别活化了细胞因子的产生以及在吞噬细胞上的共刺激分子的上调。这导致T细胞行为的调节。

[0003] 大部分哺乳动物物种具有十种与十五种之间的Toll样受体类型。已经在人类连同小鼠中鉴定了十三种TLR(简单命名为TLR1至TLR13),并且已经在其他哺乳动物物种中发现许多它们的等价型。然而,在人类中发现的某些TLR的等价型并不存在于所有哺乳动物中。例如,一种编码类似于人类中TLR10的蛋白质的基因存在于小鼠中,但是该基因显现出过去在某位点被一种反转录病毒损坏。另一方面,小鼠表达TLR11、TLR12以及TLR13,它们均不存在于人类中。其他的哺乳动物可以表达尚未在人类中发现的TLR。其他的非哺乳动物物种可以具有与哺乳动物不同的TLR,如TLR14(其在东方鲀(Takifugu pufferfish)中发现)所证实的。这可以使得使用实验动物作为人类先天免疫模型的方法复杂化。

[0004] 对于Toll样受体的综述参见以下期刊文章。霍夫曼·J.A. (Hoffmann, J.A.),《自然》(Nature), 426, 第33-38页, 2003;阿基拉S. (Akira, S.), 田K. (Takeda, K.), 和贝少T. (Kaisho, T.),《(免疫学年鉴》(Annual Rev. Immunology), 21, 第335-376页, 2003;尤勒维奇R.J. (Ulevitch, R.J.),《自然综述:免疫学》(Nature Reviews: Immunology) 4, 第512-520页, 2004。

[0005] 先前已经描述了对Toll样受体显示有活性的化合物,如WO 2000006577中的杂环衍生物、WO 98/01448和WO 99/28321中的腺嘌呤衍生物、以及WO 2009/067081中的嘧啶。

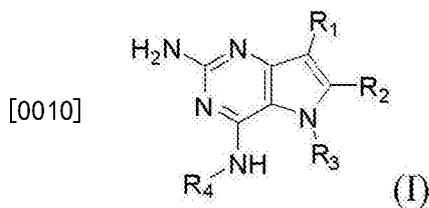
[0006] 在某些病毒感染的治疗中,可以给予干扰素(IFN- $\alpha$ )定期注射,比如说丙型肝炎病毒(HCV), (弗里德(Fried)等),聚乙二醇干扰素- $\alpha$ 联合病毒唑治疗慢性丙型肝炎病毒感染(Peginterferon- $\alpha$  plus ribavirin for chronic hepatitis C virus infection),《新英格兰医学期刊》(N Engl J Med) 2002;347:975-82)。可口服的小分子IFN诱导物提供了降低的免疫原性以及给予便利性的潜在优势。因此,新颖的IFN诱导物是用于治疗病毒感染的潜在有效的新类别药物。有关具有抗病毒效果的小分子IFN诱导物的文献的一个实例,参见德克拉克E. (De Clercq, E.);迪斯卡帕斯J. (Descamps, J.);德索梅尔P. (De Somer, P.)《科学》(Science) 1978, 200, 563-565。

[0007] 在某些类型的癌症的治疗中,干扰素 $\alpha$ 还与其他药物组合给予患者(《欧洲癌症杂志》(Eur. J. Cancer) (46) 第2849-57页,以及《癌症研究》(Cancer Res.) 1992 (52) 第1056页)。由于TLR7/8激动剂诱导显著的Th1应答的能力,它们也是感兴趣的疫苗佐剂(《人类疫苗》(Hum. Vaccines), 2009 (5), 381-394)。

[0008] 然而,对于新颖Toll样受体调节物存在一种强烈的需要,这些调节物与现有技术

的化合物相比具有优选的选择性以及改进的安全性特性 (profile)。

[0009] 根据本发明提供了一种具有化学式 (I) 的化合物



[0011] 以及其药学上可接受的盐、溶剂化物前药、立体异构体或多晶型物,其中

[0012] R<sub>1</sub>是H、氟或甲基;

[0013] R<sub>2</sub>是H、卤素或C<sub>1-3</sub>烷基;

[0014] R<sub>3</sub>是任选地被芳基取代的C<sub>1-6</sub>烷基,该芳基任选地进一步被一个或多个取代基取代,该一个或多个取代基独立地选自芳氧基、卤素、芳基、烷基氨基、二烷基氨基、杂环烷基、C<sub>1-6</sub>环烷基、C<sub>1-6</sub>烷基、羧酸、羧酸酯、羧酸酰胺、腈、或C<sub>1-6</sub>烷氧基;或

[0015] R<sub>3</sub>是任选地被C<sub>1-6</sub>烯基、C<sub>3-7</sub>环烷基或C<sub>3-7</sub>杂环烷基取代的C<sub>1-6</sub>烷基;或

[0016] R<sub>3</sub>是任选地被C<sub>1-6</sub>烷氧基取代的C<sub>1-6</sub>烷基,该C<sub>1-6</sub>烷氧基任选地进一步被芳基取代;

[0017] R<sub>4</sub>是任选地被一个或多个取代基取代的C<sub>1-8</sub>烷基,该一个或多个取代基独立地选自羟基、C<sub>1-6</sub>烷氧基、C<sub>1-6</sub>烷基、C<sub>3-7</sub>环烷基、C<sub>2-6</sub>烯基、芳基、任选地进一步被C<sub>1-6</sub>烷基取代的杂芳基、以及任选地进一步被C<sub>1-6</sub>烷基取代的C<sub>3-7</sub>环烷基;

[0018] 其条件是不包括2-氨基-4-(N-丁基氨基)-5-( $\alpha$ 甲基苄基)吡咯并[3,2-d]嘧啶。

[0019] 优选的化合物是具有化学式 (I) 的那些,其中R<sub>3</sub>是被芳基(经取代的或未经取代的)取代的C<sub>1-3</sub>烷基基团,并且R<sub>1</sub>、R<sub>2</sub>和R<sub>4</sub>是如以上所描述的。

[0020] 在一个第二实施例中是具有化学式 (I) 的化合物,其中R<sub>3</sub>和R<sub>4</sub>是被芳基取代的C<sub>1-3</sub>烷基,该芳基如以上所描述地任选地进一步被取代。

[0021] 在一个另外的实施例中是具有化学式 (I) 的那些,其中R<sub>1</sub>是氢,R<sub>2</sub>是氟,并且R<sub>3</sub>和R<sub>4</sub>是如以上所描述的。

[0022] 其他优选的实施例是具有化学式 (I) 的那些,其中R<sub>1</sub>是氟,R<sub>2</sub>是氢,并且R<sub>3</sub>和R<sub>4</sub>是如以上所描述的。

[0023] 根据在此披露的本发明,如列于表I和II中的具有以下编号#89、94、101、144、154、156、175、192、209、213及215的化合物由于其特性是令人特别感兴趣的。

[0024] 具有化学式 (I) 的化合物以及它们的药学上可接受的盐、溶剂化物或多晶型物具有作为药物的活性,特别是作为Toll样受体(尤其是TLR7和/或TLR8)调节物的活性。

[0025] 在一个另外的方面,本发明提供了一种药物组合物,该药物组合物包括具有化学式 (I) 的化合物或其药学上可接受的盐、溶剂化物或多晶型物连同一种或多种药学上可接受的赋形剂、稀释剂或载体。

[0026] 此外,根据本发明的具有化学式 (I) 的化合物或其一种药学上可接受的盐、溶剂化物或多晶型物,或者包括所述的具有化学式 (I) 的化合物或其一种药学上可接受的盐、溶剂化物或多晶型物的药物组合物可以用作药剂。

[0027] 本发明的另一个方面是:具有化学式 (I) 的化合物或其一种药学上可接受的盐、溶剂化物或多晶型物,或者包括所述的具有化学式 (I) 的化合物或其一种药学上可接受的盐、

溶剂化物或多晶型物的所述药物组合物可以相应地用于治疗涉及TLR7和/或TLR8的调节的任何障碍。

[0028] 术语“烷基”是指包含指定数目碳原子的直链或支链饱和脂肪族烃。

[0029] 术语“卤素”是指氟、氯、溴或碘。

[0030] 术语“烯基”是指由至少两个碳原子和至少一个碳-碳双键组成的如以上定义的烷基。

[0031] 术语“环烷基”是指包含指定数目碳原子的碳环。

[0032] 术语“烷氧基”是指单独键合到氧的烷基(碳和氢链),例如像甲氧基基团或乙氧基基团。

[0033] 术语“芳基”意指可任选地包括一个或两个选自N、O和S(特别是选自N和O)的杂原子的芳香族环结构。所述芳香族环结构可以具有5、6或7个环原子。特别地,所述芳香族环结构可以具有5或6个环原子。所述芳香族环结构还可以与另一芳基环稠合,提供一个二环结构(实例包括但不限于:喹啉、异喹啉、喹唑啉、苯并噁唑)。

[0034] 术语“芳氧基”是指一种芳香族环结构。所述芳香族基团单独键合到氧上(例如苯氧基)。

[0035] 术语“烯炔”是指包含特定数目碳原子的不饱和烃链,其包含至少一个碳-碳双键。

[0036] 术语“杂环”是指饱和的或部分饱和的分子,并且包括四氢呋喃、二噁烷或其他环醚。包含氮的杂环包括例如氮杂环丁烷、吗啉、哌啶、哌嗪、吡咯烷、以及类似物。其他的杂环包括例如硫代吗啉、间二氧杂环戊烷基以及环砜。

[0037] 具有化学式(I)的化合物的药学上可接受的盐包括其酸加成盐以及碱盐。合适的酸加成盐是由形成无毒盐的酸形成。合适的碱盐是由形成无毒盐的碱形成。

[0038] 本发明的化合物还可以按非溶剂化的和溶剂化的形式存在。术语“溶剂化物”在此使用以描述包括本发明的化合物以及一种或多种药学上可接受的溶剂分子(例如,乙醇)的分子络合物。

[0039] 术语“多晶型物”是指本发明的化合物以多于一种的形式或晶体结构存在的能力。

[0040] 可以将本发明的化合物以晶态的或非晶态的产物进行给予。可以通过例如沉淀、结晶、冷冻干燥、喷雾干燥或蒸发干燥的方法获得呈固体塞、粉剂或膜的这些化合物。它们可以单独给予或与一种或多种本发明的其他化合物组合给予或与一种或多种其他药物组合给予。通常,它们将作为与一种或多种药学上可接受的赋形剂相结合的配制品而给予。术语“赋形剂”在此使用以描述除本发明的一种或多种化合物之外的任何成分。赋形剂的选择大体上取决于例如具体给予模式、赋形剂对溶解性和稳定性的影响以及剂型的性质等因素。

[0041] 可以将本发明的化合物或其任何亚组配制为用于给予目的的不同药物形式。作为适当的组合物,可以提及通常用于全身性给予药物的所有组合物。为了制备本发明的药物组合物,将一种有效量的特定化合物(任选地呈加成盐形式)作为活性成分与一种药学上可接受的载体组合在均匀掺合物中,该载体可以采用多种形式,取决于用于给予的所希望的制剂的形式。令人希望地,这些药物组合物处于适合于例如口服、经直肠或经皮给予的单位剂型。例如,在制备处于口服剂型的组合物中,可使用任何常见药物介质,在口服液体剂型(例如悬浮液、糖浆剂、酏剂、乳液以及溶液)的情况中,例如像水,二醇类、油类、醇类以及类

似物；或者在粉剂、丸剂、胶囊剂和片剂的情况下，固体载体如淀粉、糖、高岭土、稀释剂、润滑剂、粘合剂、崩解剂以及类似物。因为其容易给予，片剂和胶囊剂代表了最有利的口服单位剂型，在该情况下显然使用固体药物载体。还包括在使用之前不久可以被转化为液体形式的固体形式制剂。在适合用于经皮给予的组合物中，该载体可任选地包括一种渗透增强剂和/或适合的润湿剂，可任选地与小比例的具有任何性质的适合的添加剂组合，这些添加剂并不在皮肤上引入显著的有害作用。所述添加剂可以促进对皮肤的给予和/或可以有助于制备所希望的组合物。能以不同方式给予这些组合物，例如，作为透皮贴剂、作为点剂、作为软膏剂。还可以经由吸入或吹入法借助于在本领域中采用的用于经由此方式给予的方法和制品来给予本发明的化合物。因此，大体上，本发明的化合物能以溶液、悬浮液或干燥粉剂的形式而被给予至肺部。

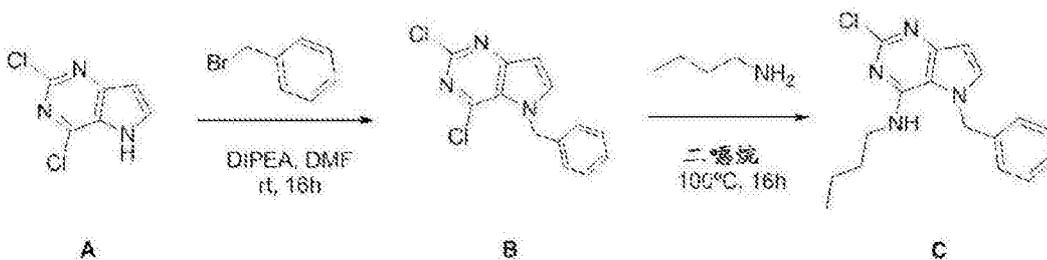
[0042] 为了便于给予和剂量的均一性，将上述药物组合物配制成单位剂型是特别有利的。如在此使用的单位剂型指的是适合作为单位剂量的物理离散单位，各单位含有预定量的活性成分，该预定量的活性成分经计算与所需药物载体相结合而产生所希望的治疗效果。此类单位剂型的实例是片剂（包括刻痕或包衣的片剂）、胶囊剂、丸剂、粉末包（powder packet）、糯米纸囊剂（wafer）、栓剂、可注射溶液或悬浮液以及类似剂型，及其分离的多个。

[0043] 在感染性疾病治疗领域中的普通技术人员将能够从下文所呈现的测试结果来确定有效量。通常认为有效日用量为从0.01mg/kg至50mg/kg体重，更优选从0.1mg/kg至10mg/kg体重。可适合地将所需剂量在1天中以合适的时间间隔分2个、3个、4个或更多个子剂量形式给予。所述子剂量可以被配制成单位剂型，例如每一单位剂型包含1至1000mg、且特别是5至200mg的活性成分。

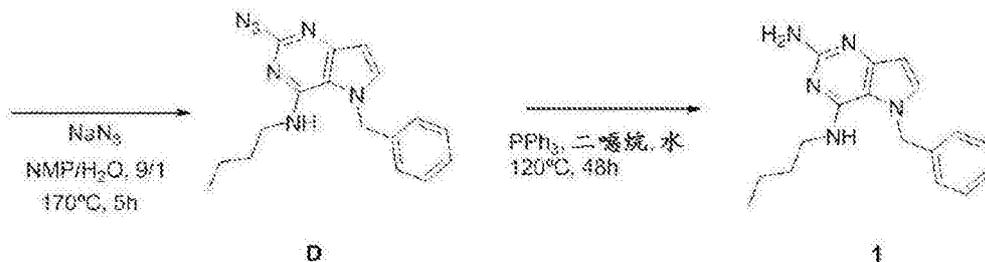
[0044] 如本领域的普通技术人员所熟知的，给予的精确剂量和频率取决于使用的具有化学式(I)的具体化合物、正在被治疗的具体病症、正在被治疗的病症的严重性、具体患者的年龄、体重和总体身体健康状况、连同个体可能服用的其他药物。此外，显然该有效量可以降低或增加，这取决于所治疗的受试者的反应和/或取决于对本发明的这些化合物开处方的医师的评估。因此以上所提及的有效量的范围仅仅是指导而不是旨在以任何程度限制本发明的范围或用途。

[0045] 实验部分

[0046] 方案1.总反应方案

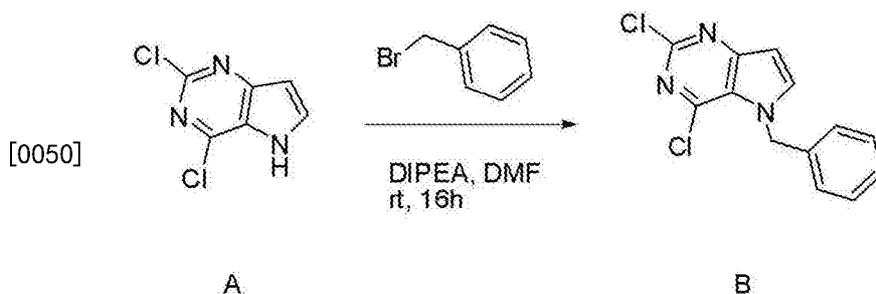


[0047]



[0048] 使用极性无质子溶剂(例如DMF)可以将方案1中的A型化合物用苄基溴进行烷基化。烷基卤化物与中间体A的反应需要强碱(例如碳酸铯)并且可能较长的反应时间和/或升高的温度。使用胺置换中间体B中的氯以形成C型化合物可能需要另外的加热或延长的反应时间,如使用氨基醇(对于制备氨基醇,参考WO 2009067081和WO 2008147697)所观察到的。用胺置换中间体B中的氯还可以在室温下在极性溶剂(例如DMF或乙腈)中进行。可以使用多种碱来帮助从B到C的反应,该碱包括但不限于以下:三乙胺、二异丙胺、碳酸铯、碳酸钾、或氢氧化钠。由以上中间体D代表的化合物中的叠氮基的还原还可以在Pd/C上在氢气氛围中进行。包含氟的中间体B、C和D可以在与未经取代的类似物相同的方案下被取代,因此,所描述的反应方案适用于化合物的两种类型。

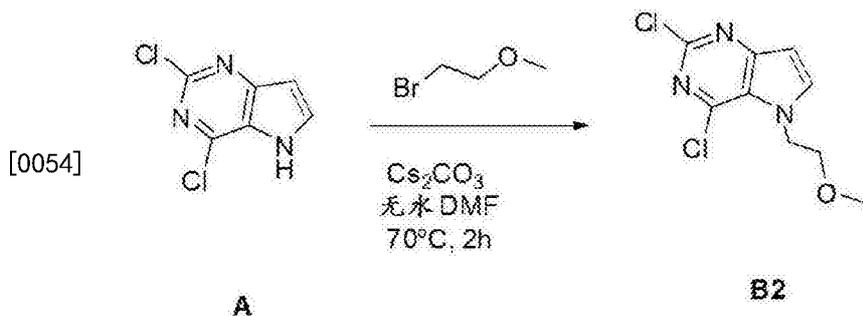
[0049] 中间体B的制备



[0051] 向一个50mL小瓶中放置2,4-二氯-5H-吡咯并[3,2-d]嘧啶[CAS 63200-54-4] (1g, 5.319mmol)、DMF (10mL)、DIPEA (2.75mL, 16mmol) 和苄基溴 (0.7mL, 5.85mmol)。将该小瓶密封并在室温下振荡16小时。将溶剂在减压下去除。将粗品经由硅胶柱层析使用庚烷至乙酸乙酯的梯度进行纯化。将最好的级分进行合并,并且将溶剂在减压下去除以提供B。

[0052] LC-MS (M+H)  $m/z = 278$ 

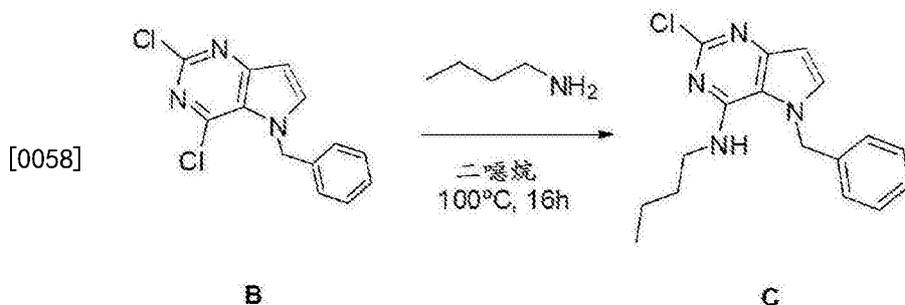
[0053] 中间体B2的制备



[0055] 向配备有磁力搅拌棒的50mL小瓶中放置A (50mg, 0.27mmol)、无水DMF (1mL)、碳酸铯 (0.259g, 0.8mmol), 并且然后放置2-溴乙基甲基醚 (0.03mL, 0.29mmol)。将该烧瓶密封, 并且允许将该反应在70°C下搅拌2小时。将溶剂在减压下去除。将粗品经由硅胶柱层析使用庚烷至乙酸乙酯的梯度进行纯化。将最好的级分进行合并, 并且将溶剂在减压下去除以提供B2。

[0056] LC-MS (M+H)  $m/z = 246$

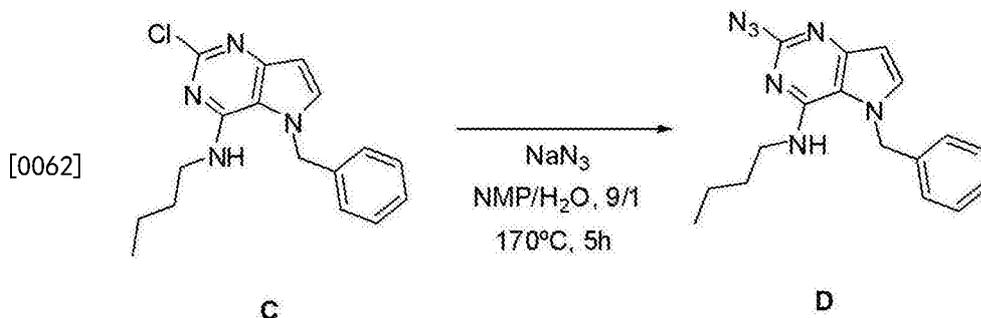
[0057] 中间体C的制备



[0059] 向配备有磁力搅拌棒的50mL圆底烧瓶中放置B (1.4g, 5.03mmol)、正丁胺 (0.59mL, 6.04mmol) 和1,4-二噁烷 (5mL)。将该烧瓶配备一个回流冷凝器并且允许在100°C下伴随着搅拌加热16小时。在冷却至室温之后, 将溶剂在减压下去除。将粗品经由硅胶柱层析使用庚烷至乙酸乙酯的梯度进行纯化。将最好的级分进行合并, 并且将溶剂在减压下去除以提供C。

[0060] LC-MS (M+H)  $m/z = 315$

[0061] 中间体D的制备

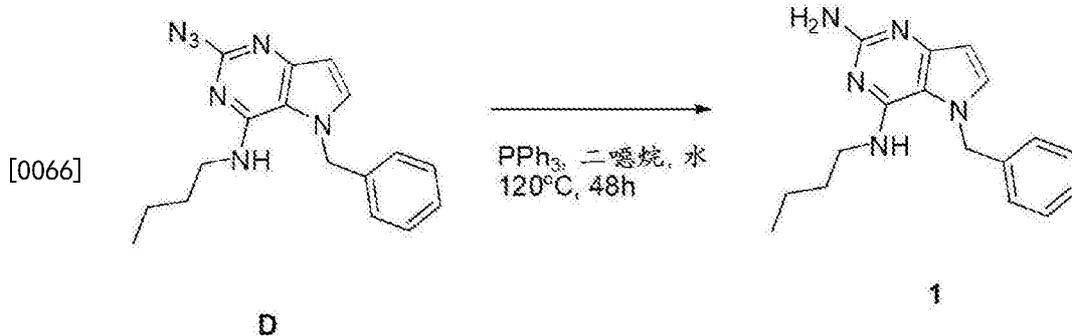


[0063] 向配备有磁力搅拌棒的玻璃小瓶中放置C (1g, 3.18mmol)、叠氮化钠 (0.62g, 9.53mmol) 和NMP:水 (9:1, 4mL)。将该玻璃小瓶密封并且将该混合物伴随着搅拌加热至170°C持续5小时。在冷却至室温之后, 将该混合物用乙酸乙酯 (20mL) 稀释并且用水洗涤 (5x 15mL)。将有机层经硫酸镁干燥, 将固体经由过滤去除并且将滤液的溶剂在减压下去除。将粗品经由硅胶柱层析使用庚烷至乙酸乙酯的梯度进行纯化。将最好的级分进行合并, 并且

将溶剂在减压下去除以提供D。

[0064] LC-MS (M+H)  $m/z$  = 322

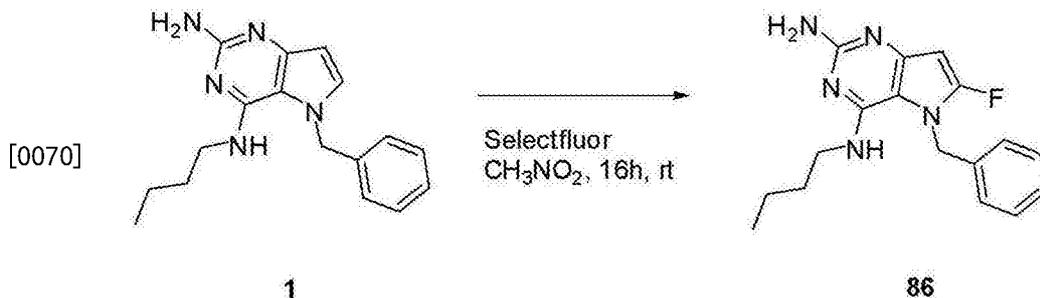
[0065] 1的制备



[0067] 向配备有磁力搅拌棒的玻璃小瓶中放置D (100mg, 0.311mmol)、1,4-二噁烷 (4mL)、水 (1mL) 和三苯基膦 (245mg, 0.93mmol)。将该玻璃小瓶密封并且将该混合物伴随着搅拌加热至120℃持续48小时。在冷却至室温之后,将溶剂在减压下去除。将粗品经由硅胶柱层析使用二氯甲烷至在二氯甲烷中10%甲醇梯度进行纯化。将最好的级分进行合并,并且将溶剂在减压下去除以提供1。

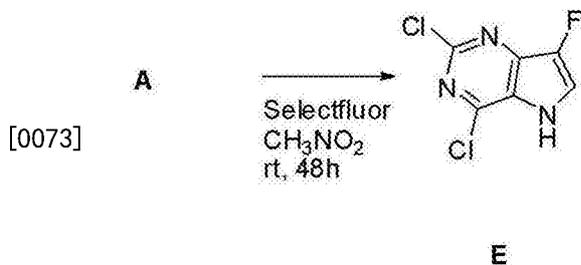
[0068] LC-MS (M+H)  $m/z$  = 296

[0069] 86的制备



[0071] 向配备有磁力搅拌棒的玻璃小瓶中放置1 (110mg, 0.372mmol)、硝基甲烷 (1.5mL) 和selectfluor (198mg, 0.56mmol)。将该玻璃小瓶密封并且将混合物在室温下搅拌16小时。将溶剂在减压下去除。将粗品经由反相层析进行纯化。将最好的级分进行合并,并且将溶剂在减压下去除以提供86。

[0072] 中间体E的制备

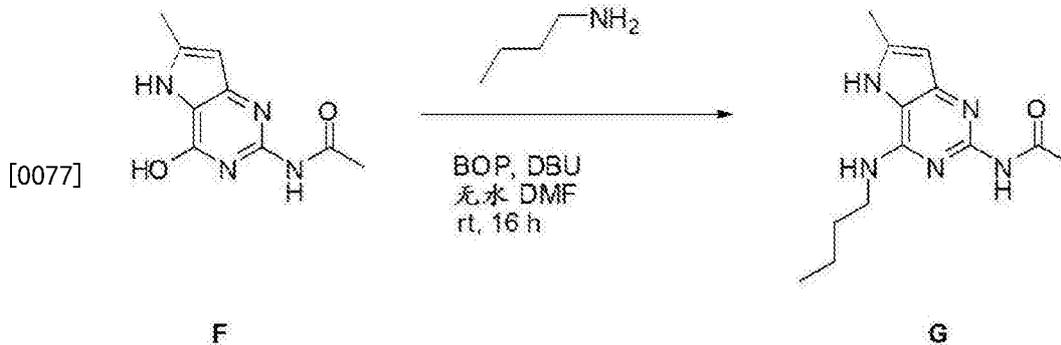


[0074] 向配备有磁力搅拌棒的玻璃小瓶中放置A (600mg, 3.19mmol)、硝基甲烷 (10mL) 和selectfluor (5.67g, 16mmol)。将该玻璃小瓶密封并且将混合物在室温下搅拌48小时。添加NaHCO<sub>3</sub> (饱和水性的, 10mL) 并且用乙酸乙酯 (3x 15mL) 萃取。将有机层进行合并,经硫酸镁干燥,通过过滤除去固体,并且在减压下去除滤液的溶剂,以提供粗品E,将其照原样用于下

一个步骤。

[0075] LC-MS (M+H)  $m/z$  = 206

[0076] 中间体G的制备



[0078] 步骤1.

[0079] 根据WO 2010006025第44页方案3中用于制备化合物9的方法来制备中间体F。例外的是采用乙酰基代替三甲基乙酰基基团。

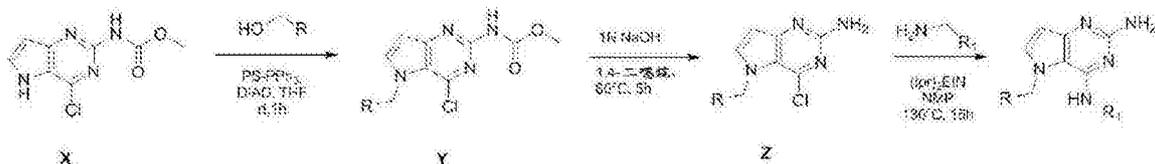
[0080] 步骤2中中间体G的制备

[0081] 向配备有磁力搅拌棒的50mL玻璃小瓶中放置F (200mg, 0.97mmol)、无水DMF (5mL)、DBU (0.435mL, 2.91mmol) 和BOP (536mg, 1.2mmol)。将该反应混合物在搅拌几分钟之后变成溶液,然后添加正丁胺 (0.48mL, 4.85mmol) 并且在室温下继续搅拌16小时。将溶剂在减压下去除,并且将粗品经由反相层析进行纯化。

[0082] LC-MS (M+H)  $m/z$  = 262

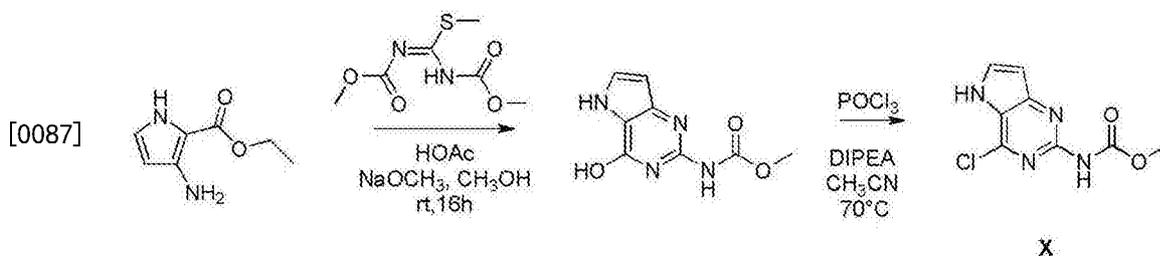
[0083] 方案2.总反应方案

[0084]



[0085] 通用程序。可以使用光延反应 (Mitsunobu) 条件在极性无质子溶剂 (例如THF) 中将方案2中的X型化合物用醇进行官能化。在碱性条件下,在1,4-二噁烷中进行氨基甲酸甲酯的裂解,以形成中间体Z。使用胺和碱 (例如NaH) 在极性溶剂 (例如NMP) 中进行中间体Z中氯的置换,以形成具有化学式 (I) 的化合物。

[0086] 中间体X的制备

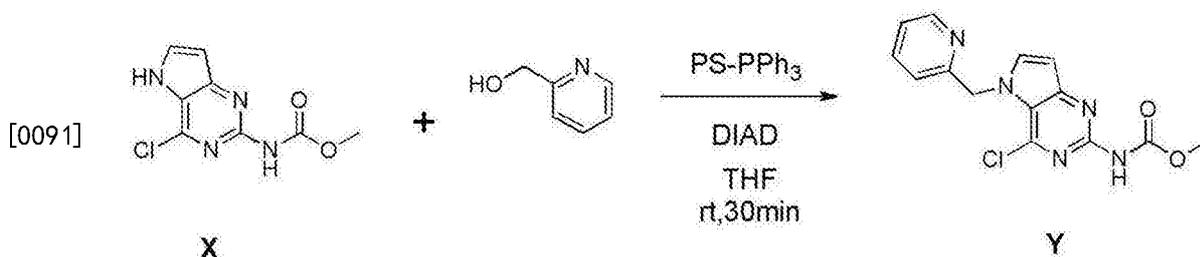


[0088] 将3-氨基-2-乙氧基羰基吡咯盐酸盐 (25.8g, 135.3mmol) 在二氯甲烷和饱和  $\text{NaHCO}_3$  之间分配,经  $\text{MgSO}_4$  干燥,过滤并蒸发至干。将残余物与1,3-双(甲氧基羰基)-2-甲基-2-硫代异脲 (32.1g, 156mmol) 和乙酸 (39mL, 677mmol) 一起溶解在甲醇 (500mL) 中并且在室

温下搅拌1小时。出现沉淀并且继续搅拌过夜。添加甲醇钠(73.1g,1353mmol)。观察到放热并且将该反应混合物搅拌过夜。将该反应混合物经由添加乙酸而调节至pH 5,并且将沉淀滤出,与水(2x 350mL)、乙腈(1x 350mL)和二异丙基醚(1x 350mL)进行研磨。将获得的N-(4-羟基-5H-吡咯并[3,2-d]嘧啶-2-基)氨基甲酸甲酯在烘箱中干燥。

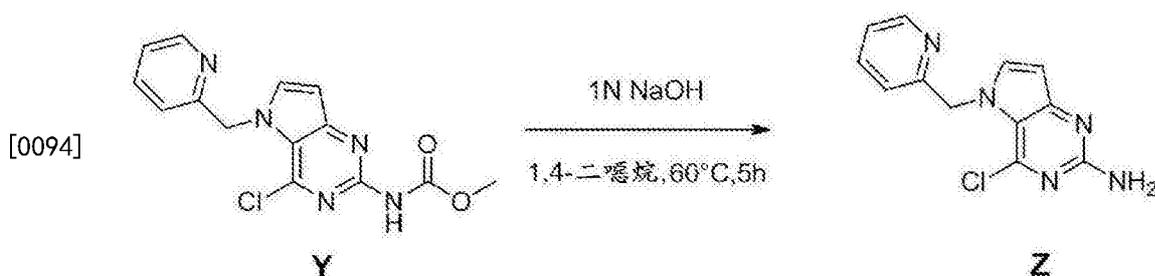
[0089] 在室温下,将N-(4-羟基-5H-吡咯并[3,2-d]嘧啶-2-基)氨基甲酸甲酯(25g,120mmol)给至500mL多颈烧瓶中的乙腈(350mL)中。添加POCl<sub>3</sub>(22.1mL,238.2mmol),并且在通过顶置式机械搅拌器(300rpm)搅拌的同时将该反应混合物加热至70℃。经由注射泵以0.2mL/min的流速逐滴添加胡宁氏碱(Hunig's base)(41.4mL,240.2mmol)。将该反应混合物冷却至室温,并且在45℃下倾倒入乙酸钠(78.8g,961mmol)在水(500mL)中的搅拌溶液里。蒸发有机物并将剩余的液体在冰浴中搅拌和冷却。将形成的固体通过过滤分离,用乙腈洗涤并且与二异丙基醚进行研磨,以变成呈固体的中间体X,将其在真空下干燥。

[0090] 中间体Y的制备

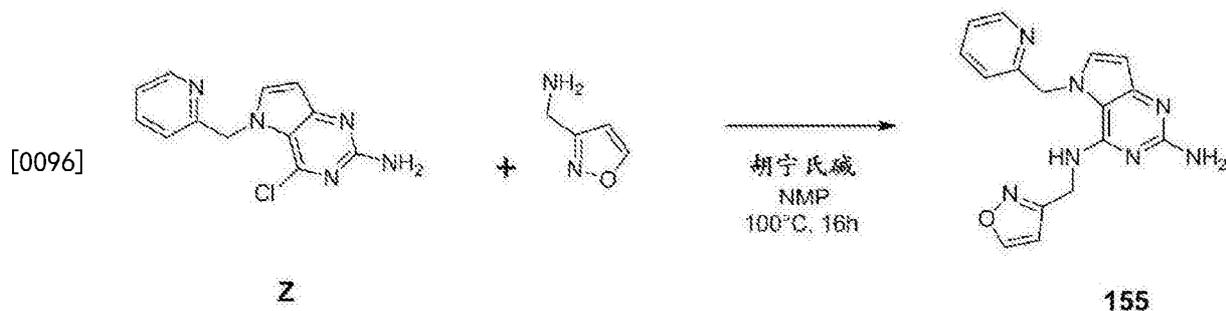


[0092] 在室温下,向中间体X(5g,22mmol)、2-吡啶甲醇(2.6mL,26.5mmol)和聚苯乙烯结合的三苯基膦(18.4g,55.2mmol)在无水THF(153mL)中的悬浮液里添加DIAD(6.9mL,33mmol),并且将该反应混合物搅拌30分钟,然后在减压下进行浓缩。将产物经由硅胶柱层析法使用二氯甲烷:甲醇100:0至90:10梯度的梯度进行纯化。收集产物级分并在减压下进行浓缩。将产物在乙腈中再结晶,通过过滤分离并且在真空下干燥,以提供呈白色固体的Y。

[0093] 中间体Z的制备



[0095] 将Y(4.5g,14.2mmol)溶解在100mL圆底烧瓶中的1,4-二噁烷(68mL)中并添加1N NaOH(34mL)。将该混合物加热至60℃持续5h。将该混合物冷却并在减压下进行浓缩。将残余物用水进行处理,并且将沉淀通过过滤分离并进行干燥,以提供Z。将产物按原样用于下一步骤中。

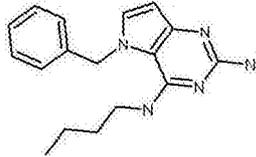


[0097] 将Z (175mg, 0.67mmol)、异噁唑-3-基-甲胺盐酸盐 (136mg, 1.0mmol) 和二异丙基乙胺 (173mg, 1.3mmol) 溶解在7mL玻璃小瓶中的NMP (2.4mL) 中。将该混合物在100°C下搅拌2h, 然后冷却并且在真空中浓缩。将其通过制备型HPLC (固定相: RP Vydac Denali C18-10 $\mu$ m, 200g, 5cm), 流动相: 在水中的0.25% NH<sub>4</sub>OAc溶液, 甲醇), 收集所希望的级分并且在真空中浓缩。将产物在乙腈中研磨, 通过过滤分离并且在真空下干燥, 以变成呈白色固体的155。

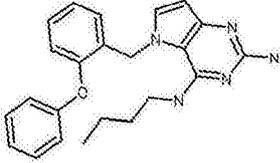
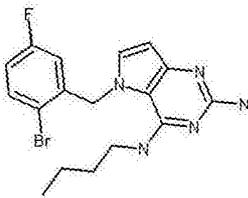
[0098] 表1. 具有化学式 (I) 的化合物及相应的分析数据。

[0099] 根据实验部分中所描述的方法制备化合物。\*R指示以R构型所绘的未知构型的纯的对映异构体。\*S指示以S构型所绘的未知构型的纯的对映异构体。

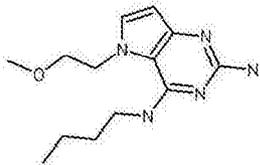
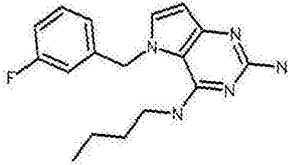
[0100]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt ( min )	LC-MS 质量发现 值
1		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 0.77 (t, J=7.3 Hz, 3 H), 0.98 - 1.11 (m, 2 H), 1.33 (dt, J=14.5, 7.2 Hz, 2 H), 3.25 - 3.30 (m, 2 H), 5.23 (s, 2 H), 5.48 (s, 6 2 H), 5.75 (t, J=5.5 Hz, 1 H), 5.98 (d, J=3.0 Hz, 1 H), 6.97 (d, J=7.0 Hz, 2 H), 7.19 - 7.35 (m, 4 H)	B, 0.88	296
2		<sup>1</sup> H NMR (300 MHz, 氯仿- <i>d</i> ) δ	A, 2.82	388

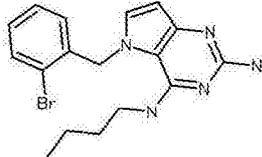
[0101]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		ppm 0.76 (t, $J=7.2$ Hz, 3 H), 1.07 (dq, $J=14.9, 7.3$ Hz, 2 H), 1.23 - 1.35 (m, 2 H), 3.31 (td, $J=6.8, 5.6$ Hz, 2 H), 4.90 (t, $J=4.9$ Hz, 1 H), 5.12 (br. s., 2 H), 5.31 (s, 2 H), 6.21 (d, $J=3.0$ Hz, 1 H), 6.71 - 6.79 (m, 1 H), 6.86 - 6.94 (m, 3 H), 6.97 - 7.05 (m, 2 H), 7.06 - 7.14 (m, 1 H), 7.20 - 7.27 (m, 1 H), 7.27 - 7.36 (m, 2 H)		
3		<sup>1</sup> H NMR (400 MHz, DMSO- $d_6$ ) $\delta$ ppm 0.75 (t, $J=7.3$ Hz, 3 H), 0.96 - 1.09 (m, 2 H), 1.28 - 1.41 (m, 2 H), 3.25 - 3.33 (m, 2 H), 5.55 (s, 4 H), 5.85 (dd, $J=9.7, 2.6$ Hz, 1 H), 5.98 (t,	A, 2.49	393

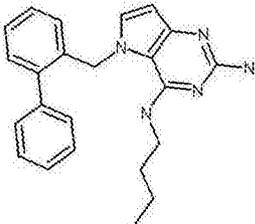
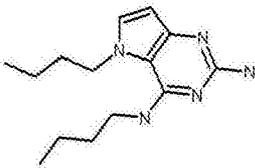
[0102]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		J=5.0 Hz, 1 H), 6.08 (d, J=3.0 Hz, 1 H), 7.11 (td, J=8.5, 3.1 Hz, 1 H), 7.30 (d, J=3.0 Hz, 1 H), 7.70 (dd, J=8.8, 5.3 Hz, 1 H)		
4		<sup>1</sup> H NMR (300 MHz, 氯仿-d) δ ppm 0.91 (t, J=7.2 Hz, 3 H), 1.30 - 1.44 (m, 2 H), 1.49 - 1.61 (m, 2 H), 3.34 (s, 3 H), 3.43 (td, J=7.1, 5.3 Hz, 2 H), 3.69 - 3.77 (m, 2 H), 4.20 - 4.29 (m, 2 H), 5.73 (br. s., 1 H), 6.20 (d, J=3.0 Hz, 1 H), 6.86 (d, J=3.2 Hz, 1 H), 7.11 (br. s., 1 H)	A, 1.95	264
5		<sup>1</sup> H NMR (300 MHz, 氯仿-d) δ ppm 0.74 (t, J=7.2 Hz, 3 H), 0.90 - 1.07 (m, 2 H), 1.11	A, 2.29	314

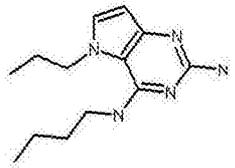
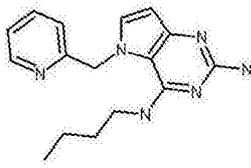
[0103]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		- 1.17 (m, 2 H), 3.18 - 3.28 (m, 2 H), 4.40 (br. s., 1 H), 4.94 (br. s., 2 H), 5.30 (s, 2 H), 6.23 (d, <i>J</i> =3.0 Hz, 1 H), 6.70 (d, <i>J</i> =8.8 Hz, 1 H), 6.79 (d, <i>J</i> =7.7 Hz, 1 H), 6.94 - 7.03 (m, 2 H), 7.30 (td, <i>J</i> =8.0, 5.8 Hz, 1 H)		
6		<sup>1</sup> H NMR (300 MHz, 氯仿- <i>d</i> ) δ ppm 0.72 (t, <i>J</i> =7.2 Hz, 3 H), 0.88 - 1.03 (m, 2 H), 1.14 - 1.27 (m, 2 H), 3.24 (td, <i>J</i> =6.7, 5.3 Hz, 2 H), 4.29 (br. s., 1 H), 4.89 (br. s., 2 H), 5.33 (s, 2 H), 6.24 (d, <i>J</i> =3.0 Hz, 1 H), 6.46 - 6.53 (m, 1 H), 6.99 (d, <i>J</i> =3.0 Hz, 1 H), 7.10 - 7.22 (m, 2 H), 7.55 - 7.60 (m,	A, 2.47	375

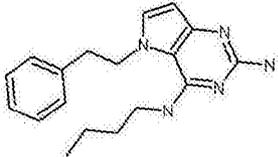
[0104]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		1 H)		
7		<sup>1</sup> H NMR (300 MHz, 氯仿-d) δ ppm 0.74 (t, <i>J</i> =7.2 Hz, 3 H), 0.86 - 1.01 (m, 2 H), 1.06 - 1.18 (m, 2 H), 3.12 - 3.22 (m, 2 H), 4.31 (t, <i>J</i> =5.0 Hz, 1 H), 5.18 (br. s., 2 H), 5.19 - 5.24 (m, 2 H), 6.20 (d, <i>J</i> =3.0 Hz, 1 H), 6.71 (d, <i>J</i> =7.7 Hz, 1 H), 6.96 (d, <i>J</i> =3.0 Hz, 1 H), 7.21 - 7.47 (m, 8 H)	A, 2.78	372
8		<sup>1</sup> H NMR (300 MHz, DMSO-d <sub>6</sub> ) δ ppm 0.84 (t, <i>J</i> =7.4 Hz, 3 H), 0.93 (t, <i>J</i> =7.3 Hz, 3 H), 1.06 - 1.27 (m, 2 H), 1.27 - 1.44 (m, 2 H), 1.50 - 1.66 (m, 4 H), 3.44 - 3.54 (m, 2 H), 4.28	A, 2.28	262

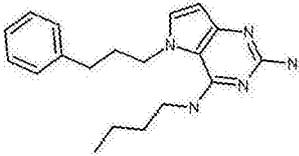
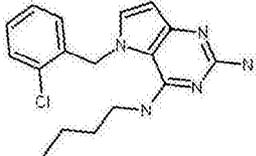
[0105]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		(t, J=6.9 Hz, 2 H), 5.99 (d, J=2.9 Hz, 1 H), 6.17 (br. s., 2 H), 6.79 (br. s., 1 H), 7.28 (d, J=2.9 Hz, 1 H)		
9		<sup>1</sup> H NMR (300 MHz, 氯仿 -d) δ ppm 0.86 (t, J=7.4 Hz, 3 H), 0.91 (t, J=7.3 Hz, 3 H), 1.36 (dq, J=15.0, 7.4 Hz, 2 H), 1.52 - 1.65 (m, 2 H), 1.76 (sxt, J=7.3 Hz, 2 H), 3.52 (td, J=7.1, 5.6 Hz, 2 H), 4.07 (t, J=7.1 Hz, 2 H), 5.17 - 5.30 (m, 1 H), 5.52 (br. s., 2 H), 6.09 (d, J=3.0 Hz, 1 H), 6.88 (d, J=3.0 Hz, 1 H)	A, 2.06	248
10		<sup>1</sup> H NMR (300 MHz, 氯仿 -d) δ ppm 0.92 (t, J=7.3 Hz, 3 H), 1.38 (dq, J=15.0, 7.3 Hz, 2	A, 2.14	297

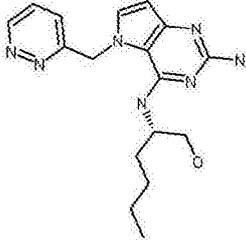
[0106]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		H), 1.56 - 1.68 (m, 2 H), 3.49 (td, J=7.1, 5.1 Hz, 2 H), 5.28 (s, 2 H), 5.78 (br. s., 2 H), 6.18 (d, J=3.0 Hz, 1 H), 7.06 (d, J=3.0 Hz, 1 H), 7.25 - 7.32 (m, 1 H), 7.34 (d, J=7.7 Hz, 1 H), 7.74 (td, J=7.7, 1.7 Hz, 1 H), 8.48 (d, J=4.4 Hz, 1 H), 8.58 (br. s., 1 H)		
11		<sup>1</sup> H NMR (300 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 0.94 (t, J=7.4 Hz, 3 H), 1.39 (dq, J=14.9, 7.4 Hz, 2 H), 1.63 (quin, J=7.3 Hz, 2 H), 2.90 (t, J=7.1 Hz, 2 H), 3.46 - 3.55 (m, 2 H), 4.55 (t, J=7.1 Hz, 2 H), 5.94 (d, J=3.0 Hz, 1 H), 6.33 (br. s., 2 H), 6.97 (br. s., 1 H),	A, 2.42	310

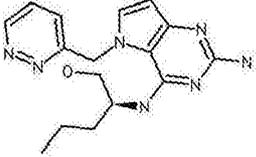
[0107]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		7.02 - 7.12 (m, 3 H), 7.16 - 7.29 (m, 3 H)		
12		<sup>1</sup> H NMR (300 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 0.90 (t, J=7.3 Hz, 3 H), 1.34 (dq, J=14.9, 7.3 Hz, 2 H), 1.57 (quin, J=7.3 Hz, 2 H), 1.91 (quin, J=7.5 Hz, 2 H), 2.41 - 2.48 (m, 2 H), 3.41 - 3.49 (m, 2 H), 4.29 (t, J=7.0 Hz, 2 H), 5.57 (s, 2 H), 5.94 (d, J=2.9 Hz, 1 H), 6.32 (t, J=5.4 Hz, 1 H), 7.10 - 7.22 (m, 4 H), 7.22 - 7.31 (m, 2 H)	A, 2.6	324
13		<sup>1</sup> H NMR (300 MHz, 氯仿- <i>d</i> ) δ ppm 0.81 (t, J=7.2 Hz, 3 H), 1.06 (dq, J=14.9, 7.3 Hz, 2 H), 1.22 - 1.35 (m, 2 H), 3.32 (td,	A, 2.47	330

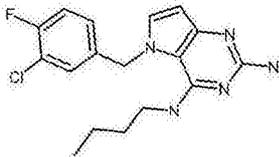
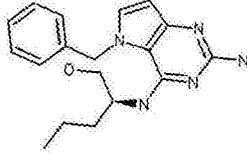
[0108]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		J=6.7, 5.4 Hz, 2 H), 4.20 (br. s., 1 H), 4.51 (br. s., 2 H), 5.44 (s, 2 H), 6.31 (d, J=3.2 Hz, 1 H), 6.63 (d, J=7.4 Hz, 1 H), 7.07 (d, J=3.0 Hz, 1 H), 7.16 - 7.25 (m, 1 H), 7.29 - 7.34 (m, 1 H), 7.47 (dd, J=8.0, 1.2 Hz, 1 H)		
14		<sup>1</sup> H NMR (400 MHz, 氯仿-d) ppm 0.89 (t, J=6.9 Hz, 3 H), 1.20 - 1.27 (m, 1 H), 1.28 - 1.41 (m, 4 H), 1.64 (q, J=7.0 Hz, 2 H), 3.61 (dd, J=11.2, 6.9 Hz, 1 H), 3.77 (dd, J=11.0, 2.8 Hz, 1 H), 4.24 (td, J=6.9, 2.8 Hz, 1 H), 4.57 (br. s., 2 H), 5.48 - 5.68 (m, 2 H), 6.21 (d, J=3.0 Hz, 1 H),	B, 0.63	342

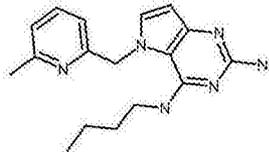
[0109]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		6.74 (d, J=6.8 Hz, 1 H), 7.10 (d, J=3.0 Hz, 1 H), 7.35 (dd, J=8.5, 1.3 Hz, 1 H), 7.51 (dd, J=8.4, 4.9 Hz, 1 H), 9.16 (dd, J=5.0, 1.3 Hz, 1 H)		
15		<sup>1</sup> H NMR (400 MHz, 甲醇-d <sub>4</sub> ) δ ppm 0.88 (t, J=7.3 Hz, 3 H), 1.13 - 1.32 (m, 3 H), 1.46 - 1.69 (m, 3 H), 2.39 (t, J=6.8 Hz, 1 H), 3.61 (d, J=5.5 Hz, 2 H), 4.31 (dd, J=8.8, 5.0 Hz, 1 H), 5.62 - 5.87 (m, 2 H), 6.13 (d, J=3.0 Hz, 1 H), 7.39 (d, J=3.0 Hz, 1 H), 7.46 (dd, J=8.5, 1.8 Hz, 1 H), 7.70 (dd, J=8.5, 5.0 Hz, 1 H), 9.14 (dd, J=4.9, 1.6 Hz, 1 H)	B, 0.55	328

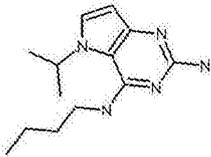
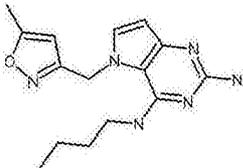
[0110]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
16		<sup>1</sup> H NMR (300 MHz, 氯仿- <i>d</i> ) $\delta$ ppm 0.77 (t, J=7.2 Hz, 3 H), 1.02 (dq, J=14.9, 7.3 Hz, 2 H), 1.15 - 1.29 (m, 2 H), 3.25 (td, J=6.8, 5.4 Hz, 2 H), 4.08 - 4.22 (m, 1 H), 4.42 (br. s., 2 H), 5.23 (s, 2 H), 6.20 (d, J=3.0 Hz, 1 H), 6.83 (ddd, J=8.5, 4.3, 2.2 Hz, 1 H), 6.95 (d, J=3.0 Hz, 1 H), 7.04 - 7.12 (m, 2 H)	A, 2.5	348
17		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) $\delta$ ppm 0.69 (t, J=7.3 Hz, 3 H), 0.80 - 0.93 (m, 2 H), 1.05 - 1.17 (m, 1 H), 1.34 - 1.45 (m, 1 H), 3.24 (br. s., 2 H), 4.06 - 4.16 (m, 1 H), 4.63 (br. s., 1 H), 5.03	B, 0.79	326

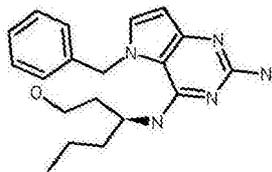
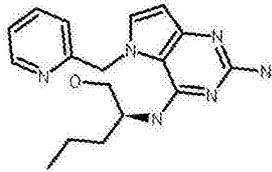
[0111]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		(d, J=8.6 Hz, 1 H), 5.24 (s, 2 H), 5.40 - 5.57 (m, 2 H), 5.99 (d, J=3.1 Hz, 1 H), 6.98 (d, J=7.0 Hz, 2 H), 7.22 - 7.35 (m, 3 H), 7.36 (d, J=2.9 Hz, 1 H)		
18		<sup>1</sup> H NMR (300 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 0.89 (t, J=7.4 Hz, 3 H), 1.18 - 1.39 (m, 2 H), 1.45 - 1.63 (m, 2 H), 2.50 (s, 3 H), 3.36 - 3.46 (m, 2 H), 5.33 (s, 2 H), 5.41 (s, 2 H), 5.96 (d, J=2.9 Hz, 1 H), 7.03 (d, J=7.6 Hz, 1 H), 7.23 (d, J=7.7 Hz, 1 H), 7.28 (t, J=5.2 Hz, 1 H), 7.40 (d, J=3.0 Hz, 1 H), 7.71 (t, J=7.7 Hz, 1 H)	A, 1.68	311

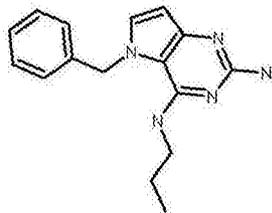
[0112]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
19		<sup>1</sup> H NMR (300 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 0.99 (t, J=7.4 Hz, 3 H), 1.26 - 1.43 (m, 2 H), 1.45 (d, J=6.3 Hz, 6 H), 1.67 (quin, J=7.3 Hz, 2 H), 3.54 - 3.63 (m, 2 H), 4.95 (dt, J=12.9, 6.4 Hz, 1 H), 6.18 (d, J=3.2 Hz, 1 H), 6.73 (br. s., 2 H), 7.29 (br. s., 1 H), 7.57 (d, J=3.2 Hz, 1 H)	A, 1.51	248
20		<sup>1</sup> H NMR (300 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 0.89 (t, J=7.3 Hz, 3 H), 1.27 (dq, J=14.9, 7.4 Hz, 2 H), 1.51 (quin, J=7.2 Hz, 2 H), 2.32 (s, 3 H), 3.26 - 3.44 (m, 2 H), 5.33 (s, 2 H), 5.51 (s, 2 H), 5.83 - 5.87 (m, 1 H), 5.97 (d, J=3.0 Hz, 1 H), 6.11 (t,	A, 1.45	301

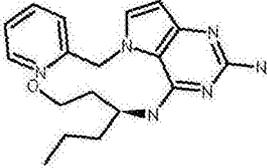
[0113]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		J=5.3 Hz, 1 H), 7.29 (d, J=3.0 Hz, 1 H)		
21		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 0.70 (t, J=7.3 Hz, 3 H), 0.82 - 0.98 (m, 2 H), 1.17 - 1.36 (m, 2 H), 1.37 - 1.48 (m, 1 H), 1.51 - 1.63 (m, 1 H), 3.21 - 6 3.31 (m, 2 H), 4.17 - 4.29 (m, 1 H), 4.49 (br. s., 1 H), 5.24 (d, J=8.5 Hz, 1 H), 5.30 (s, 2 H), 5.41 - 5.58 (m, 2 H), 6.00 (d, J=3.0 Hz, 1 H), 6.95 (s, 1 H), 6.96 (s, 1 H), 7.20 - 7.27 (m, 1 H), 7.27 - 7.34 (m, 2 H), 7.36 (d, J=3.0 Hz, 1 H)	B, 0.83	340
22		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 0.87 (t, J=7.3 Hz, 3 H), 1.15 -	B, 0.69	327

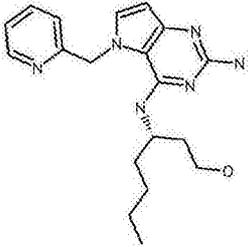
[0114]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		1.32 (m, 2 H), 1.45 - 1.59 (m, 1 H), 1.64 (td, <i>J</i> =8.0, 5.0 Hz, 1 H), 3.50 - 3.54 (m, 2 H), 3.72 - 3.79 (m, 1 H), 4.35 (td, <i>J</i> =8.5, 4.8 Hz, 1 H), 5.45 - 5.64 (m, 2 H), 6.14 (d, <i>J</i> =3.0 Hz, 1 H), 6.77 (br. s., 2 H), 7.43 (ddd, <i>J</i> =7.7, 4.9, 1.0 Hz, 1 H), 7.51 (d, <i>J</i> =7.8 Hz, 1 H), 7.63 (d, <i>J</i> =3.0 Hz, 1 H), 7.91 (td, <i>J</i> =7.7, 1.8 Hz, 1 H), 8.42 (d, <i>J</i> =7.8 Hz, 1 H), 8.50 - 8.58 (m, 1 H)		
23		<sup>1</sup> H NMR (300 MHz, 氯仿- <i>d</i> ) δ ppm 0.67 (t, <i>J</i> =7.4 Hz, 3 H), 1.25 (sxt, <i>J</i> =7.3 Hz, 2 H), 3.24 (td, <i>J</i> =7.0, 5.4 Hz, 2 H), 4.65 (br.	A, 2.15	282

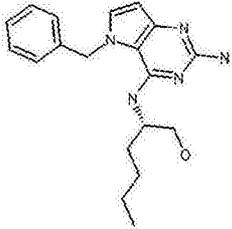
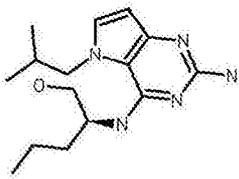
[0115]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		s., 1 H), 5.16 (br. s., 2 H), 5.39 (s, 2 H), 6.30 (d, <i>J</i> =3.0 Hz, 1 H), 7.03 - 7.13 (m, 3 H), 7.32 - 7.47 (m, 3 H)		
24		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 0.82 (t, <i>J</i> =7.40 Hz, 3 H) 1.13 - 1.24 (m, 2 H) 1.43 - 1.54 (m, 2 H) 1.55 - 1.76 (m, 2 H) 3.38 - 3.46 (m, 2 H) 4.28 - 4.37 (m, 1 H) 4.47 (br. s., 1 H) 5.35 (s, 2 H) 5.43 - 5.51 (m, 2 H) 5.97 (d, <i>J</i> =3.01 Hz, 1 H) 6.88 (d, <i>J</i> =8.28 Hz, 1 H) 7.26 (d, <i>J</i> =7.78 Hz, 1 H) 7.37 (ddd, <i>J</i> =7.53, 5.02, 1.00 Hz, 1 H) 7.43 (d, <i>J</i> =3.01 Hz, 1 H) 7.84 (td, <i>J</i> =7.65, 1.76 Hz, 1	B, 0.71	341

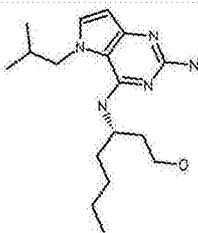
[0116]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		H) 8.53 (dt, J=4.00, 0.80 Hz, 1 H)		
25		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 0.74 - 0.85 (m, 3 H) 1.09 - 1.18 (m, 2 H) 1.18 - 1.30 (m, 2 H) 1.40 - 1.56 (m, 2 H) 1.56 - 1.65 (m, 1 H) 1.65 - 1.76 (m, 1 H) 3.34 - 3.45 (m, 2 H) 4.24 - 4.34 (m, 1 H) 4.47 (br. s., 1 H) 5.22 (s, 2 H) 5.39 - 5.53 (m, 2 H) 5.96 (d, J=2.76 Hz, 1 H) 6.75 (d, J=8.28 Hz, 1 H) 7.23 (d, J=7.78 Hz, 1 H) 7.37 (ddd, J=7.53, 4.89, 1.13 Hz, 1 H) 7.41 (d, J=3.01 Hz, 1 H) 7.83 (td, J=7.72, 1.88 Hz, 1 H) 8.50 - 8.55 (m, 1 H)	B, 0.8	355

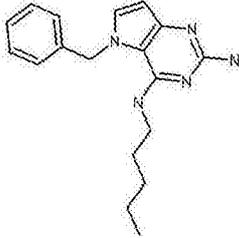
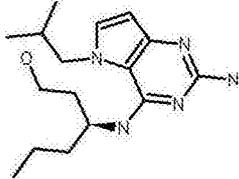
[0117]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
26		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 0.73 (t, J=7.4 Hz, 3 H), 0.77 - 0.93 (m, 2 H), 1.01 - 1.19 (m, 3 H), 1.38 - 1.51 (m, 1 H), 3.23 - 3.30 (m, 2 H), 4.04 - 6.417 (m, 1 H), 4.66 (br. s., 1 H), 5.12 (d, J=8.5 Hz, 1 H), 5.35 (s, 2 H), 5.40 - 5.60 (m, 2 H), 6.01 (d, J=3.0 Hz, 1 H), 6.95 - 7.03 (m, 2 H), 7.22 - 7.35 (m, 3 H), 7.38 (d, J=3.0 Hz, 1 H)	B, 0.86	340
27		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 0.74 (d, J=6.52 Hz, 3 H) 0.82 (d, J=6.78 Hz, 3 H) 0.92 (t, J=7.28 Hz, 3 H) 1.30 - 1.46 (m, 2 H) 1.50 - 1.69 (m, 2 H)	B, 0.76	292

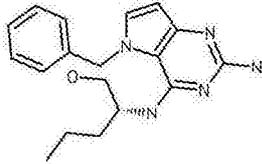
[0118]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		1.87 - 2.01 (m, 1 H) 3.43 - 3.58 (m, 2 H) 3.88 (dd, J=14.68, 8.16 Hz, 1 H) 4.12 (dd, J=14.56, 6.53 Hz, 1 H) 4.28 (m, J=8.40, 3.90 Hz, 1 H) 4.79 (br. s., 1 H) 5.22 (s, 2 H) 5.41 (d, J=8.53 Hz, 1 H) 5.89 (d, J=3.01 Hz, 1 H) 7.15 (d, J=3.01 Hz, 1 H)		
28		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 0.69 (d, J=6.9 Hz, 3 H), 0.79 (d, J=6.9 Hz, 3 H), 0.82 - 0.91 (m, 3 H), 1.20 - 1.39 (m, 4 H), 1.49 - 1.65 (m, 2 H), 1.66 - 6 1.79 (m, 2 H), 1.83 - 1.97 (m, 1 H), 3.43 - 3.58 (m, 2 H), 3.86 (dd, J=14.5, 8.5 Hz, 1	B, 0.89	320

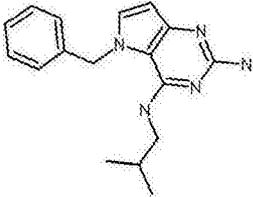
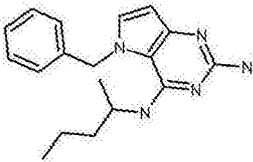
[0119]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		H), 4.12 (dd, J=14.5, 6.5 Hz, 1 H), 4.27 - 4.44 (m, 1 H), 4.71 (br. s., 1 H), 5.21 (s, 2 H), 5.75 (d, J=8.5 Hz, 1 H), 5.87 (d, J=2.8 Hz, 1 H), 7.12 (d, J=3.2 Hz, 1 H)		
29		<sup>1</sup> H NMR (300 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 0.75 - 0.85 (m, 3 H), 1.02 (d, J=7.0 Hz, 2 H), 1.11 - 1.26 (m, 2 H), 1.34 (d, J=7.6 Hz, 2 H), 3.28 (s, 2 H), 5.22 (s, 2 H), 5.49 (s, 2 H), 5.76 (s, 1 H), 5.98 (d, J=3.0 Hz, 1 H), 6.97 (d, J=6.7 Hz, 2 H), 7.17 - 7.35 (m, 4 H)	A, 2.47	310
30		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 0.76 (dd, J=11.42, 6.65 Hz, 6	B, 0.82	306

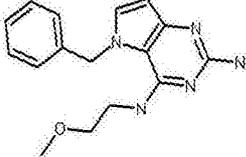
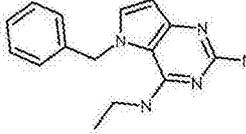
[0120]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		H) 0.90 (t, J=7.28 Hz, 3 H) 1.26 - 1.37 (m, 2 H) 1.53 - 1.63 (m, 1 H) 1.63 - 1.73 (m, 1 H) 1.74 - 1.90 (m, 3 H) 3.49 - 3.62 (m, 2 H) 4.11 - 4.22 (m, 2 H) 4.55 (m, J=6.50 Hz, 1 H) 4.79 (t, J=4.52 Hz, 1 H) 6.16 (d, J=3.01 Hz, 1 H) 7.24 (d, J=8.28 Hz, 1 H) 7.33 (br. s., 2 H) 7.44 (d, J=2.76 Hz, 1 H) 12.35 (br. s., 1 H)		
31		<sup>1</sup> H NMR (300 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 0.64 - 0.75 (m, 3 H), 0.77 - 0.97 (m, 2 H), 1.02 - 1.21 (m, 1 H), 1.30 - 1.50 (m, 1 H), 3.33 (d, J=4.3 Hz, 2 H), 4.15 (dd, J=9.2, 4.5 Hz, 1	A, 2.07	326

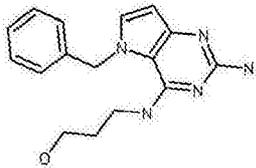
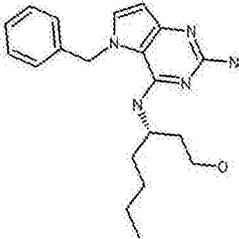
[0121]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		H), 4.69 (br. s., 1 H), 5.34 (d, <i>J</i> =8.5 Hz, 1 H), 5.42 - 5.64 (m, 2 H), 5.71 (br. s., 2 H), 6.06 (d, <i>J</i> =3.0 Hz, 1 H), 6.99 (d, <i>J</i> =6.6 Hz, 2 H), 7.17 - 7.37 (m, 3 H), 7.44 (d, <i>J</i> =3.0 Hz, 1 H)		
32		<sup>1</sup> H NMR (300 MHz, 氯仿- <i>d</i> ) δ ppm 0.57 (d, <i>J</i> =6.6 Hz, 6 H), 1.19 (s, 2 H), 1.33 - 1.52 (m, 1 H), 3.05 (dd, <i>J</i> =6.8, 5.6 Hz, 2 H), 4.61 - 4.78 (m, 1 H), 5.32 (s, 2 H), 6.25 (d, <i>J</i> =3.0 Hz, 1 H), 6.97 - 7.06 (m, 3 H), 7.26 - 7.39 (m, 3 H)	A, 2.25	296
33		<sup>1</sup> H NMR (300 MHz, 氯仿- <i>d</i> ) δ ppm 0.74 - 0.82 (m, 3 H), 0.86 (d, <i>J</i> =6.5 Hz, 3 H),	A, 2.4	310

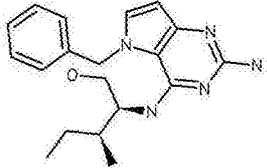
[0122]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		0.93 - 1.28 (m, 4 H), 4.01 - 4.22 (m, 1 H), 4.39 (d, <i>J</i> =7.8 Hz, 1 H), 5.05 (br. s., 2 H), 5.37 (s, 2 H), 6.29 (d, <i>J</i> =3.0 Hz, 1 H), 7.02 - 7.13 (m, 3 H), 7.32 - 7.47 (m, 3 H)		
34		<sup>1</sup> H NMR (300 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 3.24 (s, 3 H), 3.35 - 3.44 (m, 2 H), 3.57 (q, <i>J</i> =5.6 Hz, 2 H), 5.55 (s, 2 H), 5.97 (br. s., 2 H), 6.09 (d, <i>J</i> =2.9 Hz, 1 H), 6.30 (br. s., 1 H), 7.05 - 7.14 (m, 2 H), 7.25 - 7.41 (m, 3 H), 7.46 (d, <i>J</i> =3.0 Hz, 1 H)	A, 1.81	298
35		<sup>1</sup> H NMR (300 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 0.98 (t, <i>J</i> =7.1 Hz, 3 H), 3.23 - 3.44 (m, 2 H), 5.43	A, 1.96	268

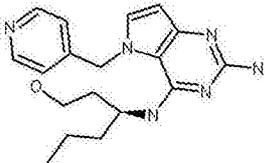
[0123]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		(s, 2 H), 5.49 (s, 2 H), 5.96 - 6.07 (m, 2 H), 7.02 (d, <i>J</i> =6.7 Hz, 2 H), 7.17 - 7.38 (m, 4 H)		
36		<sup>1</sup> H NMR (300 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 1.56 (quin, <i>J</i> =6.4 Hz, 2 H), 3.24 - 3.44 (m, 4 H), 4.45 - 4.58 (m, 1 H), 5.49 (s, 2 H), 5.61 (br. s., 2 H), 6.03 (d, <i>J</i> =2.9 Hz, 1 H), 6.19 (t, <i>J</i> =5.0 Hz, 1 H), 6.96 - 7.04 (m, 2 H), 7.19 - 7.34 (m, 3 H), 7.37 (d, <i>J</i> =3.0 Hz, 1 H)	A, 1.61	298
37		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 0.74 (t, <i>J</i> =7.3 Hz, 3 H), 0.80 - 0.95 (m, 2 H), 1.02 - 1.17 (m, 2 H), 1.19 - 1.48 (m, 3	B, 0.92	354

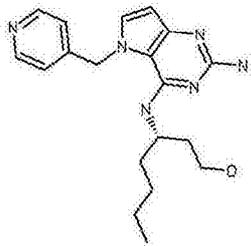
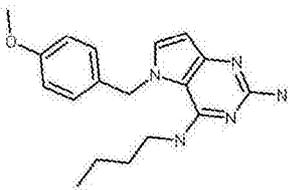
[0124]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		H), 1.51 - 1.64 (m, 1 H), 3.21 - 6 3.27 (m, 2 H), 4.20 (tt, J=8.5, 4.0 Hz, 1 H), 4.49 (br. s., 1 H), 5.18 - 5.32 (m, 3 H), 5.40 - 5.59 (m, 2 H), 6.00 (d, J=3.1 Hz, 1 H), 6.96 (d, J=7.3 Hz, 2 H), 7.19 - 7.39 (m, 4 H)		
38		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 0.62 (d, J=4.0 Hz, 3 H), 0.65 (d, J=6.8 Hz, 3 H), 0.95 - 1.04 (m, 1 H), 1.35 - 1.47 (m, 1 H), 1.89 (s, 3 H), 3.35 - 3.46 6 (m, 2 H), 3.98 - 4.07 (m, 1 H), 5.06 (d, J=8.8 Hz, 1 H), 5.42 - 5.60 (m, 4 H), 6.01 (d, J=2.9 Hz, 1 H), 6.94 - 6.98 (m, 2 H), 7.23 - 7.28 (m,	B, 0.84	340

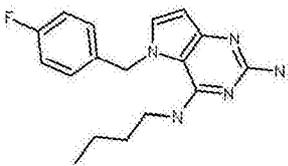
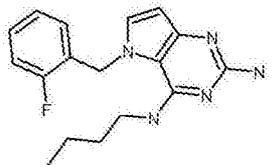
[0125]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		1 H), 7.29 - 7.35 (m, 2 H), 7.38 (d, J=3.1 Hz, 1 H)		
39		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 0.63 - 0.73 (m, 3 H), 0.75 - 0.95 (m, 2 H), 1.18 - 1.36 (m, 2 H), 1.48 (dd, J=8.9, 4.7 Hz, 1 H), 1.53 - 1.64 (m, 1 H), 3.20 - 3.28 (m, 2 H), 4.13 - 4.29 (m, 1 H), 4.50 (t, J=5.4 Hz, 1 H), 5.28 (s, 2 H), 5.37 (d, J=8.6 Hz, 1 H), 5.47 - 5.69 (m, 2 H), 6.04 (d, J=3.1 Hz, 1 H), 6.81 (d, J=5.9 Hz, 2 H), 7.36 (d, J=2.9 Hz, 1 H), 8.40 - 8.50 (m, 2 H)	B, 0.57	341

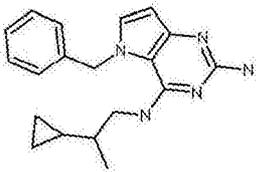
[0126]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
40		<sup>1</sup> H NMR (400 MHz, 氯仿-d) δ ppm 0.76 - 0.82 (m, 3 H), 0.87 - 1.00 (m, 2 H), 1.02 - 1.22 (m, 5 H), 1.28 - 1.41 (m, 1 H), 1.72 - 1.85 (m, 1 H), 3.34 (td, J=11.6, 2.4 Hz, 1 H), 3.44 - 3.55 (m, 1 H), 4.12 - 4.27 (m, 2 H), 4.58 (br. s., 2 H), 5.26 - 5.45 (m, 2 H), 6.27 (d, J=3.1 Hz, 1 H), 6.89 - 6.97 (m, 2 H), 7.06 (d, J=3.1 Hz, 1 H), 8.55 - 8.62 (m, 2 H)	B, 0.64	355
41		<sup>1</sup> H NMR (300 MHz, 氯仿-d) δ ppm 0.65 - 0.80 (m, 3 H) 0.89 - 1.07 (m, 2 H) 1.11 - 1.22 (m, 2 H) 3.14 - 3.28 (m, 2 H) 3.73 (s, 3 H)	A, 2.26	326

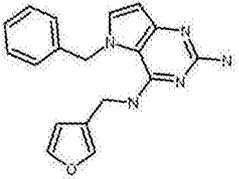
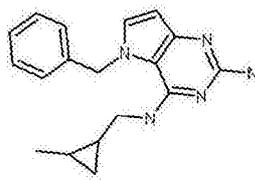
[0127]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		4.76 (br. s., 1 H) 5.08 - 5.24 (m, 2 H) 5.27 (s, 2 H) 6.18 (d, <i>J</i> =3.02 Hz, 1 H) 6.84 (d, <i>J</i> =8.66 Hz, 2 H) 6.94 (d, <i>J</i> =8.66 Hz, 2 H) 7.00 (d, <i>J</i> =3.02 Hz, 1 H)		
42		<sup>1</sup> H NMR (300 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 0.70 - 0.87 (m, 3 H) 0.97 - 1.14 (m, 2 H) 1.31 - 1.46 (m, 2 H) 3.36 - 3.40 (m, 2 H) 5.52 (s, 2 H) 5.62 (s, 2 H) 6.05 (d, <i>J</i> =3.02 Hz, 1 H) 6.11 (s, 1 H) 6.90 - 7.09 (m, 2 H) 7.09 - 7.24 (m, 2 H) 7.39 (d, <i>J</i> =3.02 Hz, 1 H)	A, 2.23	314
43		<sup>1</sup> H NMR (300 MHz, 氯仿- <i>d</i> ) δ ppm 0.67 - 0.85 (m, 3 H) 0.94 -	A, 2.27	314

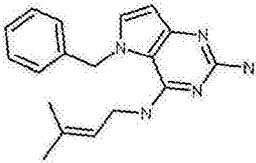
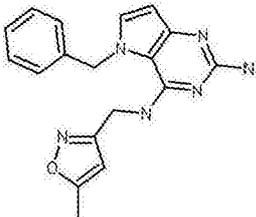
[0128]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		1.13 (m, 2 H) 1.16 - 1.33 (m, 2 H) 3.16 - 3.43 (m, 2 H) 4.33 (br. s., 1 H) 4.54 (br. s., 2 H) 5.32 (s, 2 H) 6.21 (d, <i>J</i> =3.02 Hz, 1 H) 6.67 (t, <i>J</i> =7.35 Hz, 1 H) 6.99 (d, <i>J</i> =3.02 Hz, 1 H) 7.00 - 7.13 (m, 2 H) 7.22 - 7.32 (m, 1 H)		
44		<sup>1</sup> H NMR (300 MHz, 氯仿- <i>d</i> ) δ ppm -0.07 - 0.07 (m, 2 H) 0.21 - 0.43 (m, 3 H) 0.66 - 0.75 (m, 3 H) 0.76 - 0.95 (m, 1 H) 3.22 - 3.51 (m, 2 H) 4.86 (br. s., 1 H) 5.15 (br. s., 2 H) 5.41 (s, 2 H) 6.33 (d, <i>J</i> =3.02 Hz, 1 H) 7.07 (br. s., 1 H) 7.10 (s, 2 H) 7.35 - 7.47 (m, 3	A, 2.46	322

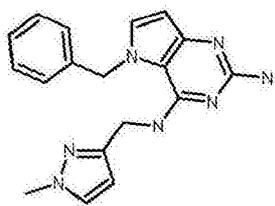
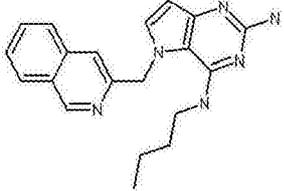
[0129]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		H)		
45		<sup>1</sup> H NMR (300 MHz, 氯仿-d) δ ppm 4.21 (d, J=4.95 Hz, 2 H) 4.48 (br. s., 1 H) 4.70 (br. s., 2 H) 5.18 - 5.30 (m, 2 H) 5.97 (s, 1 H) 6.22 (d, J=3.02 Hz, 1 H) 6.90 (dd, J=6.53, 2.13 Hz, 2 H) 6.98 (s, 1 H) 7.02 (d, J=3.02 Hz, 1 H) 7.20 - 7.29 (m, 4 H)	A, 2.09	320
46		<sup>1</sup> H NMR (300 MHz, 氯仿-d) δ ppm -0.12 - 0.09 (m, 2 H) 0.24 - 0.46 (m, 2 H) 0.89 (d, J=5.64 Hz, 3 H) 2.84 - 3.06 (m, 1 H) 3.08 - 3.25 (m, 1 H) 4.51 (br. s., 1 H) 4.63 (br. s., 2 H) 5.34 (s, 2 H) 6.23 (d, J=3.02 Hz,	A, 2.26	308

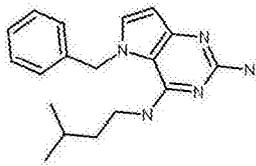
[0130]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		1 H) 7.03 (d, <i>J</i> =2.75 Hz, 2 H) 7.06 (br. s., 1 H) 7.27 - 7.40 (m, 3 H)		
47		<sup>1</sup> H NMR (300 MHz, 氯仿- <i>d</i> ) δ ppm 1.42 (s, 3 H) 1.58 (s, 3 H) 3.66 - 3.80 (m, 2 H) 4.42 (br. s., 1 H) 4.71 - 4.88 (m, 1 H) 5.02 (br. s., 2 H) 5.28 (s, 2 H) 6.21 (d, <i>J</i> =3.02 Hz, 1 H) 6.96 - 7.01 (m, 2 H) 7.02 (s, 1 H) 7.24 - 7.41 (m, 3 H)	A, 2.32	308
48		<sup>1</sup> H NMR (300 MHz, 氯仿- <i>d</i> ) δ ppm 2.28 (s, 3 H) 4.46 (d, <i>J</i> =5.22 Hz, 2 H) 4.65 (br. s., 2 H) 4.92 (br. s., 1 H) 5.30 (s, 2 H) 5.54 (s, 1 H) 6.22 (d, <i>J</i> =3.02 Hz, 1 H)	A, 1.97	335

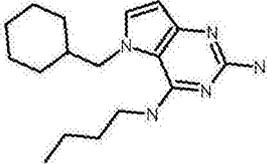
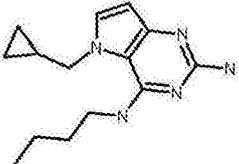
[0131]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		6.89 - 7.01 (m, 2 H) 7.03 (d, <i>J</i> =3.16 Hz, 1 H) 7.21 - 7.27 (m, 3 H)		
49		<sup>1</sup> H NMR (300 MHz, 氯仿- <i>d</i> ) δ ppm 3.79 (s, 3 H) 4.44 (d, <i>J</i> =4.67 Hz, 2 H) 5.33 (s, 2 H) 5.60 (br. s., 1 H) 5.84 (d, <i>J</i> =2.06 Hz, 1 H) 6.28 (d, <i>J</i> =3.02 Hz, 1 H) 6.43 (br. s., 2 H) 6.96 (dd, <i>J</i> =6.53, 2.82 Hz, 2 H) 7.02 (d, <i>J</i> =3.02 Hz, 1 H) 7.18 (d, <i>J</i> =2.20 Hz, 1 H) 7.21 - 7.28 (m, 3 H)	A, 1.83	334
50		<sup>1</sup> H NMR (300 MHz, 氯仿- <i>d</i> ) δ ppm 0.83 - 0.91 (m, 3 H) 1.30 - 1.41 (m, 2 H) 1.57 - 1.67 (m, 2 H) 3.44 - 3.60 (m, 2 H) 5.41 (s, 2 H)	A, 2.52	347

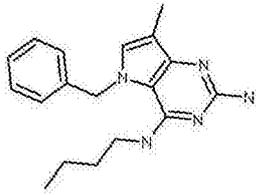
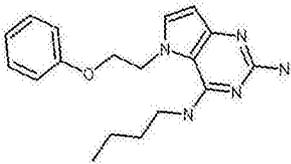
[0132]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		6.22 (br. s, 2 H) 6.21 (d, <i>J</i> =3.02 Hz, 1 H) 7.05 (d, <i>J</i> =3.02 Hz, 1 H) 7.55 - 7.65 (m, 2 H) 7.70 (t, <i>J</i> =7.49 Hz, 1 H) 7.76 - 7.86 (m, 1 H) 7.95 (d, <i>J</i> =8.11 Hz, 1 H) 8.23 (br. s., 1 H) 9.12 (s, 1 H)		
51		<sup>1</sup> H NMR (300 MHz, 氯仿- <i>d</i> ) δ ppm 0.71 (d, <i>J</i> =6.32 Hz, 6 H) 0.74 - 0.86 (m, 1 H) 0.93 - 1.05 (m, 2 H) 3.15 - 3.28 (m, 2 H) 4.59 (br. s., 1 H) 5.29 (s, 2 H) 6.18 (br. s., 2 H) 6.27 (d, <i>J</i> =3.02 Hz, 1 H) 6.97 - 7.01 (m, 2 H) 7.02 (br. s., 1 H) 7.26 - 7.42 (m, 3 H)	A, 2.45	310

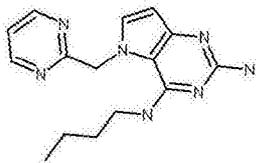
[0133]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
52		<sup>1</sup> H NMR (300 MHz, 氯仿- <i>d</i> ) δ ppm 0.89 - 0.95 (m, 1 H) 0.92 (t, <i>J</i> =7.35 Hz, 3 H) 1.00 - 1.26 (m, 4 H) 1.31 - 1.44 (m, 2 H) 1.47 - 1.75 (m, 8 H) 3.43 - 3.59 (m, 2 H) 3.83 (d, <i>J</i> =7.29 Hz, 2 H) 4.73 (br. s., 1 H) 4.93 (br. s., 2 H) 6.08 (d, <i>J</i> =3.02 Hz, 1 H) 6.81 (d, <i>J</i> =3.02 Hz, 1 H)	A, 2.68	302
53		<sup>1</sup> H NMR (300 MHz, 氯仿- <i>d</i> ) δ ppm 0.19 - 0.35 (m, 2 H) 0.50 - 0.65 (m, 2 H) 0.69 - 0.86 (m, 1 H) 0.91 (t, <i>J</i> =7.29 Hz, 3 H) 1.33 - 1.45 (m, 2 H) 1.49 - 1.65 (m, 2 H) 3.50 (td, <i>J</i> =7.11, 5.57 Hz, 2 H) 4.00 (d,	A, 2.19	260

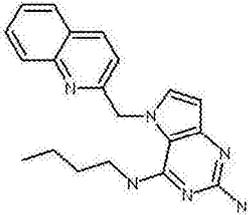
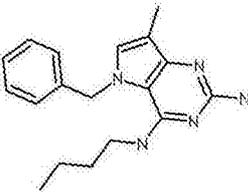
[0134]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		<i>J</i> =6.05 Hz, 2 H) 4.68 (br. s., 2 H) 4.80 (br. s., 1 H) 6.10 (d, <i>J</i> =3.02 Hz, 1 H) 6.93 (d, <i>J</i> =3.02 Hz, 1 H)		
54		<sup>1</sup> H NMR (300 MHz, 氯仿- <i>d</i> ) δ ppm 0.69 - 0.74 (m, 3 H) 0.89 - 0.97 (m, 2 H) 1.07 - 1.13 (m, 2 H) 2.21 (s, 3 H) 3.14 - 3.27 (m, 2 H) 4.66 (br. s., 1 H) 5.24 (s, 2 H) 6.40 (br. s., 2 H) 6.78 - 6.86 (m, 1 H) 6.92 - 7.05 (m, 2 H) 7.26 - 7.41 (m, 3 H)	A, 2.46	310
55		<sup>1</sup> H NMR (300 MHz, 氯仿- <i>d</i> ) δ ppm 0.96 (t, <i>J</i> =7.29 Hz, 3 H) 1.38 - 1.57 (m, 2 H) 1.58 - 1.75 (m, 2 H) 3.54 - 3.64 (m, 2 H) 4.29 -	A, 2.47	326

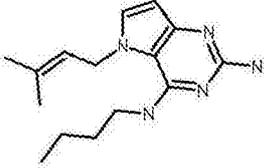
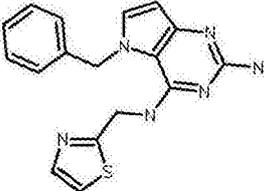
[0135]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		4.42 (m, 2 H) 4.56 (t, <i>J</i> =4.88 Hz, 2 H) 4.59 (br. s., 2 H) 5.96 (br. s., 1 H) 6.26 (d, <i>J</i> =3.02 Hz, 1 H) 6.79 - 6.91 (m, 2 H) 6.99 (d, <i>J</i> =3.02 Hz, 1 H) 7.00 - 7.08 (m, 1 H) 7.28 - 7.34 (m, 2 H)		
56		<sup>1</sup> H NMR (300 MHz, 氯仿- <i>d</i> ) δ ppm 0.93 (t, <i>J</i> =7.35 Hz, 3 H) 1.36 - 1.52 (m, 2 H) 1.52 - 1.71 (m, 2 H) 3.46 - 3.65 (m, 2 H) 5.35 (s, 2 H) 6.06 (br. s., 2 H) 6.22 (d, <i>J</i> =3.02 Hz, 1 H) 7.13 (d, <i>J</i> =3.02 Hz, 1 H) 7.31 (t, <i>J</i> =5.02 Hz, 1 H) 8.02 (br. s., 1 H) 8.71 (d, <i>J</i> =5.09 Hz, 2 H)	C, 4.68	298

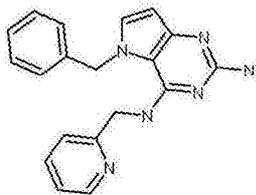
[0136]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
57		<sup>1</sup> H NMR (300 MHz, 氯仿-d) δ ppm 0.79 (t, J=7.29 Hz, 3 H) 1.22 (dd, J=15.19, 7.49 Hz, 2 H) 1.39 - 1.56 (m, 2 H) 3.29 - 3.45 (m, 2 H) 4.63 (br. s., 2 H) 5.44 (s, 2 H) 6.17 (d, J=3.02 Hz, 1 H) 7.00 (br. s., 1 H) 7.09 (d, J=3.02 Hz, 1 H) 7.18 - 7.28 (m, 1 H) 7.42 - 7.57 (m, 1 H) 7.62 - 7.83 (m, 2 H) 7.97 (d, J=8.39 Hz, 1 H) 8.10 (d, J=8.39 Hz, 1 H)	A, 2.49	347
58		<sup>1</sup> H NMR (300 MHz, 氯仿-d) δ ppm 0.69 - 0.74 (m, 3 H) 0.89 - 0.97 (m, 2 H) 1.07 - 1.13 (m, 2 H) 2.21 (s, 3 H) 3.14 - 3.27 (m, 2 H) 4.66	A, 2.56	310

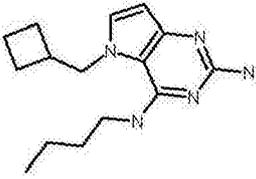
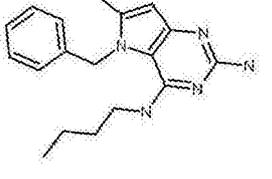
[0137]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		(br. s., 1 H) 5.24 (s, 2 H) 6.40 (br. s., 2 H) 6.78 - 6.86 (m, 1 H) 6.92 - 7.05 (m, 2 H) 7.26 - 7.41 (m, 3 H)		
59		<sup>1</sup> H NMR (300 MHz, 氯仿-d) δ ppm 0.89 (t, J=7.22 Hz, 3 H) 1.26 - 1.40 (m, 2 H) 1.41 - 1.57 (m, 2 H) 1.70 - 1.77 (m, 6 H) 3.32 - 3.51 (m, 2 H) 4.47 (br. s., 2 H) 4.66 (d, J=5.64 Hz, 2 H) 4.98 (br. s., 1 H) 5.28 - 5.41 (m, 1 H) 6.06 (d, J=3.02 Hz, 1 H) 6.84 (d, J=3.02 Hz, 1 H)	A, 2.37	274
60		<sup>1</sup> H NMR (300 MHz, 氯仿-d) δ ppm 4.47 (br. s., 2 H) 4.74 (d, J=5.50 Hz, 2 H) 5.15 (t, J=5.16 Hz, 1 H)	A, 1.86	337

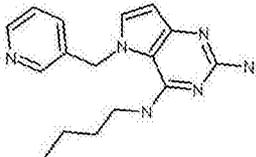
[0138]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		5.32 (s, 2 H) 6.22 (d, J=3.02 Hz, 1 H) 6.94 - 7.01 (m, 2 H) 7.03 (d, J=3.02 Hz, 1 H) 7.14 (d, J=3.30 Hz, 1 H) 7.17 - 7.27 (m, 3 H) 7.58 (d, J=3.30 Hz, 1 H)		
61		<sup>1</sup> H NMR (300 MHz, 氯仿-d) δ ppm 4.38 (d, J=5.36 Hz, 2 H) 4.49 (br. s., 2 H) 4.54 - 4.66 (m, 1 H) 5.26 (s, 2 H) 6.21 (d, J=3.02 Hz, 1 H) 6.84 - 6.92 (m, 2 H) 7.00 - 7.08 (m, 2 H) 7.08 - 7.14 (m, 1 H) 7.14 - 7.23 (m, 3 H) 8.15 - 8.23 (m, 1 H) 8.36 - 8.44 (m, 1 H)	A, 1.28	331

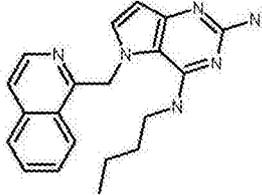
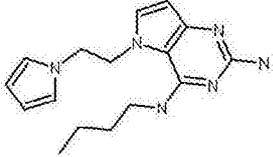
[0139]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
62		<sup>1</sup> H NMR (300 MHz, 氯仿- <i>d</i> ) δ ppm 0.92 (t, J=7.35 Hz, 3 H) 1.37 (dq, J=14.90, 7.31 Hz, 2 H) 1.52 - 1.63 (m, 2 H) 1.65 - 1.78 (m, 2 H) 1.78 - 1.90 (m, 2 H) 1.91 - 2.05 (m, 2 H) 2.47 - 2.83 (m, 2 H) 3.41 - 3.54 (m, 1 H) 4.05 (d, J=7.01 Hz, 2 H) 4.73 (br. s., 1 H) 4.89 (br. s., 2 H) 6.09 (d, J=3.02 Hz, 1 H) 6.85 (d, J=3.02 Hz, 1 H)	A, 2.33	274
63		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 0.75 (t, J=7.3 Hz, 3 H), 0.98 - 1.06 (m, 2 H), 1.32 (quin, J=7.2 Hz, 2 H), 2.27 (s, 3 H), 3.24 - 3.28 (m, 2 H), 5.25	B, 0.97	310

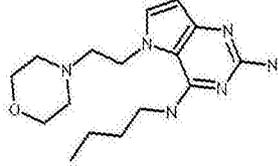
[0140]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		(br. s., 6.2 H), 5.44 (s, 2 H), 5.75 (t, J=5.4 Hz, 1 H), 5.87 (s, 1 H), 6.87 (d, J=7.0 Hz, 2 H), 7.19 - 7.25 (m, 1 H), 7.25 - 7.32 (m, 2 H)		
64		<sup>1</sup> H NMR (300 MHz, 氯仿-d) δ ppm 0.75 (t, J=7.30 Hz, 3 H) 0.89 - 1.06 (m, 2 H) 1.11 - 1.29 (m, 2 H) 3.24 - 3.34 (m, 2 H) 5.16 (br. s., 1 H) 5.47 (s, 2 H) 5.96 (br. s., 2 H) 6.21 (d, J=3.02 Hz, 1 H) 7.00 (d, J=3.02 Hz, 1 H) 7.18 - 7.26 (m, 2 H) 8.33 - 8.42 (m, 1 H) 8.49 - 8.59 (m, 1 H)	C, 4.21	297

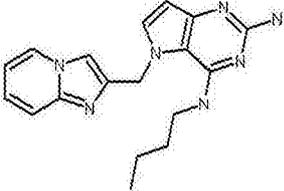
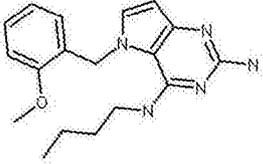
[0141]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
65		<sup>1</sup> H NMR (300 MHz, 氯仿- <i>d</i> ) δ ppm 0.95 (t, J=7.29 Hz, 3 H) 1.30 - 1.54 (m, 2 H) 1.70 (quin, J=7.32 Hz, 2 H) 3.50 (td, J=7.11, 5.02 Hz, 2 H) 4.76 (br. s., 2 H) 5.77 (s, 2 H) 6.14 (d, J=3.02 Hz, 1 H) 7.17 - 7.21 (m, 1 H) 7.62 - 7.73 (m, 3 H) 7.80 - 7.87 (m, 1 H) 8.25 - 8.34 (m, 1 H) 8.37 (d, J=5.77 Hz, 1 H) 8.59 (br. s., 1 H)	A, 2.61	347
66		<sup>1</sup> H NMR (300 MHz, 氯仿- <i>d</i> ) δ ppm 0.90 (t, J=7.22 Hz, 3 H) 1.25 - 1.40 (m, 2 H) 1.43 - 1.54 (m, 2 H) 3.29 (td, J=7.11, 5.57 Hz, 2 H) 3.87 (br. s., 1 H) 4.07 - 4.22 (m, 2 H) 4.23	A, 2.15	299

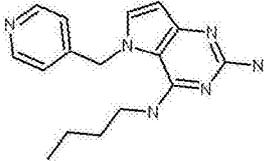
[0142]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		- 4.31 (m, 2 H) 4.61 (br. s., 2 H) 6.06 (t, J=2.06 Hz, 2 H) 6.14 (d, J=3.02 Hz, 1 H) 6.29 (t, J=2.06 Hz, 2 H) 6.70 (d, J=3.02 Hz, 1 H)		
67		<sup>1</sup> H NMR (300 MHz, 氯仿-d) δ ppm 0.92 (t, J=7.29 Hz, 3 H) 1.26 - 1.47 (m, 2 H) 1.49 - 1.67 (m, 2 H) 2.34 - 2.46 (m, 4 H) 2.72 - 2.81 (m, 2 H) 3.52 (td, J=7.22, 5.77 Hz, 2 H) 3.57 - 3.64 (m, 4 H) 4.17 - 4.24 (m, 2 H) 5.75 - 6.08 (m, 2 H) 6.19 (d, J=3.02 Hz, 1 H) 6.87 (d, J=3.02 Hz, 1 H) 8.19 (br. s., 1 H)	A, 1.16	319

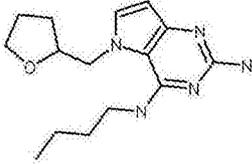
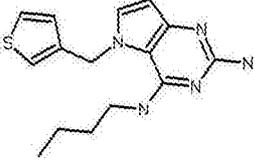
[0143]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
68		<sup>1</sup> H NMR (300 MHz, 氯仿- <i>d</i> ) δ ppm 0.90 (t, J=7.29 Hz, 3 H) 1.30 - 1.46 (m, 2 H) 1.58 - 1.73 (m, 2 H) 3.53 (td, J=7.01, 5.22 Hz, 2 H) 5.32 (s, 2 H) 5.78 - 6.11 (m, 2 H) 6.18 (d, J=3.02 Hz, 1 H) 6.78 - 6.84 (m, 1 H) 7.01 (d, J=3.02 Hz, 1 H) 7.18 - 7.24 (m, 2 H) 7.46 (d, J=9.07 Hz, 1 H) 7.54 (s, 1 H) 8.06 (d, J=6.74 Hz, 1 H) 8.92 - 9.11 (m, 0 H)	A, 1.76	336
69		<sup>1</sup> H NMR (300 MHz, 氯仿- <i>d</i> ) δ ppm 0.74 (t, J=7.30 Hz, 3 H) 0.90 - 1.12 (m, 2 H) 1.14 - 1.27 (m, 2 H) 3.20 - 3.28 (m, 2 H) 3.85 (s, 3 H)	A, 2.44	326

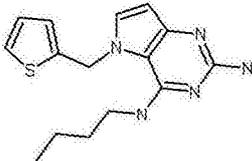
[0144]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		4.55 (br. s., 3 H) 5.22 - 5.27 (m, 2 H) 6.18 (d, J=3.02 Hz, 1 H) 6.62 (d, J=7.01 Hz, 1 H) 6.82 (t, J=7.56 Hz, 1 H) 6.87 (d, J=8.25 Hz, 1 H) 6.98 (d, J=3.02 Hz, 1 H) 7.20 - 7.27 (m, 1 H)		
70		<sup>1</sup> H NMR (300 MHz, 氯仿- <i>d</i> ) δ ppm 0.74 (t, J=7.40 Hz, 3 H) 0.88 - 1.09 (m, 2 H) 1.10 - 1.25 (m, 2 H) 3.18 - 3.28 (m, 2 H) 4.21 (br. s., 1 H) 4.66 (br. s., 2 H) 5.23 (s, 2 H) 6.22 (d, J=3.16 Hz, 2 H) 6.89 (d, J=5.77 Hz, 1 H) 6.96 (d, J=3.02 Hz, 1 H) 8.51 - 8.59 (m, 2 H)	A, 1.14	297

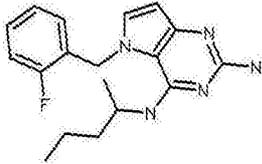
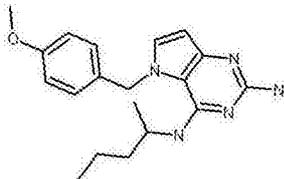
[0145]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
71		<sup>1</sup> H NMR (300 MHz, 氯仿- <i>d</i> ) δ ppm 0.91 (t, J=7.29 Hz, 3 H) 1.27 - 1.45 (m, 2 H) 1.49 - 1.67 (m, 3 H) 1.85 (d, J=7.01 Hz, 1 H) 1.91 - 2.12 (m, 2 H) 3.39 - 3.49 (m, 2 H) 3.72 (t, J=6.67 Hz, 2 H) 4.02 (dd, J=15.81, 4.54 Hz, 1 H) 4.12 - 4.23 (m, 1 H) 4.42 (dd, J=15.74, 1.72 Hz, 1 H) 5.76 - 6.13 (m, 2 H) 6.23 (d, J=3.02 Hz, 1 H) 6.82 (d, J=3.02 Hz, 1 H) 7.61 - 7.79 (m, 1 H)	A, 2.17	290
72		<sup>1</sup> H NMR (300 MHz, 氯仿- <i>d</i> ) δ ppm 0.78 (t, J=7.30 Hz, 3 H) 1.00 - 1.15 (m, 2 H) 1.16 - 1.29 (m, 2 H)	A, 2.27	302

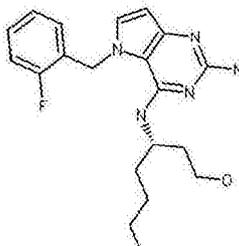
[0146]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		3.19 - 3.31 (m, 2 H) 4.46 (br. s., 1 H) 4.59 (br. s., 2 H) 5.27 (s, 2 H) 6.17 (d, J=3.02 Hz, 1 H) 6.82 (dd, J=4.95, 1.10 Hz, 1 H) 6.91 - 6.95 (m, 1 H) 6.97 (d, J=3.02 Hz, 1 H) 7.34 (dd, J=4.95, 2.89 Hz, 1 H)		
73		<sup>1</sup> H NMR (300 MHz, 氯仿-d) δ ppm 0.79 (t, J=7.20 Hz, 3 H) 1.02 - 1.33 (m, 4 H) 1.90 - 2.08 (m, 2 H) 3.27 (td, J=6.80, 5.36 Hz, 2 H) 4.58 (br. s., 2 H) 5.41 (s, 2 H) 6.19 (d, J=3.02 Hz, 1 H) 6.67 - 6.84 (m, 1 H) 6.93 (dd, J=5.02, 3.51 Hz, 1 H) 6.98 (d, J=3.16 Hz, 1 H) 7.26 (dd,	A, 2.28	302

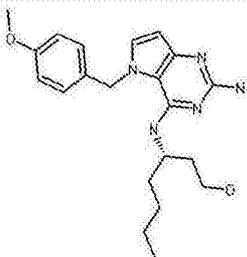
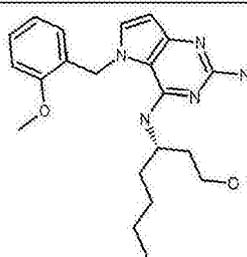
[0147]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		J=5.09, 0.96 Hz, 1 H)		
74		<sup>1</sup> H NMR (300 MHz, 氯仿-d) δ ppm 0.73 (t, J=7.20 Hz, 3 H) 0.89 (d, J=6.46 Hz, 3 H) 0.93 - 1.07 (m, 2 H) 1.07 - 1.29 (m, 2 H) 4.05 - 4.20 (m, 1 H) 4.43 (d, J=7.84 Hz, 1 H) 5.16 - 5.29 (m, 2 H) 5.33 (s, 2 H) 6.25 (d, J=3.02 Hz, 1 H) 6.68 (t, J=7.49 Hz, 1 H) 7.02 - 7.13 (m, 3 H) 7.23 - 7.34 (m, 1 H)	A, 2.53	328
75		<sup>1</sup> H NMR (300 MHz, 氯仿-d) δ ppm 0.72 (t, J=7.00 Hz, 3 H) 0.83 (d, J=6.46 Hz, 3 H) 0.86 - 1.07 (m, 2 H) 1.08 - 1.22 (m, 2 H) 3.74 (s, 3 H) 4.07 (s, 1 H) 4.57 -	A, 2.58	340

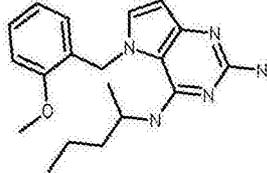
[0148]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		4.62 (m, 1 H) 5.23 (s, 2 H) 5.30 - 5.55 (m, 2 H) 6.24 (d, J=3.02 Hz, 1 H) 6.82 - 6.89 (m, 2 H) 6.90 - 6.97 (m, 2 H) 7.02 (d, J=3.02 Hz, 1 H)		
76		<sup>1</sup> H NMR (300 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 0.68 (t, J=7.20 Hz, 1 H) 0.81 - 0.95 (m, 2 H) 0.96 - 1.14 (m, 2 H) 1.16 - 1.36 (m, 2 H) 1.36 - 1.62 (m, 2 H) 3.21 - 3.28 (m, 2 H) 4.09 - 4.25 (m, 1 H) 4.39 - 4.48 (m, 1 H) 5.15 - 5.26 (m, 2 H) 5.32 - 5.39 (m, 1 H) 5.40 - 5.50 (m, 1 H) 5.55 - 5.65 (m, 1 H) 5.96 (d, J=2.90 Hz, 1 H) 6.34 - 6.44 (m, 1 H) 6.97 - 7.05 (m,	A, 2.34	372

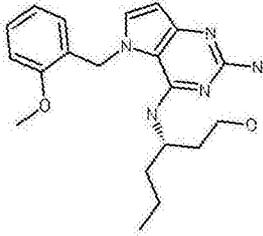
[0149]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		1 H) 7.10 - 7.30 (m, 3 H)		
77		<sup>1</sup> H NMR (300 MHz, 氯仿-d) δ ppm 0.73 (t, J=7.20 Hz, 3 H) 0.80 - 1.00 (m, 4 H) 1.00 - 1.33 (m, 2 H) 1.47 - 1.83 (m, 3 H) 3.15 - 3.26 (m, 1 H) 3.32 - 3.43 (m, 1 H) 3.72 (s, 3 H) 4.01 - 4.14 (m, 1 H) 4.22 (d, J=8.25 Hz, 1 H) 4.40 (br. s., 2 H) 5.16 - 5.29 (m, 2 H) 6.18 (d, J=3.02 Hz, 1 H) 6.80 - 6.95 (m, 4 H) 7.03 (d, J=3.02 Hz, 1 H)	A, 2.34	384
78		<sup>1</sup> H NMR (300 MHz, CDCl <sub>3</sub> ) δ 7.31 (t, J = 7.9 Hz, 1H), 7.12 (d, J = 3.0 Hz, 1H), 6.95 (d, J = 8.5 Hz, 1H), 6.89 (d, J = 7.6 Hz,	A, 2.42	384

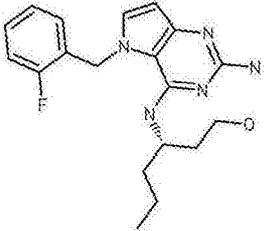
[0150]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		1H), 6.63 (d, $J = 6.9$ Hz, 1H), 6.29 (d, $J = 3.0$ Hz, 1H), 5.33 (d, $J = 6.0$ Hz, 2H), 5.02 (s, 2H), 4.60 (s, 1H), 4.20 (s, 1H), 3.92 (s, 3H), 3.50 – 3.35 (m, 1H), 3.24 (td, $J = 11.6, 2.7$ Hz, 1H), 1.86 – 1.69 (m, 2H), 1.44 – 1.29 (m, 1H), 1.29 – 0.92 (m, 6H), 0.81 (t, $J = 7.2$ Hz, 3H).		
79		<sup>1</sup> H NMR (300 MHz, CDCl <sub>3</sub> ) $\delta$ 7.34 (t, $J = 7.8$ Hz, 1H), 7.10 (d, $J = 3.0$ Hz, 1H), 6.97 (d, $J = 8.5$ Hz, 1H), 6.91 (d, $J = 7.4$ Hz, 1H), 6.65 (d, $J = 7.4$ Hz, 1H), 6.31 (d, $J = 3.0$ Hz, 1H), 5.33 (s, 2H), 4.76 (d, $J = 7.2$ Hz, 1H),	A, 2.60	340

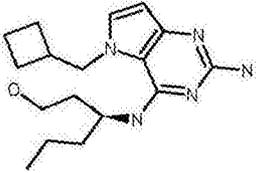
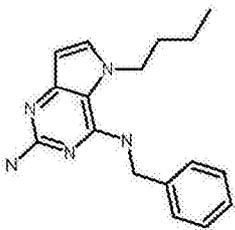
[0151]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		4.18 (dt, $J = 14.2, 6.9$ Hz, 1H), 3.93 (s, 3H), 1.24 – 0.95 (m, 6H), 0.91 (d, $J = 6.5$ Hz, 3H), 0.79 (t, $J = 7.0$ Hz, 3H).		
80		<sup>1</sup> H NMR (300 MHz, CDCl <sub>3</sub> ) $\delta$ 7.24 (t, $J = 7.8$ Hz, 1H), 7.05 (d, $J = 3.0$ Hz, 1H), 6.88 (d, $J = 8.3$ Hz, 1H), 6.83 (t, $J = 7.8$ Hz, 1H), 6.56 (d, $J = 7.3$ Hz, 1H), 6.21 (d, $J = 3.0$ Hz, 1H), 5.26 (2d, $J = 6.0$ Hz, 2H), 4.90 (s, 2H), 4.52 (d, $J = 8.3$ Hz, 1H), 4.17 (dd, $J = 9.1, 6.4$ Hz, 1H), 3.86 (s, 3H), 3.36 (ddd, $J = 11.8, 5.0, 2.7$ Hz, 1H), 3.17 (td, $J = 11.5, 2.7$ Hz, 1H), 1.77 – 1.60 (m, 1H), 1.37 – 1.13	A, 2.25	370

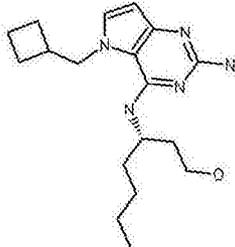
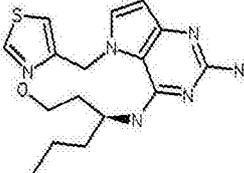
[0152]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		(m, 2H), 1.09 – 0.75 (m, 4H), 0.71 (t, <i>J</i> = 7.0 Hz, 3H).		
81		<sup>1</sup> H NMR (300 MHz, CDCl <sub>3</sub> ) δ 7.27 (dd, <i>J</i> = 13.6, 6.2 Hz, 1H), 7.09 (d, <i>J</i> = 10.1 Hz, 1H), 7.05 (d, <i>J</i> = 3.1 Hz, 1H), 7.02 (d, <i>J</i> = 7.7 Hz, 1H), 6.63 (t, <i>J</i> = 7.2 Hz, 1H), 6.24 (d, <i>J</i> = 3.0 Hz, 1H), 5.42 – 5.25 (m, 2H), 4.78 (s, 2H), 4.43 (s, 1H), 4.20 (s, 1H), 3.48 – 3.36 (m, 1H), 3.25 (td, <i>J</i> = 11.6, 2.5 Hz, 1H), 1.82 – 1.65 (m, 2H), 1.39 – 0.86 (m, 5H), 0.71 (t, <i>J</i> = 7.1 Hz, 3H).	A, 2.19	358

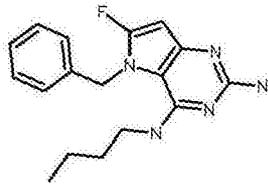
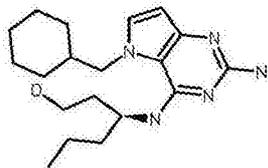
[0153]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
82		<sup>1</sup> H NMR (300 MHz, CDCl <sub>3</sub> ) δ 6.92 (d, <i>J</i> = 3.0 Hz, 1H), 6.16 (d, <i>J</i> = 3.0 Hz, 1H), 5.85 (s, 1H), 5.51 (s, 2H), 4.60 – 4.39 (m, 1H), 4.24 – 4.04 (m, 2H), 3.81 (d, <i>J</i> = 6.6 Hz, 2H), 2.71 (dt, <i>J</i> = 14.9, 7.5 Hz, 1H), 2.15 – 1.32 (m, 13H), 0.97 (t, <i>J</i> = 7.3 Hz, 3H).	A, 2.22	318
83		<sup>1</sup> H NMR (300 MHz, CDCl <sub>3</sub> ) δ 7.44 – 7.28 (m, 5H), 6.93 (d, <i>J</i> = 3.0 Hz, 1H), 6.17 (d, <i>J</i> = 3.0 Hz, 1H), 4.95 (s, 1H), 4.83 (s, 2H), 4.78 (d, <i>J</i> = 5.2 Hz, 2H), 4.03 (t, <i>J</i> = 7.2 Hz, 2H), 1.85 – 1.59 (m, 2H), 1.35 – 1.10 (m, 2H), 0.84 (t, <i>J</i>	A, 2.55	296

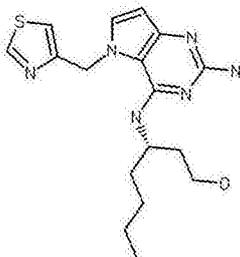
[0154]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		= 7.3 Hz, 3H).		
84		<sup>1</sup> H NMR (300 MHz, CDCl <sub>3</sub> ) δ 6.94 (d, <i>J</i> = 3.0 Hz, 1H), 6.17 (d, <i>J</i> = 3.0 Hz, 1H), 5.08 (s, 2H), 4.46 (s, 1H), 4.27 – 3.99 (m, 2H), 3.72 (d, <i>J</i> = 6.9 Hz, 2H), 8.12 – -0.50 (m, 60H), 2.71 (dd, <i>J</i> = 14.9, 7.4 Hz, 1H), 2.13 – 1.31 (m, 16H), 0.92 (t, <i>J</i> = 6.8 Hz, 3H).	A, 2.65	332
85		<sup>1</sup> H NMR (300 MHz, CDCl <sub>3</sub> ) δ 8.75 (d, <i>J</i> = 1.9 Hz, 1H), 7.19 (s, <i>J</i> = 1.9 Hz, 1H), 7.02 (d, <i>J</i> = 3.0 Hz, 2H), 6.19 (d, <i>J</i> = 3.0 Hz, 1H), 5.36 (s, 2H), 5.22 – 4.88 (m, 2H), 4.37 (s, 2H), 3.48 (dd, <i>J</i> = 23.1, 14.8 Hz, 3H), 2.03	A, 1.35	347

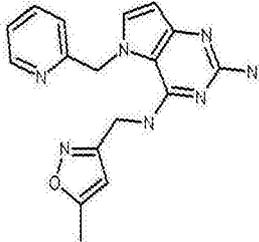
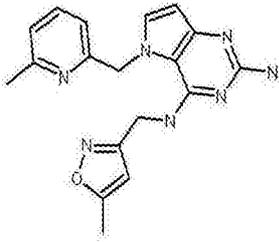
[0155]

#	结构	$^1\text{H NMR}$	LC 方法, Rt (min)	LC-MS 质量发现 值
		- 1.83 (m, 2H), 1.81 - 1.05 (m, 5H), 0.82 (dt, $J =$ 19.4, 7.1 Hz, 3H).		
86		$^1\text{H NMR}$ (300 MHz, $\text{CDCl}_3$ ) $\delta$ 7.48 - 7.28 (m, 3H), 7.15 (d, $J =$ 6.8 Hz, 2H), 5.72 (d, $J = 3.3$ Hz, 1H), 5.25 (s, 2H), 4.44 (s, 2H), 4.16 (s, 1H), 3.23 (dd, $J =$ 12.0, 6.8 Hz, 2H), 1.18 (dd, $J = 14.4,$ 7.1 Hz, 2H), 1.03 (dd, $J = 15.0, 7.1$ Hz, 2H), 0.79 (t, $J$ $= 7.1$ Hz, 3H).	A, 2.58	314
87		$^1\text{H NMR}$ (300 MHz, $\text{CDCl}_3$ ) $\delta$ 6.88 (d, $J = 3.0$ Hz, 1H), 6.13 (d, $J =$ 2.9 Hz, 1H), 5.60 (s, 1H), 5.46 (s, 2H), 4.57 - 4.45 (m, 1H), 4.00 (dd, $J = 15.0, 6.2$ Hz,	A, 1.89	346

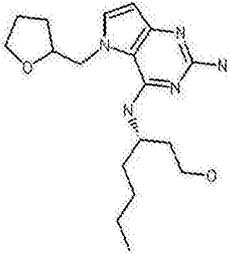
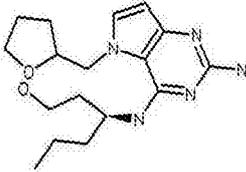
[0156]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		1H), 3.89 – 3.69 (m, 3H), 2.10 – 1.91 (m, 2H), 1.85 – 1.06 (m, 16H), 0.95 (dd, <i>J</i> = 15.9, 8.6 Hz, 3H).		
88		<sup>1</sup> H NMR (300 MHz, CDCl <sub>3</sub> ) δ 8.79 (d, <i>J</i> = 1.9 Hz, 1H), 7.19 (d, <i>J</i> = 1.6 Hz, 1H), 7.07 (s, 1H), 6.25 (d, <i>J</i> = 8.1 Hz, 1H), 6.22 (d, <i>J</i> = 3.0 Hz, 1H), 5.43 (d, <i>J</i> = 1.3 Hz, 2H), 4.42 (s, 2H), 4.34 (ddd, <i>J</i> = 11.0, 5.5, 2.9 Hz, 1H), 3.57 (dd, <i>J</i> = 11.8, 2.6 Hz, 1H), 3.44 (td, <i>J</i> = 11.7, 2.4 Hz, 2H), 2.03 – 1.87 (m, 2H), 1.70 – 1.45 (m, 2H), 1.41 – 1.18 (m, 4H), 0.87 (t, <i>J</i> = 6.5 Hz, 3H).	A, 1.51	361

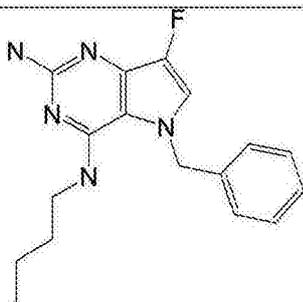
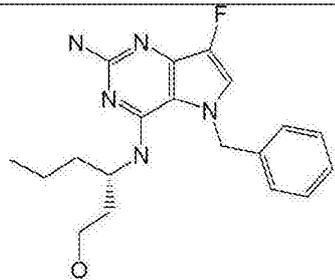
[0157]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
89		<sup>1</sup> H NMR (300 MHz, CDCl <sub>3</sub> ) δ 9.55 (s, 1H), 8.34 (d, <i>J</i> = 4.5 Hz, 1H), 7.70 (td, <i>J</i> = 7.7, 1.7 Hz, 1H), 7.30 (d, <i>J</i> = 7.8 Hz, 1H), 7.23 (dd, <i>J</i> = 7.0, 5.1 Hz, 1H), 7.04 (d, <i>J</i> = 3.0 Hz, 1H), 6.21 (d, <i>J</i> = 3.0 Hz, 1H), 5.92 (s, 3H), 5.25 (s, 2H), 4.75 (d, <i>J</i> = 5.5 Hz, 2H), 2.32 (s, 3H).	A, 1.25	336
90		<sup>1</sup> H NMR (300 MHz, CDCl <sub>3</sub> ) δ 9.39 (s, 1H), 7.63 (t, <i>J</i> = 7.7 Hz, 1H), 7.17 (s, 1H), 7.14 (d, <i>J</i> = 5.5 Hz, 1H), 7.10 (d, <i>J</i> = 3.2 Hz, 1H), 6.24 (d, <i>J</i> = 3.0 Hz, 1H), 6.01 (s, 1H), 5.33 (s, 2H), 5.27 (s, 2H), 4.83 (d, <i>J</i> = 5.6 Hz, 2H), 2.39 (s, 3H),	A, 1.37	350

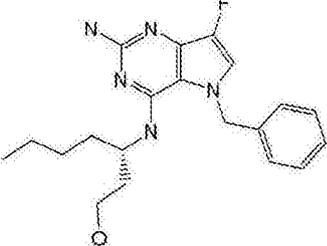
[0158]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		2.38 (s, 3H).		
91		<sup>1</sup> H NMR (300 MHz, CDCl <sub>3</sub> ) δ 6.90 (d, <i>J</i> = 3.0 Hz, 1H), 6.26 (d, <i>J</i> = 3.0 Hz, 1H), 5.49 (s, 1H), 5.34 (d, <i>J</i> = 23.9 Hz, 2H), 4.55 – 4.31 (m, 2H), 4.23 (s, 1H), 4.09 (dd, <i>J</i> = 15.8, 4.2 Hz, 1H), 3.85 – 3.49 (m, 4H), 2.15 – 1.81 (m, 6H), 1.75 – 1.54 (m, 4H), 1.54 – 1.30 (m, 3H), 0.89 (dd, <i>J</i> = 14.3, 7.3 Hz, 3H).	A, 2.22	348
92		<sup>1</sup> H NMR (300 MHz, CDCl <sub>3</sub> ) δ 6.70 (d, <i>J</i> = 2.9 Hz, 1H), 6.06 (d, <i>J</i> = 3.0 Hz, 1H), 5.43 (s, 1H), 5.31 (s, 2H), 4.26 (t, <i>J</i> = 12.8 Hz, 2H), 4.03 (s, 1H), 3.89 (dd, <i>J</i>	A, 2.00	334

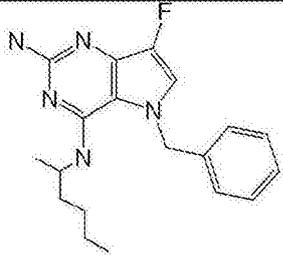
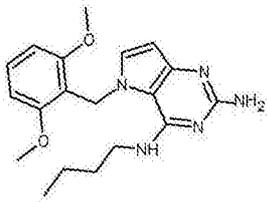
[0159]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		= 15.8, 4.3 Hz, 1H), 3.69 – 3.24 (m, 4H), 2.09 – 1.61 (m, 4H), 1.60 – 1.33 (m, 4H), 1.31 – 1.09 (m, 3H), 0.74 (t, <i>J</i> = 7.2 Hz, 3H).		
93		<sup>1</sup> H NMR (300 MHz, CDCl <sub>3</sub> ) δ 7.37 (t, <i>J</i> = 7.4 Hz, 3H), 7.08 (d, <i>J</i> = 6.6 Hz, 2H), 6.90 (d, <i>J</i> = 2.7 Hz, 1H), 5.25 (s, 2H), 4.53 (s, 2H), 4.35 (s, 1H), 3.25 (dd, <i>J</i> = 12.1, 6.8 Hz, 2H), 1.32 – 1.13 (m, 2H), 1.04 (dq, <i>J</i> = 13.9, 7.1 Hz, 2H), 0.79 (t, <i>J</i> = 7.2 Hz, 3H).	A, 2.40	314
94		<sup>1</sup> H NMR (300 MHz, CDCl <sub>3</sub> ) δ 7.38 (q, <i>J</i> = 6.2 Hz, 3H), 7.07 (d, <i>J</i> = 6.5 Hz, 2H), 6.97	A, 2.24	358

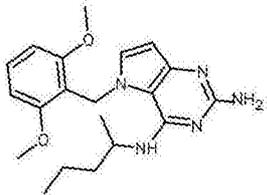
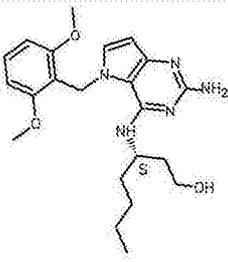
[0160]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		(d, $J = 2.7$ Hz, 1H), 5.26 (d, $J = 2.4$ Hz, 2H), 4.52 (s, 2H), 4.20 (d, $J = 11.6$ Hz, 1H), 3.42 (d, $J$ $= 11.7$ Hz, 1H), 3.22 (td, $J = 11.7,$ 2.4 Hz, 2H), 1.85 – 1.66 (m, 2H), 1.24 (d, $J = 7.1$ Hz, 2H), 0.95 (ddd, $J = 24.8,$ 13.8, 9.0 Hz, 3H), 0.75 (t, $J = 6.8$ Hz, 3H).		
95		<sup>1</sup> H NMR (300 MHz, CDCl <sub>3</sub> ) δ 7.46 – 7.31 (m, 3H), 7.07 (d, $J =$ 6.5 Hz, 2H), 6.97 (d, $J = 2.7$ Hz, 1H), 5.26 (d, $J = 3.3$ Hz, 2H), 4.55 (s, 2H), 4.32 – 4.02 (m, 1H), 3.53 – 3.33 (m, 1H), 3.22 (td, $J$ $= 11.7, 2.5$ Hz, 2H), 1.74 (ddd, $J =$ 14.3, 8.6, 4.1 Hz,	A, 2.44	372

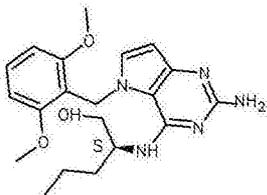
[0161]

#	结构	$^1\text{H NMR}$	LC 方法, Rt (min)	LC-MS 质量发现 值
		2H), 1.38 – 1.08 (m, 3H), 0.93 (ddd, $J = 13.8, 11.7, 4.3$ Hz, 4H), 0.80 (t, $J = 7.2$ Hz, 3H).		
96		$^1\text{H NMR}$ (300 MHz, $\text{CDCl}_3$ ) $\delta$ 7.49 – 7.30 (m, 3H), 7.08 (d, $J = 6.3$ Hz, 2H), 6.91 (d, $J = 2.7$ Hz, 1H), 5.24 (s, 2H), 4.51 (s, 2H), 4.28 – 3.96 (m, 1H), 1.08 (dddd, $J = 18.0, 16.8, 13.6, 10.8$ Hz, 7H), 0.85 (d, $J = 6.4$ Hz, 3H), 0.77 (dd, $J = 9.4, 4.5$ Hz, 3H).	A, 2.55	328
97		$^1\text{H NMR}$ (300 MHz, $\text{DMSO}-d_6$ ) $\delta$ ppm 0.94 (t, $J=7.4$ Hz, 3 H), 1.29 - 1.47 (m, 2 H), 1.61 (t, $J=7.1$ Hz, 2 H), 3.46 (q, $J=6.7$ Hz, 2 H), 3.80 (s, 6 H),	A, 2.79	356

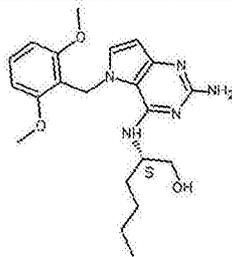
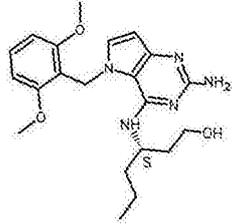
[0162]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		5.17 (s, 2 H), 5.31 (s, 2 H), 5.80 (d, <i>J</i> =2.9 Hz, 1 H), 6.33 (t, <i>J</i> =5.4 Hz, 1 H), 6.66 - 6.83 (m, 3 H), 7.38 (t, <i>J</i> =8.5 Hz, 1 H)		
98		<sup>1</sup> H NMR (300 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 0.91 (t, <i>J</i> =7.29 Hz, 3 H) 1.14 - 1.43 (m, 5 H) 1.46 - 1.72 (m, 2 H) 3.79 (s, 6 H) 4.41 - 4.60 (m, 1 H) 5.32 - 5.49 (m, 2 H) 6.02 (d, <i>J</i> =3.02 Hz, 1 H) 6.72 - 6.88 (m, 5 H) 6.92 (d, <i>J</i> =3.02 Hz, 1 H) 7.40 (t, <i>J</i> =8.39 Hz, 1 H)	A, 2.97	370
99		<sup>1</sup> H NMR (300 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 0.79 - 0.93 (m, 3 H) 1.18 - 1.39 (m, 4 H) 1.49 - 1.86 (m, 4 H)	A, 2.70	414

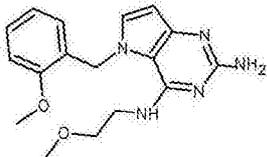
[0163]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		3.41 - 3.54 (m, 2 H) 3.78 (s, 6 H) 4.30 - 4.48 (m, 1 H) 4.56 - 4.70 (m, 1 H) 5.10 - 5.24 (m, 2 H) 5.32 (s, 2 H) 5.78 - 5.83 (m, 1 H) 5.85 - 5.93 (m, 1 H) 6.76 (s, 3 H) 7.30 - 7.44 (m, 1 H)		
100		<sup>1</sup> H NMR (300 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 0.74 - 1.01 (m, 3 H) 1.19 - 1.44 (m, 2 H) 1.46 - 1.74 (m, 2 H) 3.45 - 3.58 (m, 2 H) 3.80 (s, 6 H) 4.24 - 4.43 (m, 1 H) 4.75 - 4.88 (m, 1 H) 5.11 - 5.22 (m, 2 H) 5.23 - 5.36 (m, 2 H) 5.74 - 5.81 (m, 1 H) 5.81 - 5.85 (m, 1 H) 6.78 (s, 3 H) 7.29 - 7.44 (m, 1	A, 2.49	386

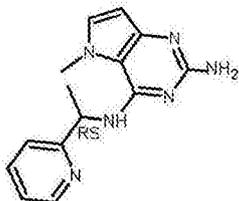
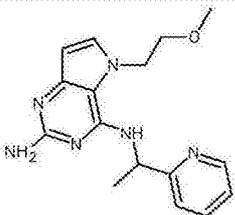
[0164]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		H)		
101		<sup>1</sup> H NMR (300 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 0.75 - 0.93 (m, 3 H) 1.19 - 1.40 (m, 4 H) 1.45 - 1.61 (m, 1 H) 1.61 - 1.78 (m, 1 H) 3.44 - 3.63 (m, 2 H) 3.80 (s, 6 H) 4.31 (d, J=4.95 Hz, 1 H) 4.81 (br. s., 1 H) 5.17 (s, 2 H) 5.30 (s, 2 H) 5.78 (d, J=8.52 Hz, 1 H) 5.83 (d, J=3.02 Hz, 1 H) 6.69 - 6.82 (m, 1 H) 6.69 - 6.82 (m, 2 H) 7.37 (t, J=8.39 Hz, 1 H)	A, 2.69	400
102		<sup>1</sup> H NMR (300 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 0.89 (t, J=7.40 Hz, 3 H) 1.20 - 1.42 (m, 2 H) 1.44 - 1.85 (m, 4 H) 3.42 - 3.54 (m, 2 H) 3.78 (s, 6 H)	A, 2.57	400

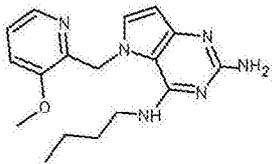
[0165]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		4.32 - 4.51 (m, 1 H) 4.56 - 4.69 (m, 1 H) 5.12 - 5.23 (m, 2 H) 5.32 (s, 2 H) 5.81 (d, J=2.90 Hz, 1 H) 5.85 - 5.93 (m, 1 H) 6.71 - 6.79 (m, 3 H) 7.31 - 7.44 (m, 1 H)		
103		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 3.17 (s, 3 H) 3.31 - 3.42 (m, 3 H) 3.45 - 3.56 (m, 3 H) 3.86 (s, 3 H) 5.11 (br. s., 2 H) 5.35 (s, 2 H) 5.62 (t, J=5.05 Hz, 1 H) 5.97 (d, J=2.83 Hz, 1 H) 6.60 - 6.69 (m, 1 H) 6.84 (td, J=7.47, 0.81 Hz, 1 H) 7.05 (d, J=8.07 Hz, 1 H) 7.18 (d, J=3.23 Hz, 1 H) 7.22 - 7.33 (m, 1 H)	D, 0.74	328

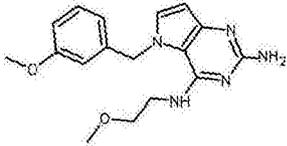
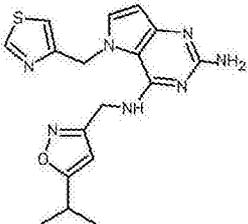
[0166]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
104		<sup>1</sup> H NMR (300 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 1.56 (d, J=6.87 Hz, 3 H) 4.01 (s, 3 H) 5.26 (s, 2 H) 5.49 (t, J=7.01 Hz, 1 H) 5.89 (d, J=2.89 Hz, 1 H) 6.67 (d, J=7.42 Hz, 1 H) 7.14 (d, J=2.89 Hz, 1 H) 7.28 (dd, J=7.01, 5.22 Hz, 1 H) 7.50 (d, J=7.84 Hz, 1 H) 7.78 (td, J=7.70, 1.65 Hz, 1 H) 8.56 (d, J=4.67 Hz, 1 H)	A, 1.23	269
105		<sup>1</sup> H NMR (300 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 1.53 (d, J=6.87 Hz, 3 H) 3.24 (s, 3 H) 3.68 (t, J=4.81 Hz, 2 H) 4.42 (t, J=4.81 Hz, 2 H) 5.24 (s, 2 H) 5.47 (t, J=7.01 Hz, 1 H) 5.94 (d,	A, 1.45	313

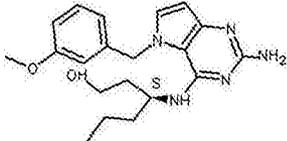
[0167]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		J=2.89 Hz, 1 H) 6.93 (d, J=7.42 Hz, 1 H) 7.20 (d, J=3.02 Hz, 1 H) 7.26 (dd, J=7.22, 5.02 Hz, 1 H) 7.47 (d, J=7.84 Hz, 1 H) 7.75 (td, J=7.63, 1.37 Hz, 1 H) 8.55 (d, J=4.81 Hz, 1 H)		
106		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 0.95 (t, J=7.37 Hz, 3 H) 1.37 - 1.46 (m, 2 H) 1.64 (quin, J=7.26 Hz, 2 H) 3.42 (td, J=6.93, 5.28 Hz, 2 H) 3.90 (s, 3 H) 5.18 (s, 2 H) 5.38 (s, 2 H) 5.89 (d, J=3.08 Hz, 1 H) 7.21 (d, J=3.08 Hz, 1 H) 7.42 (dd, J=8.47, 4.73 Hz, 1 H) 7.54 - 7.60 (m, 2 H) 8.11 (dd, J=4.73, 1.21 Hz, 1 H)	D, 0.90	327

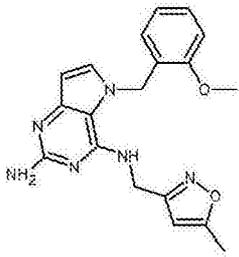
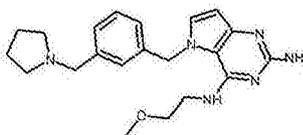
[0168]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
107		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 3.20 (s, 3 H) 3.36 (t, J=6.05 Hz, 2 H) 3.47 - 3.54 (m, 2 H) 3.71 (s, 3 H) 5.29 (s, 2 H) 5.42 (s, 2 H) 5.88 (t, J=5.50 Hz, 1 H) 6.00 (d, J=2.86 Hz, 1 H) 6.61 (d, J=7.48 Hz, 1 H) 6.63 - 6.66 (m, 1 H) 6.83 (dd, J=8.14, 2.20 Hz, 1 H) 7.23 (t, J=7.92 Hz, 1 H) 7.35 (d, J=3.08 Hz, 1 H)	D, 0.71	328
108		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 1.21 (d, J=7.04 Hz, 6 H) 3.02 (m, J=6.60, 6.60, 6.60, 6.60, 6.60 Hz, 0 H) 4.64 (d, J=5.72 Hz, 2 H) 5.35 (s, 2 H) 5.56 (s, 2 H) 5.97	D, 0.77	370

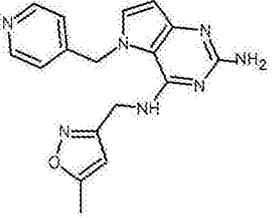
[0169]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		(d, J=3.08 Hz, 1 H) 6.01 (d, J=0.66 Hz, 1 H) 7.24 (t, J=5.83 Hz, 1 H) 7.32 (d, J=3.08 Hz, 1 H) 7.40 (d, J=1.98 Hz, 1 H) 9.03 (d, J=1.76 Hz, 1 H)		
109		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 0.70 (t, J=7.04 Hz, 3 H) 0.84 - 0.95 (m, 2 H) 1.17 - 1.35 (m, 2 H) 1.38 - 1.46 (m, 1 H) 1.53 - 1.62 (m, 1 H) 3.23 - 3.34 (m, 2 H) 3.68 (s, 3 H) 4.22 (dt, J=8.53, 4.43 Hz, 1 H) 4.49 (t, J=5.50 Hz, 1 H) 5.14 (d, J=8.58 Hz, 1 H) 5.23 (s, 2 H) 5.45 (q, J=16.95 Hz, 2 H) 5.98 (d, J=2.86 Hz, 1 H) 6.48 (d, J=7.70 Hz, 1 H) 6.56 - 6.58	D, 0.8	370

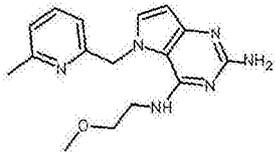
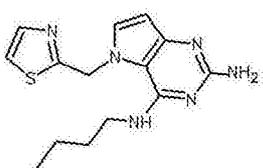
[0170]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		(m, 1 H) 6.82 (dd, J=8.14, 2.20 Hz, 1 H) 7.21 (t, J=7.92 Hz, 1 H) 7.34 (d, J=3.08 Hz, 1 H)		
110		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.30 (s, 3 H) 3.80 (s, 3 H) 4.55 (d, J=5.72 Hz, 2 H) 5.34 (s, 2 H) 5.41 (s, 2 H) 5.71 (d, J=0.88 Hz, 1 H) 5.99 (d, J=2.86 Hz, 1 H) 6.44 (dd, J=7.59, 1.43 Hz, 1 H) 6.50 (t, J=5.83 Hz, 1 H) 6.80 (td, J=7.43, 0.99 Hz, 1 H) 7.01 (d, J=7.48 Hz, 1 H) 7.21 - 7.27 (m, 2 H)	D, 0.79	365
111		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 1.59 - 1.70 (m, 4 H) 2.28 - 2.39 (m, 4 H) 3.18 (s, 3 H) 3.32 (t,	E, 1.18	381

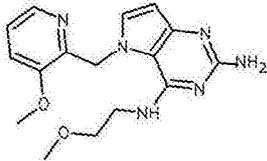
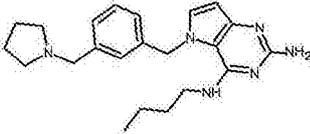
[0171]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		J=6.46 Hz, 2 H) 3.44 - 3.50 (m, 4 H) 5.26 (s, 2 H) 5.43 (s, 2 H) 5.86 (t, J=4.84 Hz, 1 H) 5.97 (d, J=2.83 Hz, 1 H) 6.84 - 6.90 (m, 0 H) 7.03 (s, 1 H) 7.15 (m, J=7.67 Hz, 1 H) 7.22 (t, J=7.30 Hz, 1 H) 7.32 (d, J=3.23 Hz, 1 H)		
112		<sup>1</sup> H NMR (300 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.29 (s, 3 H) 4.55 (d, J=5.50 Hz, 2 H) 5.55 (s, 1 H) 5.61 (s, 2 H) 5.68 (br. s., 2 H) 6.11 (d, J=2.89 Hz, 1 H) 6.83 (d, J=5.64 Hz, 2 H) 6.92 (t, J=5.43 Hz, 1 H) 7.43 (d, J=3.02 Hz, 1 H) 8.44 (d, J=5.77 Hz, 2 H)	A, 0.994	336

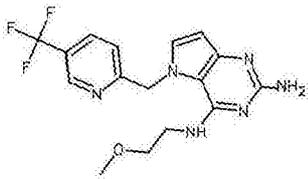
[0172]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
113		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.60 (s, 3 H) 3.22 (s, 3 H) 3.52 (t, J=5.70 Hz, 2 H) 3.72 (q, J=5.58 Hz, 2 H) 5.71 (br. s., 2 H) 6.26 (d, J=3.08 Hz, 1 H) 7.21 (d, J=7.48 Hz, 1 H) 7.34 - 7.58 (m, 3 H) 7.72 (d, J=2.86 Hz, 1 H) 7.94 (t, J=7.70 Hz, 1 H) 8.81 - 8.97 (m, 1 H) 12.60 (br. s., 1 H)	E, 1.28	313
114		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 0.87 (t, J=7.37 Hz, 3 H) 1.18 - 1.32 (m, 2 H) 1.50 (quin, J=7.21 Hz, 2 H) 3.33 - 3.38 (m, 2 H) 5.27 (s, 2 H) 5.79 (s, 2 H) 5.99 (d, J=3.08 Hz, 1 H) 6.47 (t, J=5.28 Hz,	E, 1.6	303

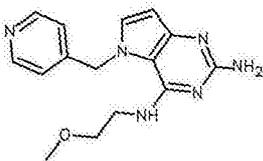
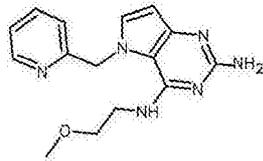
[0173]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		1 H) 7.35 (d, J=2.86 Hz, 1 H) 7.67 (d, J=3.08 Hz, 1 H) 7.77 (d, J=3.30 Hz, 1 H)		
115		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 3.30 (s, 3 H) 3.52 - 3.57 (m, 2 H) 3.57 - 3.64 (m, 2 H) 3.90 (s, 3 H) 5.23 (s, 2 H) 5.37 (s, 2 H) 5.90 (d, J=3.08 Hz, 1 H) 7.21 (d, J=2.86 Hz, 1 H) 7.41 (dd, J=8.36, 4.62 Hz, 1 H) 7.54 (dd, J=8.58, 1.10 Hz, 1 H) 7.80 (t, J=4.95 Hz, 1 H) 8.12 (dd, J=4.73, 1.21 Hz, 1 H)	D, 0.68	329
116		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 0.78 (t, J=7.30 Hz, 3 H) 1.01 - 1.11 (m, 2 H) 1.33	D, 0.73	379

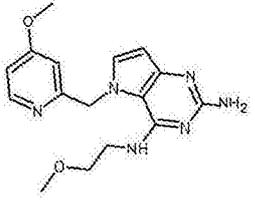
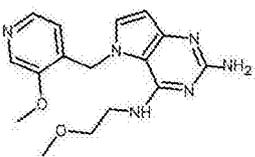
[0174]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		(quin, J=7.26 Hz, 2 H) 1.62 - 1.68 (m, 4 H) 2.31 - 2.37 (m, 4 H) 3.25 - 3.29 (m, 2 H) 3.48 (s, 2 H) 5.21 (s, 2 H) 5.47 (s, 2 H) 5.69 (t, J=5.39 Hz, 1 H) 5.97 (d, J=2.86 Hz, 1 H) 6.79 (d, J=7.48 Hz, 1 H) 7.01 (s, 1 H) 7.15 (d, J=7.70 Hz, 1 H) 7.21 (t, J=7.59 Hz, 1 H) 7.31 (d, J=2.86 Hz, 1 H)		
117		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 3.15 (s, 3 H) 3.35 (t, J=5.83 Hz, 2 H) 3.50 (q, J=5.65 Hz, 2 H) 5.30 (s, 2 H) 5.63 (s, 2 H) 6.01 (d, J=3.08 Hz, 1 H) 6.56 (t, J=5.39 Hz, 1 H) 7.17 (d, J=8.36 Hz, 1 H)	D, 0.77	367

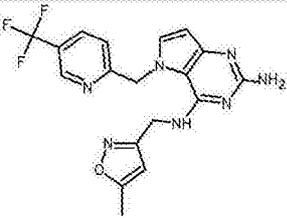
[0175]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		7.39 (d, J=3.08 Hz, 1 H) 8.21 (dd, J=8.36, 1.98 Hz, 1 H) 8.91 - 8.94 (m, 1 H)		
118		<sup>1</sup> H NMR (300 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 3.15 (s, 3 H) 3.25 - 3.31 (m, 2 H) 3.47 (d, J=5.77 Hz, 2 H) 5.32 (s, 2 H) 5.53 (s, 2 H) 5.97 (s, 1 H) 6.03 (d, J=2.89 Hz, 1 H) 6.91 (d, J=5.91 Hz, 2 H) 7.36 (d, J=3.02 Hz, 1 H) 8.47 (d, J=5.91 Hz, 2 H)	A, 0.83	299
119		<sup>1</sup> H NMR (300 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 3.26 (s, 3 H) 3.44 - 3.52 (m, 2 H) 3.52 - 3.62 (m, 2 H) 5.30 (s, 2 H) 5.44 (s, 2 H) 5.96 (d, J=3.02 Hz, 1 H) 7.29 (d, J=7.70 Hz,	A, 0.83	299

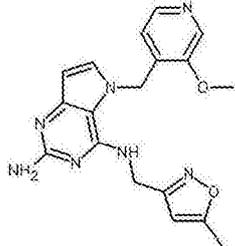
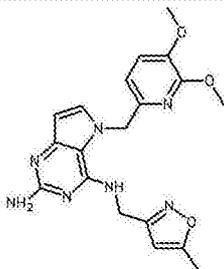
[0176]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		1 H) 7.33 - 7.45 (m, 1 H) 7.33 - 7.45 (m, 2 H) 7.83 (td, J=7.70, 1.65 Hz, 1 H) 8.56 (d, J=4.26 Hz, 1 H)		
120		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 3.25 - 3.29 (m, 3 H) 3.47 - 3.54 (m, 2 H) 3.54 - 3.61 (m, 2 H) 3.81 (s, 3 H) 5.25 (s, 2 H) 5.33 (s, 2 H) 5.94 (d, J=3.08 Hz, 1 H) 6.95 (dd, J=5.72, 2.64 Hz, 1 H) 6.98 (d, J=2.42 Hz, 1 H) 7.39 (d, J=3.08 Hz, 1 H) 7.74 (t, J=5.06 Hz, 1 H) 8.37 (d, J=5.72 Hz, 1 H)	D, 0.65	329
121		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 3.18 (s, 3 H) 3.38 (t, J=5.70 Hz, 2 H) 3.51 (q,	D, 0.52	329

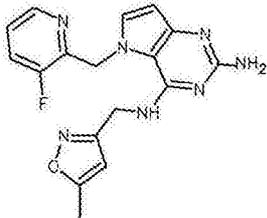
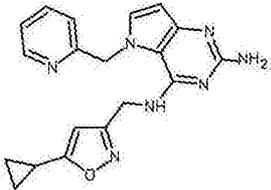
[0177]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		J=5.65 Hz, 2 H) 3.91 (s, 3 H) 5.31 (s, 2 H) 5.40 (s, 2 H) 5.95 - 6.00 (m, 2 H) 7.08 (d, J=5.72 Hz, 1 H) 7.21 (d, J=3.08 Hz, 1 H) 7.65 (s, 1 H) 8.38 (d, J=5.72 Hz, 1 H)		
122		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.28 (s, 3 H) 4.56 (d, J=5.94 Hz, 2 H) 5.38 (s, 2 H) 5.68 (s, 2 H) 5.76 (d, J=0.88 Hz, 1 H) 6.05 (d, J=3.08 Hz, 1 H) 7.04 (d, J=8.36 Hz, 1 H) 7.08 (t, J=5.83 Hz, 1 H) 7.41 (d, J=3.08 Hz, 1 H) 8.16 (dd, J=8.36, 1.98 Hz, 1 H) 8.82 - 8.85 (m, 1 H)	D, 0.80	404

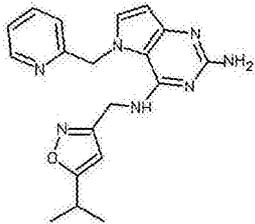
[0178]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
123		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.31 (s, 3 H) 3.85 (s, 3 H) 4.56 (d, J=5.72 Hz, 2 H) 5.37 (s, 2 H) 5.44 (s, 2 H) 5.82 (s, 1 H) 6.01 (d, J=3.08 Hz, 1 H) 6.70 (t, J=5.72 Hz, 1 H) 7.05 (d, J=5.72 Hz, 1 H) 7.22 (d, J=2.86 Hz, 1 H) 7.53 (s, 1 H) 8.37 (d, J=5.50 Hz, 1 H)	D, 0.58	366
124		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.31 (s, 3 H) 3.71 (s, 3 H) 3.72 (s, 3 H) 4.60 (d, J=5.72 Hz, 2 H) 5.32 - 5.37 (m, 4 H) 5.86 (s, 1 H) 5.99 (d, J=2.86 Hz, 1 H) 6.55 (d, J=7.92 Hz, 1 H) 6.83 (t, J=5.83 Hz, 1 H) 7.19 (d,	D, 0.70	396

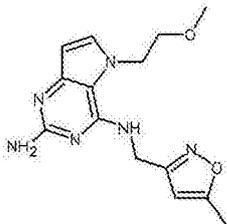
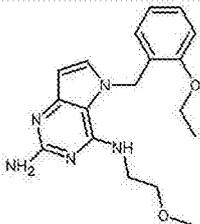
[0179]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		J=7.92 Hz, 1 H) 7.34 (d, J=2.86 Hz, 1 H)		
125		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.34 (s, 3 H) 4.63 (d, J=5.50 Hz, 2 H) 5.36 (s, 2 H) 5.58 (d, J=1.76 Hz, 2 H) 5.97 (d, J=3.08 Hz, 1 H) 6.06 (d, J=0.88 Hz, 1 H) 7.26 (dd, J=3.08, 0.88 Hz, 1 H) 7.44 - 7.49 (m, 1 H) 7.62 (t, J=5.72 Hz, 1 H) 7.78 (ddd, J=9.90, 8.47, 1.21 Hz, 1 H) 8.21 - 8.24 (m, 1 H)	D, 0.67	354
126		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 0.76 - 0.83 (m, 2 H) 0.99 - 1.04 (m, 2 H) 2.06 (tt, J=8.47, 4.95 Hz, 1 H) 4.59 (d, J=5.50 Hz, 2 H)	D, 0.74	362

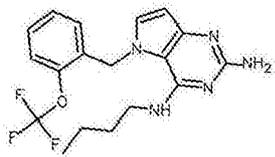
[0180]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		5.36 (s, 2 H) 5.48 (s, 2 H) 5.90 (s, 1 H) 5.99 (d, J=2.86 Hz, 1 H) 7.14 - 7.17 (m, 1 H) 7.31 - 7.35 (m, 1 H) 7.40 (d, J=2.86 Hz, 1 H) 7.74 (t, J=5.61 Hz, 1 H) 7.76 - 7.82 (m, 1 H) 8.40 - 8.43 (m, 1 H)		
127		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 1.19 (d, J=7.04 Hz, 6 H) 2.94 - 3.08 (m, 1 H) 4.63 (d, J=5.72 Hz, 2 H) 5.37 (s, 2 H) 5.49 (s, 2 H) 5.93 (s, 1 H) 5.99 (d, J=3.08 Hz, 1 H) 7.15 (d, J=7.92 Hz, 1 H) 7.32 (dd, J=7.04, 5.06 Hz, 1 H) 7.41 (d, J=2.86 Hz, 1 H) 7.74 (t, J=5.61 Hz, 1 H) 7.78 (td, J=7.70,	D, 0.79	364

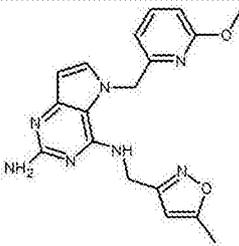
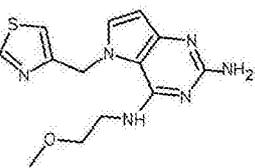
[0181]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		1.76 Hz, 1 H) 8.40 (d, J=4.18 Hz, 1 H)		
128		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.35 (d, J=0.66 Hz, 3 H) 3.15 (s, 3 H) 3.55 (t, J=5.06 Hz, 2 H) 4.36 (t, J=4.95 Hz, 2 H) 4.62 (d, J=5.72 Hz, 2 H) 5.31 (s, 2 H) 5.92 (d, J=3.08 Hz, 1 H) 6.18 (d, J=0.88 Hz, 1 H) 6.84 (t, J=5.83 Hz, 1 H) 7.17 (d, J=3.08 Hz, 1 H)	E, 1.09	303
129		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 1.38 (t, J=6.9 Hz, 3 H), 3.15 (s, 3 H), 3.27 - 3.33 (m, 2 H), 3.47 (q, J=5.6 Hz, 2 H), 4.10 (q, J=7.0 Hz, 2 H), 5.29 (s, 2 H), 5.37 (s, 2 H), 5.72 (t, J=5.4 Hz, 1 H),	E, 1.52	342

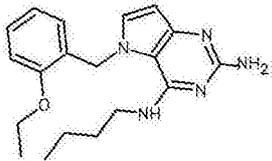
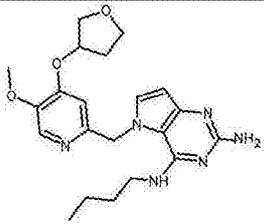
[0182]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		5.97 (d, J=2.9 Hz, 1 H), 6.59 (dd, J=7.5, 1.5 Hz, 1 H), 6.79 - 6.85 (m, 1 H), 7.02 (d, J=7.7 Hz, 1 H), 7.20 - 7.27 (m, 2 H)		
130	 <p>The chemical structure shows a central benzimidazole ring system. One nitrogen of the benzimidazole is substituted with a 2-(2,4-difluorophenoxy)ethyl group. The other nitrogen is substituted with a 2-(2-aminoimidazol-5-yl)ethyl group. The amino group is at the 2-position of the imidazole ring.</p>	<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 0.71 - 0.78 (m, 3 H), 0.96 - 1.08 (m, 2 H), 1.28 - 1.38 (m, 2 H), 3.22 - 3.29 (m, 2 H), 5.28 (s, 2 H), 5.59 (s, 2 H), 5.77 - 6 (t, J=5.4 Hz, 1 H), 6.03 (d, J=3.1 Hz, 1 H), 6.35 (d, J=7.7 Hz, 1 H), 7.19 - 7.25 (m, 1 H), 7.28 (d, J=3.1 Hz, 1 H), 7.35 - 7.40 (m, 2 H) <b>SLAST_1343_1.1</b> <b>esp</b>	E, 1.84	380

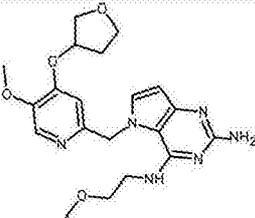
[0183]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
131		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.29 - 2.33 (m, 3 H) 3.71 (s, 3 H) 4.59 (d, J=5.72 Hz, 2 H) 5.36 (s, 2 H) 5.44 (s, 2 H) 5.82 - 5.85 (m, 1 H) 6.01 (d, J=3.08 Hz, 1 H) 6.50 (d, J=7.26 Hz, 1 H) 6.70 (d, J=8.14 Hz, 1 H) 6.90 (t, J=5.72 Hz, 1 H) 7.36 (d, J=2.86 Hz, 1 H) 7.62 (dd, J=8.25, 7.37 Hz, 1 H)	D, 0.74	366
132		<sup>1</sup> H NMR (300 MHz, 氯仿- <i>d</i> ) δ ppm 3.30 (s, 3 H) 3.47 - 3.60 (m, 2 H) 3.68 (m, J=5.10, 5.10, 5.10 Hz, 2 H) 5.37 (s, 2 H) 5.77 (br. s., 2 H) 6.20 (d, J=3.02 Hz, 1 H) 7.02 (d, J=3.16 Hz, 1 H) 7.23 - 7.31	A, 1.61	305

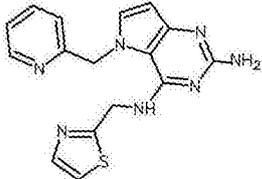
[0184]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		(m, 1 H) 7.85 (br. s., 1 H) 8.78 (d, J=1.79 Hz, 1 H)		
133		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 0.79 (t, J=7.3 Hz, 3 H), 1.09 (dq, J=15.0, 7.4 Hz, 2 H), 1.30 - 1.35 (m, 2 H), 1.38 (t, J=6.9 Hz, 3 H), 3.24 - 3.29 (m, 2 6 H), 4.10 (q, J=6.9 Hz, 2 H), 5.22 (s, 2 H), 5.39 (s, 2 H), 5.50 (t, J=5.4 Hz, 1 H), 5.96 (d, J=2.9 Hz, 1 H), 6.48 (dd, J=7.5, 1.3 Hz, 1 H), 6.77 - 6.84 (m, 1 H), 7.03 (d, J=7.9 Hz, 1 H), 7.20 - 7.26 (m, 2 H)	D, 1.0	340
134		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 0.91 (t, J=7.4 Hz, 3 H), 1.29 - 1.39 (m, 2 H), 1.54	D, 0.82	413

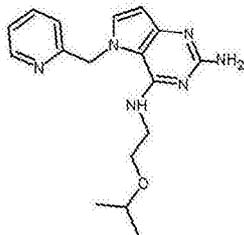
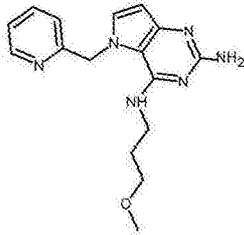
[0185]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		- 1.65 (m, 2 H), 1.84 - 1.94 (m, 1 H), 2.17 - 2.30 (m, 1 H), 3.37 - 6 3.44 (m, 2 H), 3.70 - 3.79 (m, 2 H), 3.82 (s, 3 H), 3.83 - 3.90 (m, 2 H), 4.97 - 5.04 (m, 1 H), 5.22 (s, 2 H), 5.30 (s, 2 H), 5.93 (d, J=3.1 Hz, 1 H), 7.03 (s, 1 H), 7.40 (d, J=2.9 Hz, 1 H), 7.47 (t, J=5.1 Hz, 1 H), 8.10 (s, 1 H)		
135		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 0.91 (t, J=7.4 Hz, 3 H), 1.29 - 1.39 (m, 2 H), 1.54 - 1.65 (m, 2 H), 1.84 - 1.94 (m, 1 H), 2.17 - 2.30 (m, 1 H), 3.37 - 6 3.44 (m, 2 H), 3.70 - 3.79 (m, 2 H), 3.82 (s, 3 H), 3.83 - 3.90	D, 0.64	415

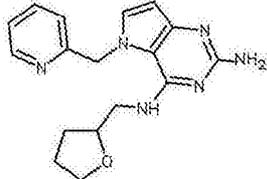
[0186]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		(m, 2 H), 4.97 - 5.04 (m, 1 H), 5.22 (s, 2 H), 5.30 (s, 2 H), 5.93 (d, J=3.1 Hz, 1 H), 7.03 (s, 1 H), 7.40 (d, J=2.9 Hz, 1 H), 7.47 (t, J=5.1 Hz, 1 H), 8.10 (s, 1 H)		
136		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 4.94 (d, J=5.9 Hz, 2 H), 5.37 (s, 2 H), 5.53 (s, 2 H), 6.01 (d, J=3.1 Hz, 1 H), 7.15 (d, J=7.7 Hz, 1 H), 7.31 (ddd, J=7.7, 6 4.8, 1.1 Hz, 1 H), 7.43 (d, J=3.1 Hz, 1 H), 7.52 (d, J=3.3 Hz, 1 H), 7.71 (d, J=3.3 Hz, 1 H), 7.78 (td, J=7.7, 2.0 Hz, 1 H), 8.10 (t, J=5.8 Hz, 1 H), 8.42 - 8.46 (m, 1 H)	D, 0.60	338

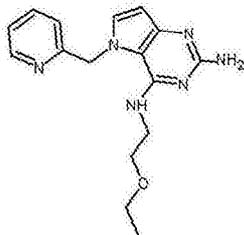
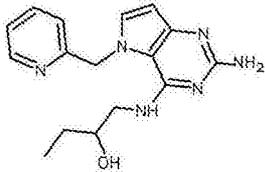
[0187]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
137		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 1.05 (d, J=6.2 Hz, 6 H), 3.46 - 3.59 (m, 5 H), 5.27 (s, 2 H), 5.44 (s, 2 H), 5.96 (d, J=3.1 Hz, 1 H), 7.17 - 7.25 (m, 2 H), 6.731 - 7.39 (m, 2 H), 7.77 - 7.85 (m, 1 H), 8.51 - 8.59 (m, 1 H)	D, 0.73	327
138		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 1.78 (quin, J=6.6 Hz, 2 H), 3.20 (s, 3 H), 3.28 - 3.32 (m, 2 H), 3.37 - 3.44 (m, 2 H), 5.25 (s, 2 H), 5.47 (s, 2 H), 5.96 (d, J=2.9 Hz, 1 H), 7.01 (t, J=5.2 Hz, 1 H), 7.16 (d, J=7.9 Hz, 1 H), 7.32 - 7.39 (m, 2 H), 7.81 (td, J=7.7, 1.8 Hz,	D, 0.63	313

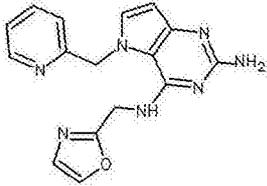
[0188]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		1 H), 8.53 - 8.56 (m, 1 H)		
139		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 1.47 - 1.58 (m, 1 H), 1.72 - 1.88 (m, 3 H), 3.39 - 3.54 (m, 2 H), 3.58 - 3.66 (m, 1 H), 3.70 - 3.78 (m, 1 H), 4.00 (quin, 6 J=6.2 Hz, 1 H), 5.26 (s, 2 H), 5.38 - 5.50 (m, 2 H), 5.96 (d, J=2.9 Hz, 1 H), 7.24 (d, J=7.7 Hz, 1 H), 7.30 (t, J=5.4 Hz, 1 H), 7.35 (ddd, J=7.6, 5.0, 1.1 Hz, 1 H), 7.39 (d, J=3.1 Hz, 1 H), 7.82 (td, J=7.7, 1.8 Hz, 1 H), 8.55 (ddd, J=4.8, 1.5, 0.9 Hz, 1 H)	D, 0.65	325

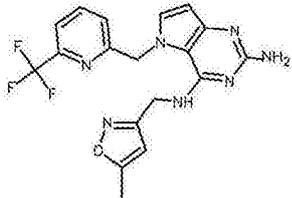
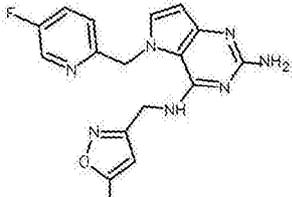
[0189]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
140		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 1.08 (t, J=7.0 Hz, 3 H), 3.43 (q, J=7.0 Hz, 2 H), 3.48 - 3.59 (m, 4 H), 5.27 (s, 2 H), 5.44 (s, 2 H), 5.96 (d, J=3.1 Hz, 1.6 H), 7.23 - 7.31 (m, 2 H), 7.35 (ddd, J=7.6, 5.0, 1.1 Hz, 1 H), 7.38 (d, J=3.1 Hz, 1 H), 7.81 (td, J=7.7, 1.8 Hz, 1 H), 8.53 - 8.57 (m, 1 H)	D, 0.66	313
141		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 0.87 (t, J=7.4 Hz, 3 H), 1.21 - 1.33 (m, 1 H), 1.33 - 1.45 (m, 1 H), 3.26 - 3.33 (m, 1 H), 3.45 (dt, J=13.1, 5.4 Hz, 1 H), 3.50 - 3.60 (m, 1 H), 4.81 (br.	D, 0.58	313

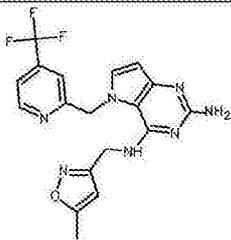
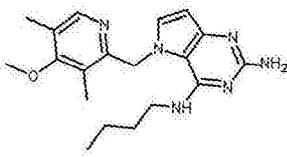
[0190]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		s., 1 H), 5.27 (s, 2 H), 5.47 (s, 2 H), 5.96 (d, J=3.1 Hz, 1 H), 7.17 - 7.26 (m, 2 H), 7.34 (ddd, J=7.7, 4.8, 1.1 Hz, 1 H), 7.38 (d, J=3.1 Hz, 1 H), 7.81 (td, J=7.7, 1.8 Hz, 1 H), 8.52 - 8.56 (m, 1 H)		
142		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 4.79 (d, J=5.7 Hz, 2 H), 5.31 (s, 2 H), 5.47 (s, 2 H), 5.99 (d, J=2.9 Hz, 1 H), 7.14 (d, J=0.7 Hz, 1 H), 7.28 - 7.36 (m, 2 6 H), 7.42 (d, J=2.9 Hz, 1 H), 7.81 (td, J=7.7, 1.8 Hz, 1 H), 7.99 (d, J=0.9 Hz, 1 H), 8.06 (t, J=5.6 Hz, 1 H), 8.40 - 8.45 (m, 1 H)	D, 0.57	322

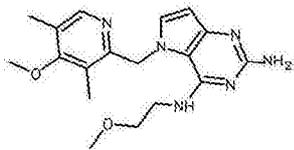
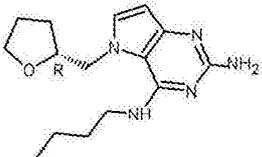
[0191]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
143		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.23 - 2.32 (m, 3 H) 4.53 (d, J=5.94 Hz, 2 H) 5.40 (s, 2 H) 5.67 - 5.71 (m, 3 H) 6.07 (d, J=3.08 Hz, 1 H) 6.90 (d, J=7.92 Hz, 1 H) 6.96 (t, J=5.83 Hz, 1 H) 7.41 (d, J=3.08 Hz, 1 H) 7.81 (d, J=7.70 Hz, 1 H) 8.01 (t, J=7.92 Hz, 1 H)	E, 1.43	404
144		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.31 - 2.35 (m, 3 H) 4.59 (d, J=5.72 Hz, 2 H) 5.36 (s, 2 H) 5.52 (s, 2 H) 5.89 (d, J=0.88 Hz, 1 H) 6.00 (d, J=3.08 Hz, 1 H) 7.11 (dd, J=8.69, 4.51 Hz, 1 H) 7.28 (t, J=5.83 Hz, 1 H) 7.39 (d,	E, 1.49	354

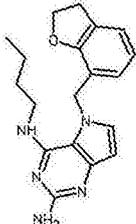
[0192]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		J=3.08 Hz, 1 H) 7.70 (td, J=8.80, 2.86 Hz, 1 H) 8.42 (d, J=2.86 Hz, 1 H)		
145		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.31 (d, J=0.66 Hz, 3 H) 4.59 (d, J=5.72 Hz, 2 H) 5.38 (s, 2 H) 5.64 (s, 2 H) 5.84 (d, J=0.66 Hz, 1 H) 6.02 (d, J=3.08 Hz, 1 H) 7.29 (t, J=5.72 Hz, 1 H) 7.42 - 7.45 (m, 2 H) 7.69 - 7.72 (m, 1 H) 8.71 (d, J=5.06 Hz, 1 H)	D, 0.79	404
146		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 0.93 (t, J=7.3 Hz, 3 H), 1.37 (dq, J=15.0, 7.3 Hz, 2 H), 1.56 - 1.66 (m, 2 H), 2.21 (s, 3 H), 2.33 (s, 3 H), 3.36 - 3.42 (m, 6 3 H),	E, 1.83	355

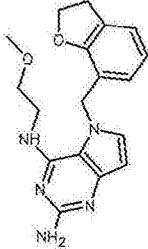
[0193]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		3.72 (s, 3 H), 5.21 (s, 2 H), 5.44 (s, 2 H), 5.92 (d, J=3.1 Hz, 1 H), 7.30 (d, J=3.1 Hz, 1 H), 7.85 (t, J=5.1 Hz, 1 H), 8.21 (s, 1 H) SLAST_1354_1.1. esp M07(s)		
147		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.21 (s, 3 H), 2.34 (s, 3 H), 3.28 (s, 3 H), 3.50 - 3.60 (m, 4 H), 3.72 (s, 3 H), 5.25 (s, 2 H), 5.42 (s, 2 H), 5.92 (d, J=3.1 6 Hz, 1 H), 7.31 (d, J=2.9 Hz, 1 H), 8.14 (t, J=4.7 Hz, 1 H), 8.22 (s, 1 H) SLAST_1354_2.1. esp M04(m)	E, 1.45	357
148		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 0.93 (t, J=7.4 Hz, 3 H), 1.38 (dq,	D, 0.81	290

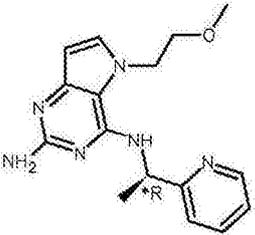
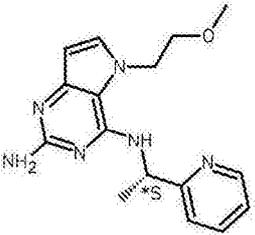
[0194]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		J=14.9, 7.4 Hz, 2 H), 1.47 - 1.67 (m, 4 H), 1.69 - 1.84 (m, 1 H), 1.85 - 1.99 (m, 1 H), 6 3.34 - 3.42 (m, 2 H), 3.56 - 3.74 (m, 2 H), 4.01 - 4.11 (m, 1 H), 4.17 (dd, J=15.2, 6.2 Hz, 1 H), 4.37 (dd, J=15.2, 2.9 Hz, 1 H), 5.26 (s, 2 H), 5.91 (d, J=3.1 Hz, 1 H), 6.51 (t, J=5.2 Hz, 1 H), 7.14 (d, J=2.9 Hz, 1 H)		
149		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 0.83 (t, J=7.4 Hz, 3 H), 1.17 (dq, J=14.9, 7.4 Hz, 2 H), 1.42 (quin, J=7.3 Hz, 2 H), 3.21 (t, J=8.7 Hz, 2 H), 3.29 - 3.35 6 (m, 2 H), 4.60 (t, J=8.7 Hz, 2 H),	E, 1.72	338

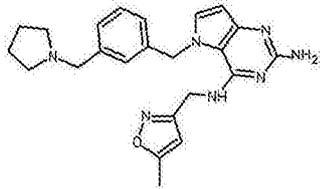
[0195]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		5.23 (s, 2 H), 5.34 (s, 2 H), 5.71 (t, J=5.3 Hz, 1 H), 5.95 (d, J=2.9 Hz, 1 H), 6.46 (d, J=7.7 Hz, 1 H), 6.72 (t, J=7.6 Hz, 1 H), 7.14 (d, J=6.6 Hz, 1 H), 7.23 (d, J=3.1 Hz, 1 H)		
150		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 3.16 - 3.24 (m, 5 H), 3.40 (t, J=5.8 Hz, 2 H), 3.52 (q, J=5.6 Hz, 2 H), 4.60 (t, J=8.7 Hz, 2 H), 5.28 (s, 2 H), 5.31 (s, 2 H), 5.92 (t, J=5.5 Hz, 1 H), 5.95 (d, J=2.9 Hz, 1 H), 6.58 (d, J=7.5 Hz, 1 H), 6.73 (t, J=7.5 Hz, 1 H), 7.14 (d, J=6.6 Hz, 1 H), 7.22 (d, J=2.9 Hz, 1 H)	E, 1.4	340

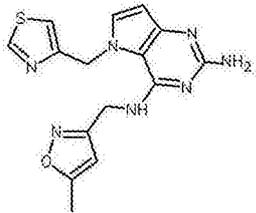
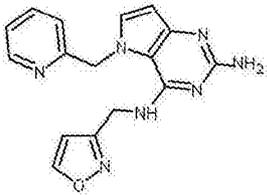
[0196]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
151		<sup>1</sup> H NMR (400 MHz, 氯仿- <i>d</i> ) δ ppm 1.58 (d, J=6.8 Hz, 3 H), 3.29 (s, 3 H), 3.70 - 3.79 (m, 2 H), 4.32 - 4.41 (m, 2 H), 4.50 (br. s., 2 H), 5.49 (t, J=6.8 Hz, 1 H), 6.17 (d, J=3.1 Hz, 1 H), 6.91 (d, J=3.1 Hz, 1 H), 7.14 (ddd, J=7.5, 4.8, 1.1 Hz, 2 H), 7.33 (d, J=7.7 Hz, 1 H), 7.61 (td, J=7.6, 1.8 Hz, 1 H), 8.50 - 8.60 (m, 1 H)	E, 1.2	313
152		<sup>1</sup> H NMR (400 MHz, 氯仿- <i>d</i> ) δ ppm 1.59 (d, J=6.8 Hz, 3 H), 3.31 (s, 3 H), 3.71 - 3.82 (m, 2 H), 4.39 (d, J=5.1 Hz, 2 H), 4.42 (br. s., 2 H), 5.50 (t, J=6.7 Hz, 1 H), 6.18 (d, J=2.9 Hz,	E, 1.44	313

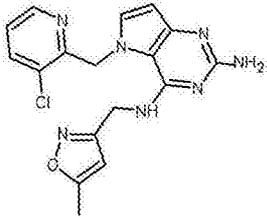
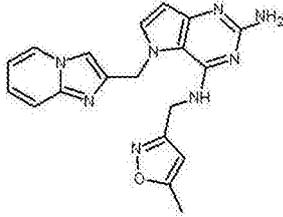
[0197]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		1 H), 6.93 (d, J=3.1 Hz, 1 H), 7.10 - 7.20 (m, 2 H), 7.35 (d, J=7.9 Hz, 1 H), 7.63 (td, J=7.6, 1.8 Hz, 1 H), 8.53 - 8.60 (m, 1 H)		
153		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 1.63 (dt, J=6.66, 3.16 Hz, 4 H) 2.27 (s, 3 H) 2.28 - 2.34 (m, 4 H) 3.44 (s, 2 H) 4.54 (d, J=5.72 Hz, 2 H) 5.32 (s, 2 H) 5.48 (s, 2 H) 5.56 (d, J=0.88 Hz, 1 H) 6.01 (d, J=2.86 Hz, 1 H) 6.61 (t, J=5.94 Hz, 1 H) 6.76 (d, J=7.26 Hz, 1 H) 6.98 (s, 1 H) 7.12 - 7.20 (m, 2 H) 7.35 (d, J=2.86 Hz, 1 H)	E, 1.07	418

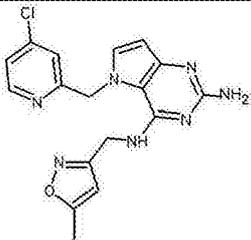
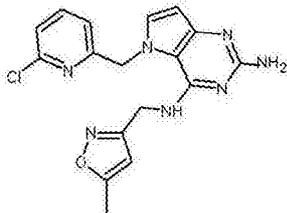
[0198]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
154		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.34 (s, 3 H) 4.62 (d, J=5.72 Hz, 2 H) 5.34 (s, 2 H) 5.55 (s, 2 H) 5.97 (d, J=3.08 Hz, 1 H) 6.02 (s, 1 H) 7.28 (t, J=5.83 Hz, 1 H) 7.32 (d, J=2.86 Hz, 1 H) 7.40 (d, J=1.98 Hz, 1 H) 9.04 (d, J=1.98 Hz, 1 H)	E, 1.14	342
155		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 4.70 (d, J=5.72 Hz, 2 H) 5.37 (s, 2 H) 5.48 (s, 2 H) 5.98 (d, J=3.08 Hz, 1 H) 6.38 (d, J=1.76 Hz, 1 H) 7.20 (d, J=7.70 Hz, 1 H) 7.32 (ddd, J=7.54, 5.01, 1.10 Hz, 1 H) 7.41 (d, J=3.08 Hz, 1 H) 7.79 (td,	E, 1.34	322

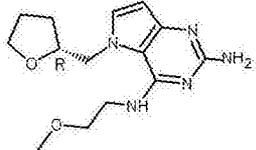
[0199]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		J=7.70, 1.76 Hz, 1 H) 7.87 (t, J=5.61 Hz, 1 H) 8.39 - 8.42 (m, 1 H) 8.77 (d, J=1.76 Hz, 1 H)		
156		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.34 (d, J=0.66 Hz, 3 H) 4.62 (d, J=5.50 Hz, 2 H) 5.36 (s, 2 H) 5.62 (s, 2 H) 5.97 (d, J=3.08 Hz, 1 H) 6.03 (d, J=0.66 Hz, 1 H) 7.29 (d, J=3.08 Hz, 1 H) 7.42 (dd, J=8.14, 4.84 Hz, 1 H) 7.68 (t, J=5.72 Hz, 1 H) 8.00 (dd, J=8.14, 1.54 Hz, 1 H) 8.32 (dd, J=4.73, 1.43 Hz, 1 H)	D, 0.74	370
157		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.27 (s, 3 H) 4.68 (d, J=5.72 Hz, 2 H) 5.33 (s, 2 H)	D, 0.65	375

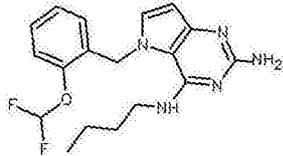
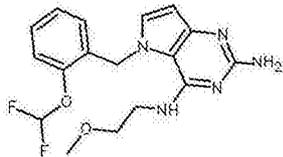
[0200]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		5.48 (s, 2 H) 5.94 (d, J=2.86 Hz, 1 H) 6.01 (s, 1 H) 6.89 (td, J=6.77, 1.21 Hz, 1 H) 7.26 (ddd, J=9.08, 6.66, 1.21 Hz, 1 H) 7.35 - 7.38 (m, 2 H) 7.79 (s, 1 H) 8.30 (t, J=5.72 Hz, 1 H) 8.51 (dt, J=6.82, 1.10 Hz, 1 H)		
158		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.33 (s, 3 H) 4.60 (d, J=5.72 Hz, 2 H) 5.38 (s, 2 H) 5.52 (s, 2 H) 5.89 (s, 1 H) 6.01 (d, J=3.08 Hz, 1 H) 7.18 - 7.22 (m, 1 H) 7.39 - 7.50 (m, 3 H) 8.41 (d, J=5.50 Hz, 1 H)	E, 1.35	370
159		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.31 (s, 3 H) 4.56 (d, J=5.72 Hz,	D, 0.73	370

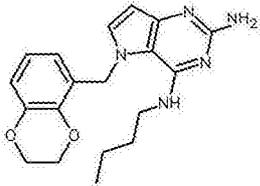
[0201]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		2 H) 5.39 (s, 2 H) 5.56 (s, 2 H) 5.75 (s, 1 H) 6.05 (d, J=3.08 Hz, 1 H) 6.68 (d, J=7.48 Hz, 1 H) 6.99 (t, J=5.83 Hz, 1 H) 7.38 (d, J=2.86 Hz, 1 H) 7.41 (d, J=7.92 Hz, 1 H) 7.78 (t, J=7.81 Hz, 1 H)		
160		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 1.46 - 1.70 (m, 2 H), 1.70 - 1.83 (m, 1 H), 1.87 - 1.99 (m, 1 H), 3.29 (s, 3 H), 3.48 - 3.56 (m, 3 H), 3.56 - 3.65 (m, 2 H), 6 3.68 - 3.77 (m, 1 H), 4.05 (qd, J=6.7, 2.8 Hz, 1 H), 4.14 (dd, J=15.1, 6.5 Hz, 1 H), 4.35 (dd, J=15.1, 2.8 Hz, 1 H), 5.23 (s, 2 H), 5.92 (d, J=2.9 Hz,	D, 0.58	292

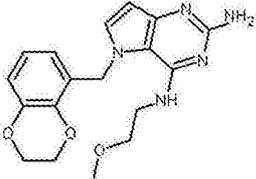
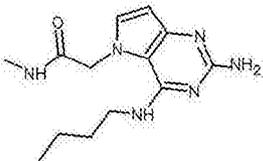
[0202]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		1 H), 6.61 (t, J=4.8 Hz, 1 H), 7.15 (d, J=3.1 Hz, 1 H)		
161		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 0.76 (t, J=7.3 Hz, 3 H), 1.05 (dq, J=15.0, 7.3 Hz, 2 H), 1.30 - 1.40 (m, 2 H), 3.24 - 3.30 (m, 2 H), 5.26 (s, 2 H), 5.51 (s, 6 2 H), 5.70 (t, J=5.5 Hz, 1 H), 6.00 (d, J=2.9 Hz, 1 H), 6.36 - 6.41 (m, 1 H), 7.06 - 7.12 (m, 1 H), 7.20 - 7.25 (m, 2 H), 7.29 (t, J=73.8 Hz, 1 H), 7.30 - 7.36 (m, 1 H)	D, 0.94	362
162		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 3.13 (s, 3 H), 3.32 - 3.35 (m, 2 H), 3.46 (q, J=5.6 Hz, 2 H), 5.32 (s, 2 H), 5.48 (s, 2 H),	D, 0.78	364

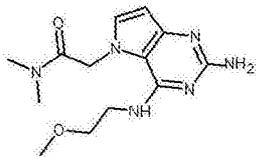
[0203]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		5.80 (t, J=5.4 Hz, 1 H), 6.01 (d, 6 J=3.1 Hz, 1 H), 6.51 (dd, J=7.7, 1.3 Hz, 1 H), 7.08 - 7.14 (m, 1 H), 7.20 - 7.25 (m, 2 H), 7.28 (t, J=73.8 Hz, 1 H), 7.31 - 7.36 (m, 1 H)		
163		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 0.80 (t, J=7.3 Hz, 3 H), 1.12 (dq, J=15.0, 7.4 Hz, 2 H), 1.34 - 1.44 (m, 2 H), 3.26 - 3.31 (m, 2 H), 4.23 - 4.30 (m, 2 H), 6.430 - 4.37 (m, 2 H), 5.24 (s, 2 H), 5.38 (s, 2 H), 5.59 (t, J=5.4 Hz, 1 H), 5.96 (d, J=3.1 Hz, 1 H), 6.02 (dd, J=7.6, 1.4 Hz, 1 H), 6.68 (t, J=7.8 Hz, 1 H), 6.77 (dd,	D, 0.9	354

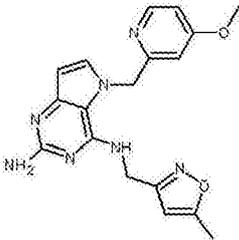
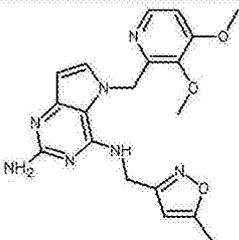
[0204]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		J=8.1, 1.5 Hz, 1 H), 7.20 (d, J=2.9 Hz, 1 H)		
164		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 3.16 (s, 3 H), 3.35 - 3.40 (m, 2 H), 3.51 (q, J=5.6 Hz, 2 H), 4.24 - 4.31 (m, 2 H), 4.31 - 4.37 (m, 2 H), 5.35 (s, 2 H), 6.537 (br. s., 2 H), 5.78 (t, J=5.4 Hz, 1 H), 5.97 (d, J=3.1 Hz, 1 H), 6.16 (dd, J=7.7, 1.5 Hz, 1 H), 6.70 (t, J=7.8 Hz, 1 H), 6.76 - 6.81 (m, 1 H), 7.22 (d, J=2.9 Hz, 1 H)	D, 0.74	356
165		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 3.16 (s, 3 H), 3.35 - 3.40 (m, 2 H), 3.51 (q, J=5.6 Hz, 2 H), 4.24 - 4.31 (m, 2 H), 4.31	D, 0.6	277

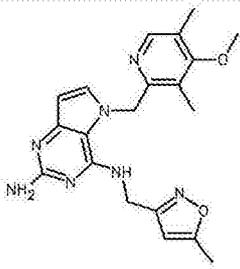
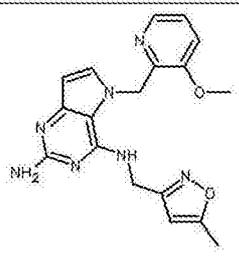
[0205]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		- 4.37 (m, 2 H), 5.35 (s, 2 H), 6 5.37 (br. s., 2 H), 5.78 (t, J=5.4 Hz, 1 H), 5.97 (d, J=3.1 Hz, 1 H), 6.16 (dd, J=7.7, 1.5 Hz, 1 H), 6.70 (t, J=7.8 Hz, 1 H), 6.76 - 6.81 (m, 1 H), 7.22 (d, J=2.9 Hz, 1 H)		
166		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 0.92 (t, J=7.4 Hz, 3 H), 1.37 (dq, J=15.0, 7.3 Hz, 2 H), 1.51 - 1.62 (m, 2 H), 2.63 (d, J=4.6 Hz, 3 H), 3.33 - 3.41 (m, 2 6 H), 4.74 (s, 2 H), 5.40 (br. s., 2 H), 5.94 (d, J=2.9 Hz, 1 H), 6.93 (t, J=5.2 Hz, 1 H), 7.11 (d, J=3.1 Hz, 1 H), 8.31 (d, J=4.4 Hz, 1 H)	D, 0.42	293

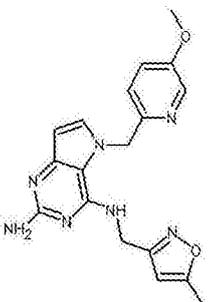
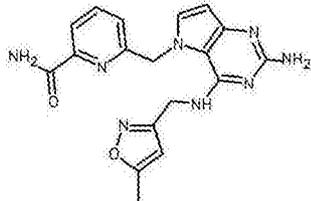
[0206]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
167		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.34 (s, 3 H) 3.78 (s, 3 H) 4.63 (d, J=5.50 Hz, 2 H) 5.33 - 5.39 (m, 4 H) 5.97 (d, J=3.08 Hz, 1 H) 6.02 (s, 1 H) 6.90 (d, J=2.42 Hz, 1 H) 6.93 (dd, J=5.72, 2.42 Hz, 1 H) 7.41 (d, J=3.08 Hz, 1 H) 8.16 (t, J=5.61 Hz, 1 H) 8.22 (d, J=5.94 Hz, 1 H)	D, 0.7	366
168		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.36 (s, 3 H) 3.79 (s, 3 H) 3.88 (s, 3 H) 4.66 (d, J=5.50 Hz, 2 H) 5.33 (s, 2 H) 5.36 (s, 2 H) 5.94 (d, J=2.86 Hz, 1 H) 6.18 (s, 1 H) 7.14 (d, J=5.72 Hz, 1 H) 7.23 (d, J=3.08 Hz,	E, 1.62	396

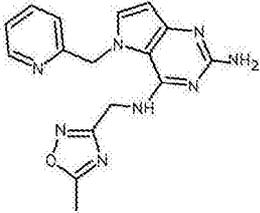
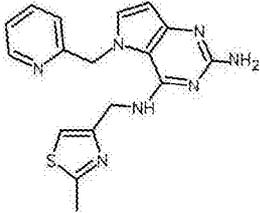
[0207]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		1 H) 8.00 (d, J=5.50 Hz, 1 H) 8.50 (t, J=5.50 Hz, 1 H)		
169		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.17 (s, 3 H) 2.31 (s, 3 H) 2.35 (s, 3 H) 3.71 (s, 3 H) 4.63 (d, J=5.50 Hz, 2 H) 5.32 (s, 2 H) 5.44 (s, 2 H) 5.94 (d, J=3.08 Hz, 1 H) 6.10 (s, 1 H) 7.33 (d, J=2.86 Hz, 1 H) 8.01 (s, 1 H) 8.49 (t, J=5.50 Hz, 1 H)	E, 1.76	394
170		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.35 (s, 3 H) 3.88 (s, 3 H) 4.66 (d, J=5.50 Hz, 2 H) 5.33 (s, 2 H) 5.40 (s, 2 H) 5.93 (d, J=2.86 Hz, 1 H) 6.13 (s, 1 H) 7.23 (d, J=3.08 Hz, 1 H)	E, 1.59	366

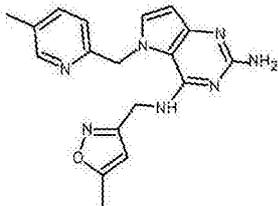
[0208]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		7.38 (dd, J=8.36, 4.62 Hz, 1 H) 7.52 (d, J=7.92 Hz, 1 H) 7.92 (dd, J=4.62, 1.10 Hz, 1 H) 8.19 (t, J=5.50 Hz, 1 H)		
171		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.33 (s, 3 H) 3.79 (s, 3 H) 4.63 (d, J=5.50 Hz, 2 H) 5.34 (s, 2 H) 5.40 (s, 2 H) 5.96 (d, J=2.86 Hz, 1 H) 5.98 (d, J=0.88 Hz, 1 H) 7.20 (d, J=8.58 Hz, 1 H) 7.37 - 7.41 (m, 2 H) 7.79 (t, J=5.72 Hz, 1 H) 8.09 (d, J=2.64 Hz, 1 H)	E, 1.53	366
172		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.27 (s, 3 H) 4.56 (d, J=5.72 Hz, 2 H) 5.35 (s, 2 H) 5.59 - 5.64 (m, 3 H) 6.04 (d, J=3.08	E, 1.1	379

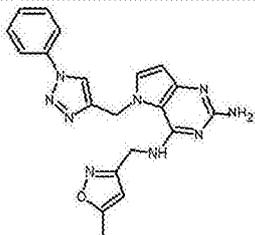
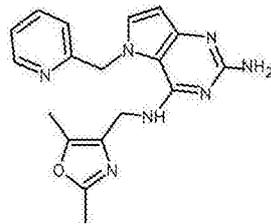
[0209]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		Hz, 1 H) 6.84 (t, J=5.83 Hz, 1 H) 7.03 (dd, J=6.05, 2.75 Hz, 1 H) 7.45 (d, J=2.86 Hz, 1 H) 7.65 (br. s., 1 H) 7.80 (br. s., 1 H) 7.86 - 7.92 (m, 2 H)		
173		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.55 (s, 3 H) 4.76 (d, J=5.50 Hz, 2 H) 5.30 (s, 2 H) 5.46 (s, 2 H) 5.98 (d, J=2.86 Hz, 1 H) 7.31 - 7.36 (m, 2 H) 7.42 (d, J=3.08 Hz, 1 H) 7.81 (td, J=7.70, 1.76 Hz, 1 H) 8.06 (t, J=5.61 Hz, 1 H) 8.44 - 8.47 (m, 1 H)	E, 1.34	337
174		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.63 (s, 3 H) 4.67 (d, J=5.28 Hz, 2 H) 5.32 (s, 2 H)	D, 0.66	352

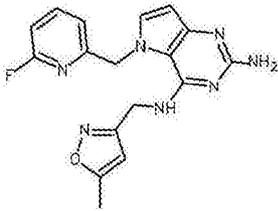
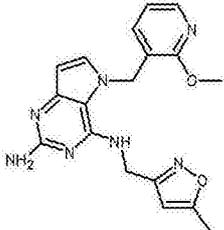
[0210]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		5.49 (s, 2 H) 5.98 (d, J=2.86 Hz, 1 H) 7.02 (s, 1 H) 7.23 (d, J=7.70 Hz, 1 H) 7.33 (dd, J=6.93, 5.17 Hz, 1 H) 7.40 (d, J=3.08 Hz, 1 H) 7.75 - 7.83 (m, 2 H) 8.43 (d, J=4.40 Hz, 1 H)		
175		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.25 (s, 3 H) 2.34 (s, 3 H) 4.62 (d, J=5.50 Hz, 2 H) 5.34 (s, 2 H) 5.42 (s, 2 H) 5.96 - 5.99 (m, 2 H) 7.12 (d, J=7.92 Hz, 1 H) 7.39 (d, J=2.86 Hz, 1 H) 7.60 (dd, J=8.03, 2.09 Hz, 1 H) 7.84 (t, J=5.61 Hz, 1 H) 8.22 - 8.25 (m, 1 H)	D, 0.72	350

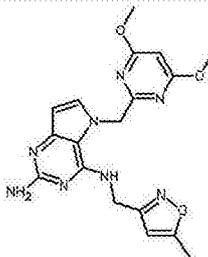
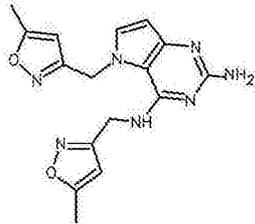
[0211]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
176		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.22 (s, 3 H) 4.67 (d, J=5.72 Hz, 2 H) 5.35 (s, 2 H) 5.63 (s, 2 H) 5.98 (d, J=3.08 Hz, 1 H) 6.07 - 6.09 (m, 1 H) 7.07 (t, J=5.83 Hz, 1 H) 7.34 (d, J=3.08 Hz, 1 H) 7.46 - 7.51 (m, 1 H) 7.55 - 7.61 (m, 2 H) 7.79 - 7.84 (m, 2 H) 8.57 (s, 1 H)	E, 1.35	402
177		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.25 (s, 3 H) 2.32 (s, 3 H) 4.37 (d, J=5.06 Hz, 2 H) 5.26 (s, 2 H) 5.40 (s, 2 H) 5.95 (d, J=3.08 Hz, 1 H) 7.31 - 7.37 (m, 2 H) 7.39 (d, J=3.08 Hz, 1 H) 7.77 - 7.82 (m, 2 H) 8.45	E, 1.23	350

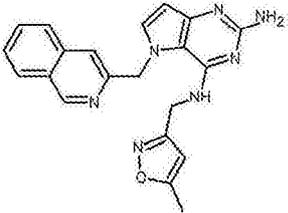
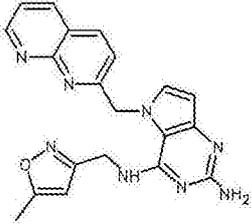
[0212]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		- 8.48 (m, 1 H)		
178		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.30 (s, 3 H) 4.56 (d, J=5.72 Hz, 2 H) 5.38 (s, 2 H) 5.54 (s, 2 H) 5.75 - 5.80 (m, 1 H) 6.04 (d, J=2.86 Hz, 1 H) 6.66 (dd, J=7.37, 2.31 Hz, 1 H) 6.87 (t, J=5.83 Hz, 1 H) 7.06 (dd, J=8.14, 2.20 Hz, 1 H) 7.36 (d, J=2.86 Hz, 1 H) 7.85 - 7.92 (m, 1 H)	F, 4	354
179		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.30 (s, 3 H) 3.90 (s, 3 H) 4.53 (d, J=5.72 Hz, 2 H) 5.38 (s, 2 H) 5.42 (s, 2 H) 5.72 (s, 1 H) 6.03 (d, J=3.08 Hz, 1 H) 6.60 - 6.65 (m, 2 H) 6.84 (dd, J=7.26, 5.06	E, 1.27	366

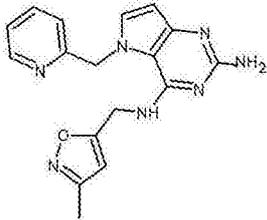
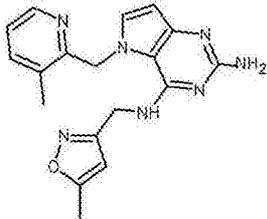
[0213]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		Hz, 1 H) 7.27 (d, J=2.86 Hz, 1 H) 8.05 (dd, J=4.95, 1.65 Hz, 1 H)		
180		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.31 (s, 3 H) 3.69 (s, 6 H) 4.58 (d, J=5.50 Hz, 2 H) 5.33 (s, 2 H) 5.43 (s, 2 H) 5.92 (s, 1 H) 5.99 (d, J=2.64 Hz, 1 H) 6.11 (s, 1 H) 6.80 (t, J=5.61 Hz, 1 H) 7.27 (d, J=2.64 Hz, 1 H)	E, 1.34	397
181		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.30 (s, 3 H) 2.34 (s, 3 H) 4.61 (d, J=5.72 Hz, 2 H) 5.38 (s, 2 H) 5.52 (s, 2 H) 5.83 (s, 1 H) 6.00 (d, J=3.08 Hz, 1 H) 6.04 (s, 1 H) 6.85 (t, J=5.72 Hz, 1 H) 7.29 (d, J=3.08 Hz, 1 H)	E, 1.17	340

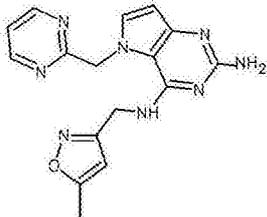
[0214]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
182		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.20 (s, 3 H) 4.63 (d, J=5.72 Hz, 2 H) 5.34 (s, 2 H) 5.64 (s, 2 H) 5.82 (s, 1 H) 6.01 (d, J=3.08 Hz, 1 H) 7.45 (d, J=3.08 Hz, 1 H) 7.58 (s, 1 H) 7.66 - 7.70 (m, 1 H) 7.75 - 7.80 (m, 2 H) 7.85 - 7.89 (m, 1 H) 8.13 (d, J=8.14 Hz, 1 H) 9.20 (s, 1 H)	E, 1.47	386
183		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.07 (s, 1 H) 2.14 (s, 3 H) 4.57 (d, J=5.72 Hz, 2 H) 5.35 (s, 1 H) 5.77 - 5.82 (m, 3 H) 6.06 (d, J=2.86 Hz, 1 H) 7.18 (d, J=8.36 Hz, 1 H) 7.51 (d, J=2.86 Hz, 1 H) 7.56 (t, J=5.72 Hz,	E, 1.03	387

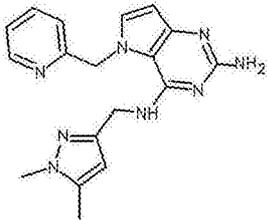
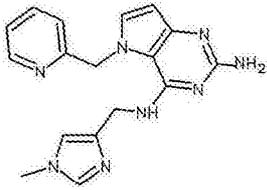
[0215]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		1 H) 7.64 (dd, J=8.14, 4.18 Hz, 1 H) 8.45 (d, J=8.36 Hz, 2 H) 9.09 (dd, J=4.07, 1.65 Hz, 1 H)		
184		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.16 (s, 3 H) 4.71 (d, J=5.50 Hz, 2 H) 5.37 (s, 2 H) 5.50 (s, 2 H) 5.95 (s, 1 H) 5.99 (d, J=2.86 Hz, 1 H) 7.18 (d, J=7.70 Hz, 1 H) 7.35 (dd, J=6.82, 5.06 Hz, 1 H) 7.42 (d, J=3.08 Hz, 1 H) 7.81 (td, J=7.65, 1.65 Hz, 1 H) 7.88 (t, J=5.50 Hz, 1 H) 8.47 (d, J=4.40 Hz, 1 H)	E, 1.11	336
185		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.34 (s, 3 H) 2.42 (s, 3 H) 4.63 (d, J=5.72 Hz, 2 H)	E, 1.35	350

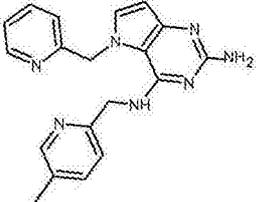
[0216]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		5.34 (s, 2 H) 5.49 (s, 2 H) 5.95 (d, J=2.86 Hz, 1 H) 6.07 (s, 1 H) 7.27 (dd, J=7.70, 4.84 Hz, 1 H) 7.32 (d, J=3.08 Hz, 1 H) 7.66 (d, J=7.48 Hz, 1 H) 8.17 (dd, J=4.73, 0.99 Hz, 1 H) 8.35 (t, J=5.61 Hz, 1 H)		
186		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.31 - 2.36 (m, 3 H) 4.58 (d, J=5.72 Hz, 2 H) 5.34 (s, 2 H) 5.62 (s, 2 H) 5.93 (d, J=0.66 Hz, 1 H) 5.97 (d, J=3.08 Hz, 1 H) 7.13 (t, J=5.61 Hz, 1 H) 7.30 (d, J=3.08 Hz, 1 H) 7.43 (t, J=4.95 Hz, 1 H) 8.72 (d, J=5.06 Hz, 2 H)	E, 0.98	337

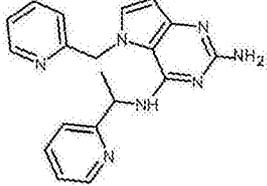
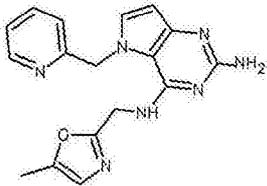
[0217]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
187		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.17 (s, 3 H) 3.65 (s, 3 H) 4.46 (d, J=5.28 Hz, 2 H) 5.29 (s, 2 H) 5.44 (s, 2 H) 5.76 (s, 1 H) 5.96 (d, J=3.08 Hz, 1 H) 7.20 (d, J=7.92 Hz, 1 H) 7.30 - 7.34 (m, 1 H) 7.38 (d, J=3.08 Hz, 1 H) 7.51 (t, J=5.28 Hz, 1 H) 7.78 (td, J=7.70, 1.76 Hz, 1 H) 8.39 (d, J=4.18 Hz, 1 H)	E, 1.16	349
188		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 3.57 (s, 3 H) 4.45 (d, J=5.06 Hz, 2 H) 5.34 (br. s., 2 H) 5.44 (s, 2 H) 5.97 (d, J=2.86 Hz, 1 H) 6.76 (s, 1 H) 7.24 (d, J=7.70 Hz, 1 H) 7.33 (dd, J=7.04, 5.28 Hz, 1 H)	E, 0.92	335

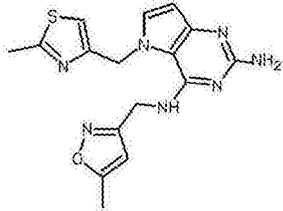
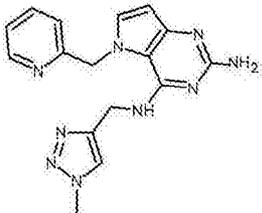
[0218]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		H) 7.39 (d, J=2.86 Hz, 1 H) 7.47 (s, 1 H) 7.64 (t, J=4.84 Hz, 1 H) 7.77 - 7.83 (m, 1 H) 8.43 (d, J=4.40 Hz, 1 H)		
189		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.25 (s, 3 H) 4.67 (d, J=5.50 Hz, 2 H) 5.26 (s, 2 H) 5.54 (s, 2 H) 5.99 (d, J=2.86 Hz, 1 H) 6.97 (d, J=7.92 Hz, 1 H) 7.13 (d, J=7.92 Hz, 1 H) 7.32 (ddd, J=6.93, 5.61, 0.88 Hz, 1 H) 7.41 (d, J=3.08 Hz, 1 H) 7.43 (dd, J=8.14, 1.98 Hz, 1 H) 7.62 (t, J=5.61 Hz, 1 H) 7.79 (td, J=7.70, 1.76 Hz, 1 H) 8.30 - 8.32 (m, 1 H) 8.43 (dd, J=4.95, 0.77 Hz, 1 H)	E, 1.27	346

[0219]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
190		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 1.52 (d, J=6.82 Hz, 3 H) 5.21 (s, 2 H) 5.43 (quin, J=6.82 Hz, 1 H) 5.48 - 5.60 (m, 2 H) 5.97 (d, J=2.86 Hz, 1 H) 7.18 - 7.25 (m, 1 H) 7.27 - 7.39 (m, 3 H) 7.44 (d, J=2.86 Hz, 1 H) 7.63 - 7.69 (m, 1 H) 7.76 (d, J=7.26 Hz, 1 H) 7.80 - 7.88 (m, 1 H) 8.46 - 8.52 (m, 2 H)	E, 1.31	346
191		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.23 (d, J=1.10 Hz, 3 H) 4.72 (d, J=5.50 Hz, 2 H) 5.31 (s, 2 H) 5.47 (s, 2 H) 5.98 (d, J=2.86 Hz, 1 H) 6.73 (d, J=1.10 Hz, 1 H) 7.28 - 7.36	E, 1.11	336

[0220]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		(m, 2 H) 7.42 (d, J=3.08 Hz, 1 H) 7.81 (td, J=7.70, 1.76 Hz, 1 H) 7.99 (t, J=5.50 Hz, 1 H) 8.40 - 8.44 (m, 1 H)		
192		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.34 (d, J=0.7 Hz, 3 H), 2.53 (s, 3 H), 4.64 (d, J=5.7 Hz, 2 H), 5.35 (s, 2 H), 5.41 (s, 2 H), 5.95 (d, J=3.1 Hz, 1 H), 6 6.08 (d, J=0.7 Hz, 1 H), 7.27 (s, 1 H), 7.31 (d, J=3.1 Hz, 1 H), 7.57 (t, J=5.7 Hz, 1 H)	D, 0.7	356
193		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 3.98 (s, 3 H) 4.62 (d, J=5.28 Hz, 2 H) 5.36 (s, 2 H) 5.44 (s, 2 H) 5.96 (d, J=2.86 Hz, 1 H)	E, 0.93	336

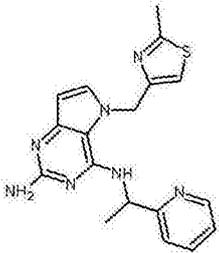
[0221]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		7.25 (d, J=7.70 Hz, 1 H) 7.31 - 7.35 (m, 1 H) 7.38 (d, J=3.08 Hz, 1 H) 7.77 - 7.83 (m, 2 H) 7.89 (t, J=5.39 Hz, 1 H) 8.41 (dd, J=4.84, 0.66 Hz, 1 H)		
194		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 1.52 (d, J=7.04 Hz, 3 H) 5.21 (s, 2 H) 5.43 (quin, J=7.04 Hz, 1 H) 5.47 - 5.58 (m, 2 H) 5.97 (d, J=2.86 Hz, 1 H) 7.19 - 7.23 (m, 1 H) 7.28 - 7.38 (m, 3 H) 7.44 (d, J=3.08 Hz, 1 H) 7.66 (td, J=7.70, 1.76 Hz, 1 H) 7.76 (d, J=7.26 Hz, 1 H) 7.84 (td, J=7.70, 1.76 Hz, 1 H) 8.47 - 8.51 (m, 2 H)。	E, 1.27	346

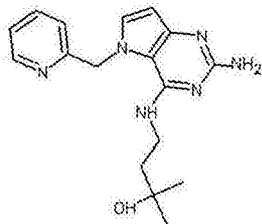
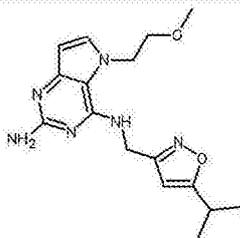
[0222]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
195		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 1.52 (d, J=6.82 Hz, 3 H) 5.21 (s, 2 H) 5.42 (quin, J=6.99 Hz, 1 H) 5.47 - 5.58 (m, 2 H) 5.97 (d, J=2.86 Hz, 1 H) 7.19 - 7.23 (m, 1 H) 7.28 - 7.38 (m, 3 H) 7.44 (d, J=3.08 Hz, 1 H) 7.66 (td, J=7.65, 1.65 Hz, 1 H) 7.77 (d, J=7.26 Hz, 1 H) 7.84 (td, J=7.59, 1.32 Hz, 1 H) 8.47 - 8.51 (m, 2 H)	E, 1.27	346
196		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.56 (s, 3 H) 3.90 (s, 3 H) 4.81 (d, J=5.72 Hz, 2 H) 5.27 (s, 2 H) 5.40 (s, 2 H) 5.93 (d, J=3.08 Hz, 1 H) 7.25 (d, J=3.08 Hz,	E, 1.24	367

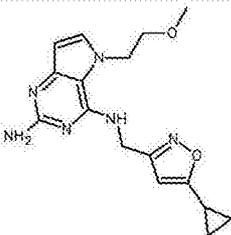
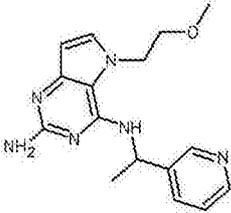
[0223]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		1 H) 7.40 (dd, J=8.36, 4.84 Hz, 1 H) 7.52 - 7.56 (m, 1 H) 7.98 (dd, J=4.84, 1.10 Hz, 1 H) 8.41 (t, J=5.50 Hz, 1 H)		
197		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 1.55 (d, J=7.0 Hz, 3 H), 2.58 (s, 3 H), 5.22 (s, 2 H), 5.41 - 5.49 (m, 1 H), 5.46 (d, J=6.8 Hz, 2 H), 5.94 (d, J=3.1 Hz, 1 H), 6.73 (d, J=3.1 Hz, 1 H), 7.23 (ddd, J=7.5, 4.8, 0.9 Hz, 1 H), 7.34 (d, J=3.1 Hz, 1 H), 7.38 (d, J=8.1 Hz, 1 H), 7.40 (s, 1 H), 7.47 (d, J=7.5 Hz, 1 H), 7.69 (td, J=7.7, 1.8 Hz, 1 H), 8.47 - 8.54 (m, 1 H)	E, 1.37	366

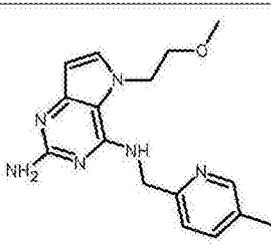
[0224]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
198		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 1.15 (s, 6 H) 1.69 - 1.74 (m, 2 H) 3.57 - 3.64 (m, 2 H) 5.62 (s, 2 H) 6.22 (d, J=2.86 Hz, 1 H) 7.34 - 7.48 (m, 4 H) 7.67 (d, J=3.08 Hz, 1 H) 7.91 (td, J=7.70, 1.76 Hz, 1 H) 8.56 - 8.59 (m, 1 H) 8.79 (t, J=4.80 Hz, 1 H) 12.51 (br. s., 1 H)	E, 1.09	327
199		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 1.21 (d, J=7.04 Hz, 6 H) 2.97 - 3.10 (m, 1 H) 3.14 - 3.18 (m, 3 H) 3.56 (t, J=4.95 Hz, 2 H) 4.37 (t, J=5.06 Hz, 2 H) 4.65 (d, J=5.72 Hz, 2 H) 5.37 (s, 2 H) 5.93 (d, J=3.08 Hz, 2 H)	D, 0.74	331

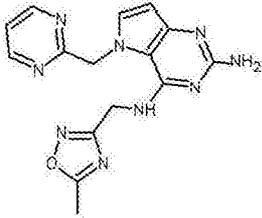
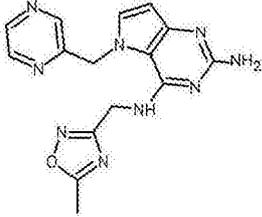
[0225]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		1 H) 6.18 (s, 1 H) 6.86 (t, J=5.61 Hz, 1 H) 7.17 (d, J=3.08 Hz, 1 H)		
200		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 0.78 - 0.90 (m, 2 H) 0.94 - 1.06 (m, 2 H) 2.03 - 2.17 (m, 1 H) 3.11 - 3.18 (m, 3 H) 3.55 (t, J=5.06 Hz, 2 H) 4.36 (t, J=5.06 Hz, 2 H) 4.61 (d, J=5.72 Hz, 2 H) 5.36 (s, 2 H) 5.92 (d, J=3.08 Hz, 1 H) 6.15 (s, 1 H) 6.84 (t, J=5.72 Hz, 1 H) 7.17 (d, J=3.08 Hz, 1 H)	D, 0.69	329
201		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 1.54 (d, J=7.04 Hz, 3 H) 3.20 (s, 3 H) 3.63 (dt, J=5.94, 3.19 Hz, 2 H) 4.32 -	D, 0.6	313

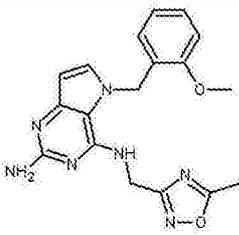
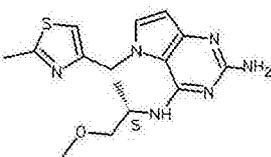
[0226]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		4.50 (m, 2 H) 5.23 (s, 2 H) 5.42 (t, J=7.04 Hz, 1 H) 5.92 (d, J=2.86 Hz, 1 H) 6.68 (d, J=7.04 Hz, 1 H) 7.18 (d, J=3.08 Hz, 1 H) 7.34 (ddd, J=7.87, 4.68, 0.66 Hz, 1 H) 7.84 (dt, J=7.92, 1.76 Hz, 1 H) 8.42 (dd, J=4.62, 1.54 Hz, 1 H) 8.68 (d, J=2.20 Hz, 1 H)		
202		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.27 (s, 3 H) 3.17 - 3.19 (m, 3 H) 3.61 (t, J=5.06 Hz, 2 H) 4.40 (t, J=5.06 Hz, 2 H) 4.70 (d, J=5.50 Hz, 2 H) 5.23 (s, 2 H) 5.92 (d, J=3.08 Hz, 1 H) 6.96 (t, J=5.61 Hz, 1 H) 7.17 (d, J=2.86 Hz, 1 H)	D, 0.64	313

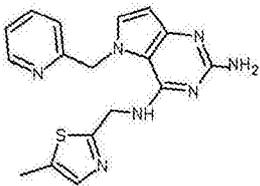
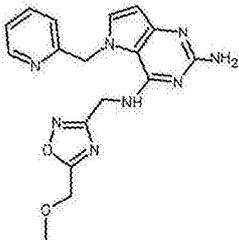
[0227]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		7.27 (d, J=7.92 Hz, 1 H) 7.55 (dd, J=8.03, 1.65 Hz, 1 H) 8.26 - 8.42 (m, 1 H)		
203		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.54 (s, 3 H) 4.72 (d, J=5.72 Hz, 2 H) 5.30 (s, 2 H) 5.59 (s, 2 H) 5.98 (d, J=3.08 Hz, 1 H) 7.30 - 7.35 (m, 2 H) 7.45 (t, J=4.95 Hz, 1 H) 8.75 (d, J=4.84 Hz, 2 H)	D, 0.48	338
204		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.54 (s, 3 H) 4.71 (d, J=5.72 Hz, 2 H) 5.33 (s, 2 H) 5.63 (s, 2 H) 6.02 (d, J=3.08 Hz, 1 H) 7.22 - 7.30 (m, 1 H) 7.41 (d, J=3.08 Hz, 1 H) 8.43 (s, 1 H) 8.52 (dd, J=2.42, 1.54 Hz, 1 H)	E, 0.92	338

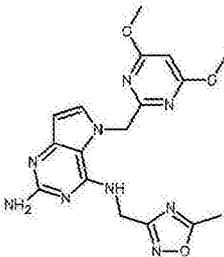
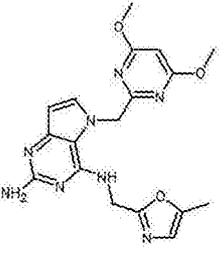
[0228]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		H) 8.56 (d, J=2.42 Hz, 1 H)		
205		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.57 (s, 3 H) 3.80 (s, 3 H) 4.85 (d, J=5.72 Hz, 2 H) 5.56 (s, 2 H) 6.24 (d, J=2.86 Hz, 1 H) 6.84 - 6.90 (m, 2 H) 7.03 (d, J=8.14 Hz, 1 H) 7.28 - 7.34 (m, 1 H) 7.40 (d, J=2.86 Hz, 1 H) 7.49 (br. s., 2 H) 8.22 - 8.28 (m, 1 H) 12.89 (br. s., 1 H)	E, 1.31	366
206		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 1.21 (d, J=6.6 Hz, 3 H), 2.65 (s, 3 H), 3.27 (s, 3 H), 3.32 - 3.35 (m, 1 H), 3.47 (dd, J=9.2, 5.1 Hz, 1 H), 4.35 - 4.55 (m, 6 1 H), 5.25 (s, 2 H), 5.36	E, 1.33	333

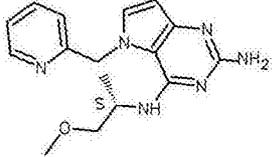
[0229]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		(d, J=4.8 Hz, 2 H), 5.92 (d, J=3.1 Hz, 1 H), 6.76 (d, J=7.5 Hz, 1 H), 7.30 (d, J=3.1 Hz, 1 H), 7.40 (s, 1 H)		
207		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.37 (s, 3 H) 4.97 (d, J=5.06 Hz, 2 H) 5.81 (s, 2 H) 6.31 (d, J=2.86 Hz, 1 H) 7.37 (d, J=7.70 Hz, 1 H) 7.43 (s, 1 H) 7.47 - 7.52 (m, 1 H) 7.57 (br. s., 1 H) 7.75 (d, J=3.08 Hz, 1 H) 7.97 (t, J=7.70 Hz, 1 H) 8.53 (d, J=4.62 Hz, 1 H) 9.50 (br. s., 1 H) 12.88 (br. s., 1 H)	E, 1.21	352
208		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 3.37 (s, 3 H) 4.72 (s, 2 H) 4.82 (d, J=5.72 Hz, 2 H)	E, 1.15	367

[0230]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		5.29 (s, 2 H) 5.46 (s, 2 H) 5.96 - 6.00 (m, 1 H) 7.29 - 7.37 (m, 2 H) 7.42 (d, J=3.08 Hz, 1 H) 7.81 (td, J=8.00, 1.50 Hz, 1 H) 8.12 (t, J=6.16 Hz, 1 H) 8.45 - 8.50 (m, 1 H)		
209		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.49 (s, 3 H) 3.71 (s, 6 H) 4.70 (d, J=5.72 Hz, 2 H) 5.27 (s, 2 H) 5.41 (s, 2 H) 5.98 (d, J=2.86 Hz, 1 H) 6.11 (s, 1 H) 6.79 (t, J=5.61 Hz, 1 H) 7.28 (d, J=2.86 Hz, 1 H)	E, 1.23	398
210		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.19 (d, J=1.10 Hz, 3 H) 3.68 (s, 6 H) 4.77 (d, J=5.72 Hz, 2 H)	E, 1.27	397

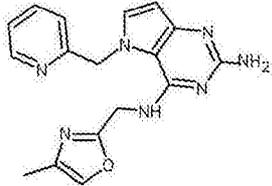
[0231]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		5.68 (s, 2 H) 6.12 (s, 1 H) 6.28 (d, J=3.08 Hz, 1 H) 6.70 (d, J=1.32 Hz, 1 H) 7.45 (br. s., 1 H) 7.59 (d, J=3.08 Hz, 1 H) 8.12 (t, J=5.50 Hz, 1 H) 12.59 - 12.72 (m, 1 H)		
211		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 1.17 (d, J=6.60 Hz, 3 H) 3.23 - 3.30 (m, 4 H) 3.43 (dd, J=9.02, 5.06 Hz, 1 H) 4.36 - 4.44 (m, 1 H) 5.27 (br. s., 2 H) 5.36 - 5.47 (m, 2 H) 5.95 (d, J=2.64 Hz, 1 H) 7.19 (d, J=7.04 Hz, 1 H) 7.33 - 7.43 (m, 3 H) 7.85 (t, J=7.37 Hz, 1 H) 8.55 (d, J=3.96 Hz, 1 H)	E, 1.21	313

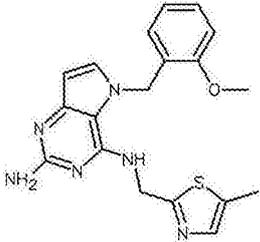
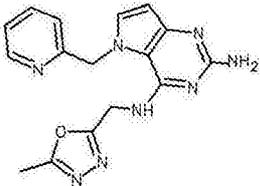
[0232]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
212		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 1.18 (d, J=6.60 Hz, 3 H) 3.25 (s, 3 H) 3.29 (s, 3 H) 3.32 - 3.35 (m, 1 H) 3.45 (dd, J=9.35, 5.17 Hz, 1 H) 3.61 (t, J=4.73 Hz, 2 H) 4.28 - 4.39 (m, 2 H) 4.44 (dt, J=12.71, 6.30 Hz, 1 H) 5.32 (br. s., 2 H) 5.93 (br. s., 1 H) 6.24 (d, J=7.70 Hz, 1 H) 7.16 (s, 1 H)	E, 1.21	280
213		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.25 (d, J=1.10 Hz, 3 H) 3.89 (s, 3 H) 4.76 (d, J=5.50 Hz, 2 H) 5.29 (s, 2 H) 5.40 (s, 2 H) 5.93 (d, J=3.08 Hz, 1 H) 6.76 (d, J=1.10 Hz, 1 H) 7.25 (d,	E, 1.29	366

[0233]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		J=3.08 Hz, 1 H) 7.39 (dd, J=8.36, 4.62 Hz, 1 H) 7.53 (dd, J=8.36, 1.10 Hz, 1 H) 7.94 (dd, J=4.73, 1.21 Hz, 1 H) 8.36 (t, J=5.61 Hz, 1 H)		
214		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.05 (d, J=1.32 Hz, 3 H) 4.73 (d, J=5.72 Hz, 2 H) 5.31 (s, 2 H) 5.47 (s, 2 H) 5.98 (d, J=3.08 Hz, 1 H) 7.29 - 7.35 (m, 2 H) 7.42 (d, J=3.08 Hz, 1 H) 7.67 (d, J=1.10 Hz, 1 H) 7.81 (td, J=7.70, 1.76 Hz, 1 H) 7.99 (t, J=5.61 Hz, 1 H) 8.41 - 8.45 (m, 1 H)	E, 1.17	336

[0234]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
215		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.31 (s, 3 H) 3.80 (s, 3 H) 4.77 (d, J=5.72 Hz, 2 H) 5.34 (s, 2 H) 5.43 (s, 2 H) 6.01 (d, J=2.86 Hz, 1 H) 6.46 - 6.50 (m, 1 H) 6.80 (t, J=7.26 Hz, 1 H) 6.90 (t, J=5.83 Hz, 1 H) 7.00 (d, J=8.14 Hz, 1 H) 7.20 - 7.27 (m, 2 H) 7.31 (d, J=1.10 Hz, 1 H)	E, 1.42	381
216		<sup>1</sup> H NMR (400 MHz, DMSO- <i>d</i> <sub>6</sub> ) δ ppm 2.43 (s, 3 H) 4.85 (d, J=5.72 Hz, 2 H) 5.33 (s, 2 H) 5.49 (s, 2 H) 5.99 (d, J=3.08 Hz, 1 H) 7.24 (d, J=7.70 Hz, 1 H) 7.34 (ddd, J=7.54, 4.90, 0.99 Hz, 1 H) 7.43 (d, J=3.08 Hz, 1 H)	E, 0.98	337

[0235]

#	结构	<sup>1</sup> H NMR	LC 方法, Rt (min)	LC-MS 质量发现 值
		7.80 (td, J=7.70, 1.76 Hz, 1 H) 8.03 (t, J=5.61 Hz, 1 H) 8.44 - 8.47 (m, 1 H)		

[0236] 分析方法。

[0237] 所有化合物通过LC-MS根据以下LC-MS方法进行表征：

[0238] 方法A. 使用菲罗门 (Phenomenex) 的Kinetex柱 (XB-C18, 50x 4.6mm I.D. 2.6m), 保持在35℃。MS检测: API-ES正电离模式, 质量范围100-1200。PDA检测 ( $\lambda = 190-400\text{nm}$ )。使用以下梯度, 用2 $\mu\text{L}$ 注射:

[0239]

溶剂 A	H <sub>2</sub> O + 0.1%甲酸		
溶剂 B	乙腈		
时 间 (min)	%A	%B	流 速 (mL/min)
0.0	95	5	3.0
4.2	5	95	3.0
4.9	5	95	3.0
5.0	95	5	3.0

[0240] 方法B. 在桥联的乙基硅氧烷/硅石混合物 (BEH) C18柱 (1.7 $\mu\text{m}$ , 2.1 $\times$ 50m; 沃特斯 (Waters) Acquity) 上以0.8mL/min的流速进行反相UPLC (超高效液相色谱法)。使用两个流动相 (在H<sub>2</sub>O/乙腈95/5中的10mM乙酸铵; 流动相B: 乙腈) 来运行一个梯度条件: 在1.3分钟内从95%A和5%B至5%A和95%B, 并且保持0.7分钟。使用0.75 $\mu\text{L}$ 的注射体积。对于正电离模式的锥孔电压是30V, 并且对于负电离模式的锥孔电压是30V。

[0241] 方法C. 在40℃下, 在沃特斯XTerra C18柱 (100x 4.6mm I.D. 3.5 $\mu\text{m}$ 颗粒) 上以1.6mL/min的流速进行分析。进行梯度洗脱如下: 在7.5min内从在水/乙腈90:10中的100%乙酸铵 (25mM) 溶液至乙腈/甲醇50:50的混合物; 在1.0min内从生成的组合物至100%乙腈; 100%乙腈持续1.5min; 在3.0分钟内从100%乙腈至在水/乙腈90:10 (25mM) 中的100%乙酸铵 (25mM) 溶液。标准注射体积是3 $\mu\text{L}$ 。对于UV采样范围设置在200-400nm。

[0242] 方法D.使用Acquity UPLC(沃特斯) 系统进行LC测量,该系统包括二元泵、样品组织器(sample organizer)、柱加热器(设定为55℃)、二极管阵列检测器(DAD)以及如在以下对应方法中指定的柱。来自该柱的流被分流到MS光谱仪。MS检测器被配置有一个电喷雾电离源。通过使用0.02秒的驻留时间在0.18秒内从100至1000扫描获得质谱。毛细管针电压是3.5kV并且该源温度保持在140℃。使用氮作为雾化器气体。在桥联的乙基硅氧烷/硅石混合物(BEH) C18柱(1.7μm, 2.1x 50mm;沃特斯公司(Waters) Acquity) 上进行反相UPLC(超高效液相层析),流速为0.8mL/min。使用两个流动相(在H<sub>2</sub>O/乙腈95/5中的10mM乙酸铵;流动相B:乙腈)来运行一个梯度条件:在1.3分钟内从95%A和5%B至5%A和95%B,并且保持0.3分钟。使用0.5μL的注射体积。对于正电离模式的锥孔电压是10V,并且对于负电离模式的锥孔电压是20V。

[0243] 方法E

[0244]

仪器	柱	流动相	梯度	流量 ----- - 柱温	运行 时间
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[0245]

沃特斯 (Waters): Acquity ® UPLC®- DAD 和 SQD	沃特斯: HSS T3 (1.8 μm, 2.1*100 mm)	A: 10 mM CH <sub>3</sub> COONH <sub>4</sub> 于 95% H <sub>2</sub> O + 5% CH <sub>3</sub> CN 中 B: CH <sub>3</sub> CN	从 100% A 在 2.10 min 中到 5% A, 在 0.90 min 中到 0% A, 在 0.5 min 中到 5% A	0.8 ----- - 55	3.5
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[0246] 方法F

[0247]

仪器	柱	流动相	梯度	流量 ----- - 柱温	运行 时间
沃特斯 (Waters) ): Alliance ®-DAD- ZQ 和 ELSD 2000 阿 尔泰克 (Alltec h)	沃特斯 (Waters): Xterra MS C18 (3.5 µm, 4.6*100 mm)	A: 25mM CH <sub>3</sub> COONH <sub>4</sub> 于 95% H <sub>2</sub> O + 5% CH <sub>3</sub> CN 中, B: CH <sub>3</sub> CN, C: CH <sub>3</sub> OH, D: (40% CH <sub>3</sub> CN 和 40% CH <sub>3</sub> OH 和 20% H <sub>2</sub> O 与 0.25% CH <sub>3</sub> COOH	在 6.5 min 内从 100% A 至 1% A、49% B 和 50% C, 在 0.5 min 内至 1% A 和 99% B, 在 1 min 内至 100% D, 保持 1.0 min, 在 0.5 min 内至 100% A 并 保持 1.5 min。	1.6 ----- - 40	11

[0248] 具有化学式(I)的化合物的生物活性

[0249] 生物测定说明

[0250] TLR7和TLR8活性的评估

[0251] 在细胞报告子测定中使用用TLR7或TLR8表达载体以及NFκB-luc报告子构建体瞬时转染了的HEK293细胞对这些化合物活化人TLR7和/或TLR8的能力进行评估。

[0252] 简而言之,使HEK293细胞生长在培养基(补充有10%FCS和2mM谷氨酰胺的DMEM)中。对于在10cm平皿中的细胞的转染,用胰蛋白酶-EDTA将细胞分散,用CMV-TLR7或TLR8质粒(750ng)、NFκB-luc质粒(375ng)和转染试剂的混合物对细胞进行转染,并且在37°C下在湿润的5%CO<sub>2</sub>气氛下孵育过夜。然后将转染的细胞用胰蛋白酶-EDTA分散,在PBS中洗涤并且在培养基中重悬至 $1.67 \times 10^5$ 个细胞/mL的密度。然后将三十微升的细胞分配至384-孔板中的每一个孔中,在孔中已经存在10µL的化合物(在4%DMSO中)。在37°C、5%CO<sub>2</sub>下孵育6小时后,通过向每个孔中添加15µL的Steady Lite Plus底物(珀金埃尔默公司(Perkin Elmer))并且在ViewLux ultraHTS微孔板成像仪(microplate imager)(珀金埃尔默公司)上进行读出来确定荧光素酶活性。从按一式四份进行的测量值生成剂量反应曲线。对每个化合物的最低有效浓度(LEC)值进行确定,该最低有效浓度值被定义为引发超出测定的标准偏差至少两倍的效应的浓度。

[0253] 在384-孔板中,使用化合物的类似稀释系列和每孔30µL的用CMV-TLR7构建体单独转染的细胞( $1.67 \times 10^5$ 细胞/mL)对化合物毒性进行平行确定。在37°C、5%CO<sub>2</sub>下孵育6小时

后,通过每孔中添加15 $\mu$ l的ATP lite (珀金埃尔默公司)并且在ViewLux ultraHTS微孔板成像仪(珀金埃尔默公司)上读数来测量细胞活力。数据以CC<sub>50</sub>进行报告。

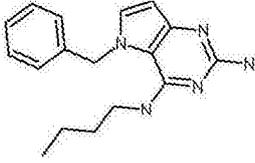
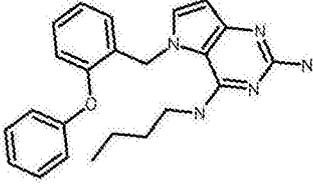
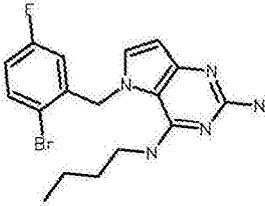
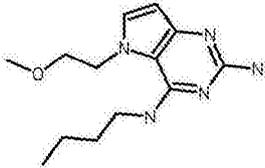
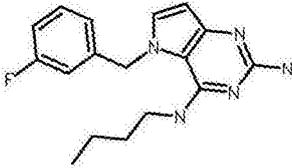
[0254] 平行地,使用一种相似稀释系列的化合物(在4%DMSO中的10 $\mu$ L的化合物)和每孔30 $\mu$ L的周NF $\kappa$ B-luc报告基因构建体单独转染的细胞(1.67x 10<sup>5</sup>个细胞/mL)。在37 $^{\circ}$ C、5%CO<sub>2</sub>下孵育后6小时,通过向每个孔中添加15 $\mu$ l的Steady Lite Plus底物(珀金埃尔默公司)并且在ViewLux ultraHTS微孔板成像仪(珀金埃尔默公司)上进行读出来确定荧光素酶活性。将计数器屏数据报道为LEC。

[0255] ISRE启动子元件的活化

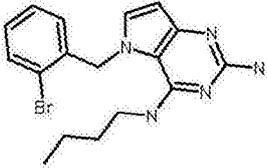
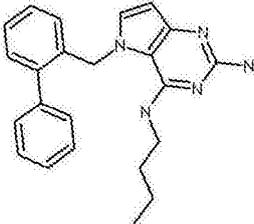
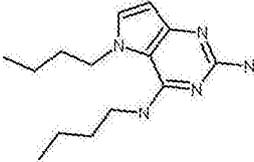
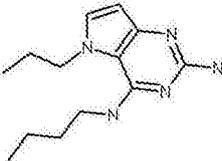
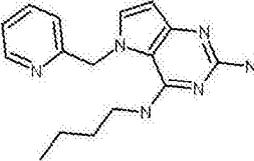
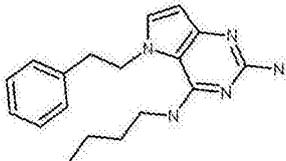
[0256] 还通过测量由来自PBMC的条件培养基造成的干扰素刺激应答元件(ISRE)的活化而对这些化合物诱导IFN-I的潜力进行了评估。具有序列GAAACTGAACT的ISRE元件高度响应于STAT1-STAT2-IRF9转录因子,在IFN-I结合至它们的受体IFNAR(Clontech,PT3372-5W)时被活化。来自Clontech(参考号631913)的质粒pISRE-Luc包含5个这种ISRE元件拷贝,随后是萤火虫荧光素酶ORF。建立一种稳定转染pISRE-Luc(HEK-ISRE1uc)的HEK293细胞系来分析PBMC条件细胞培养基。

[0257] 简言之,从至少两个供体的血沉棕黄层使用标准的Ficoll离心方案来制备PBMC。将分离的PBMC重悬于补充有10%人AB血清的RPMI培养基中,并且将2x 10<sup>5</sup>个细胞/孔分配至含有化合物(70 $\mu$ L总体积)的384-孔板中。孵育过夜后,将10 $\mu$ L的上清液转移至包含5x10<sup>3</sup>HEK-ISRE1uc细胞/孔(30 $\mu$ L)(前一天铺板)的384-孔板。经24小时孵育后,通过测定荧光素酶活性(使用40 $\mu$ L/孔Steady Lite Plus底物(珀金埃尔默公司),并且用ViewLux ultraHTS微孔板成像仪(珀金埃尔默公司)测量)而对ISRE元件的活化进行测量。各个化合物对HEK-ISRE1uc细胞的刺激活性被报告为LEC值,该LEC值定义为施用至PBMC导致荧光素酶活性至少超出测定标准偏差两倍的化合物浓度。LEC进而指示在转移定义量的PBMC培养基时ISRE活化的程度。将重组干扰素 $\alpha$ -2a(罗扰素-A)用作标准对照化合物。

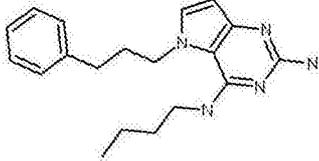
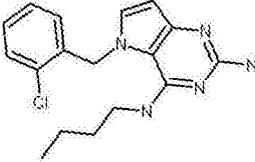
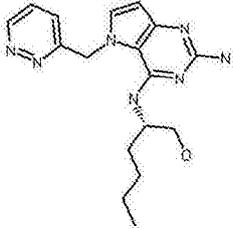
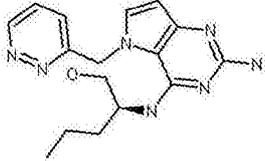
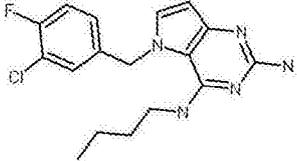
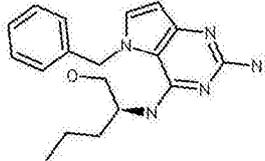
[0258] 表2.具有化学式(I)的化合物的活性。在以上描述的HEK 293NF- $\kappa$ B计数器屏测定中,所有化合物均显示无活性(LEC>25 $\mu$ M)。

#	结构	TLR7 LEC ( $\mu\text{M}$ )	TLR8 LEC ( $\mu\text{M}$ )	PBMC LEC ( $\mu\text{M}$ )
1		0.20	> 25	0.20
2		0.50	> 25	0.60
3		2.6	> 25	1.2
4		0.60	13.5	0.4
5		0.30	> 25	0.2

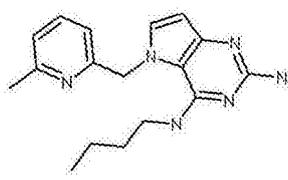
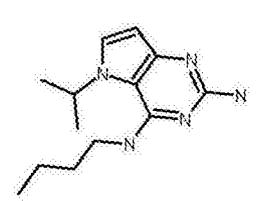
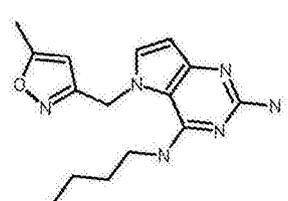
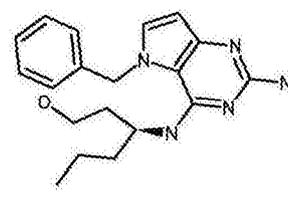
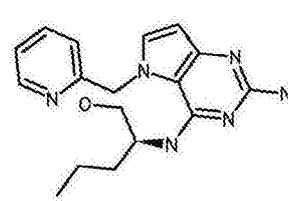
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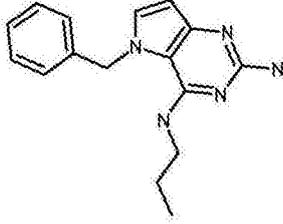
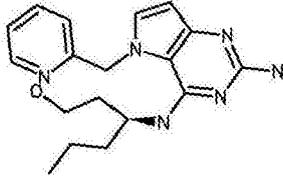
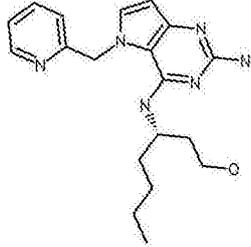
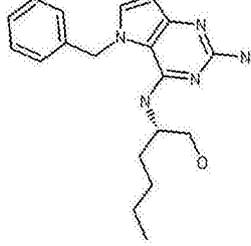
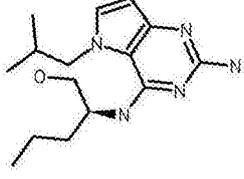
#	结构	TLR7 LEC ( $\mu\text{M}$ )	TLR8 LEC ( $\mu\text{M}$ )	PBMC LEC ( $\mu\text{M}$ )
6		1.3	> 25	0.7
7		0.61	> 25	0.8
8		0.49	1.7	0.15
9		0.53	2.1	0.22
10		0.15	> 25	0.06
11		1.5	3.5	0.56

[0260]

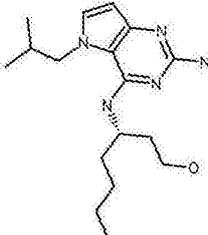
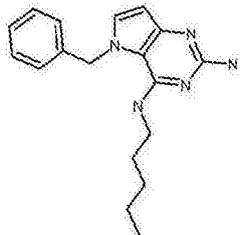
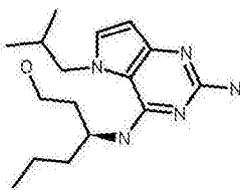
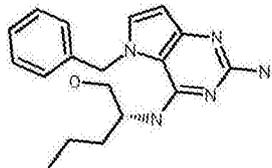
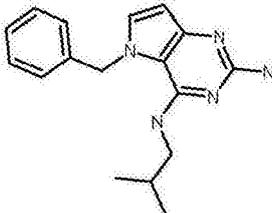
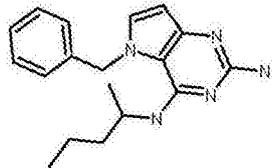
#	结构	TLR7 LEC ( $\mu\text{M}$ )	TLR8 LEC ( $\mu\text{M}$ )	PBMC LEC ( $\mu\text{M}$ )
12		0.14	0.7	0.05
13		0.80	> 25	0.89
14		0.52	6,57	0.01
15		5.84	> 25	0.1
16		0.89	> 25	0.6
17		0.07	12,5	0.01

[0261]

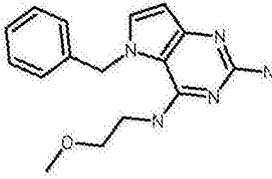
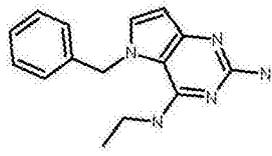
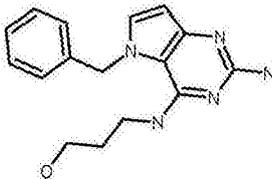
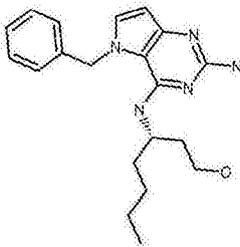
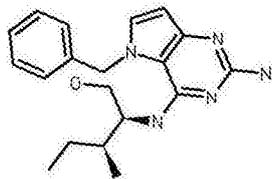
#	结构	TLR7 LEC ( $\mu\text{M}$ )	TLR8 LEC ( $\mu\text{M}$ )	PBMC LEC ( $\mu\text{M}$ )
18		0.07	> 25	0.01
19		2.5	7.06	0.62
[0262] 20		0.14	1.3	0.02
21		0.009	7.4	0.0007
22		0.48	9.2	0.02

#	结构	TLR7 LEC ( $\mu\text{M}$ )	TLR8 LEC ( $\mu\text{M}$ )	PBMC LEC ( $\mu\text{M}$ )
23		0.83	> 25	0.27
24		0.02	6.47	0.0007
25		0.01	2.84	0.001
26		0.03	1.95	0.002
27		0.15	0.85	0.17

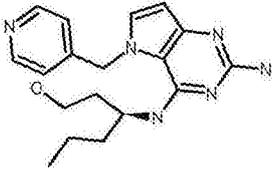
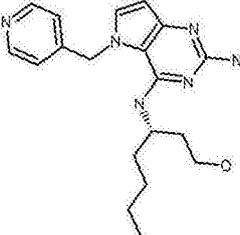
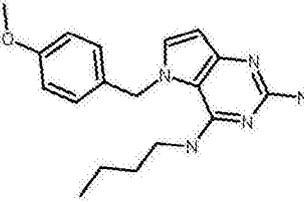
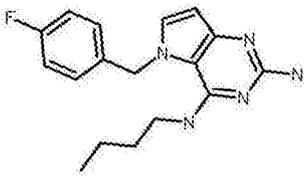
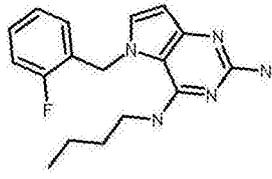
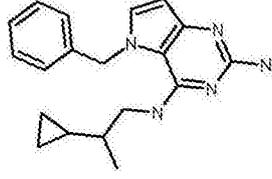
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#	结构	TLR7 LEC ( $\mu\text{M}$ )	TLR8 LEC ( $\mu\text{M}$ )	PBMC LEC ( $\mu\text{M}$ )
28		0.11	1.1	0.03
29		0.15	> 25	0.04
30		0.16	0.67	0.05
31		0.22	> 25	0.16
32		0.91	> 25	0.52
33		0.03	> 25	0.04

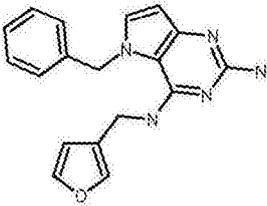
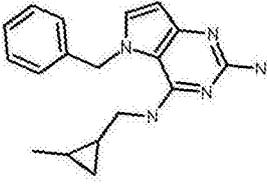
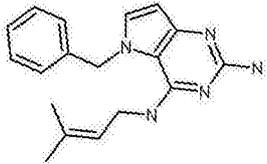
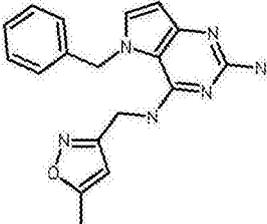
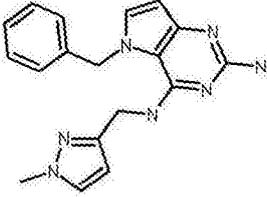
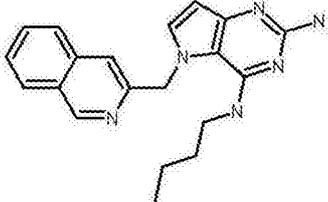
[0264]

#	结构	TLR7 LEC ( $\mu\text{M}$ )	TLR8 LEC ( $\mu\text{M}$ )	PBMC LEC ( $\mu\text{M}$ )
34		0.91	> 25	0.54
35		1.49	> 25	0.70
36		1.06	> 25	0.59
37		0.005	> 25	0.007
38		0.54	> 25	0.63

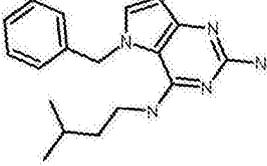
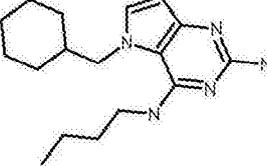
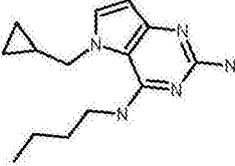
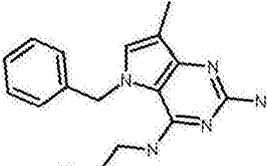
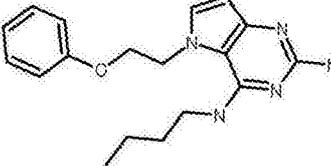
[0265]

#	结构	TLR7 LEC ( $\mu\text{M}$ )	TLR8 LEC ( $\mu\text{M}$ )	PBMC LEC ( $\mu\text{M}$ )
39		0.17	> 25	0.009
40		0.12	24.61	0.004
41		0.09	> 25	0.11
42		0.28	> 25	0.16
43		0.11	> 25	0.17
44		1.51	> 25	2.45

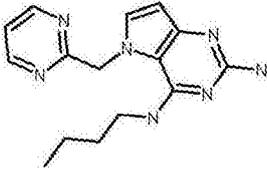
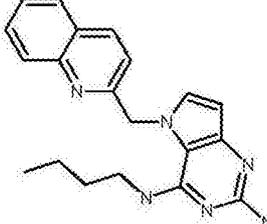
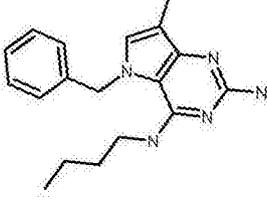
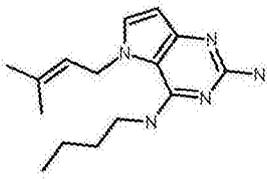
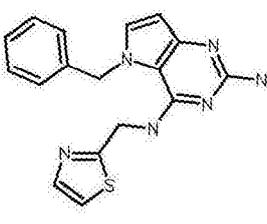
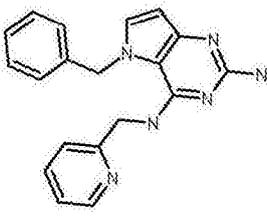
[0266]

#	结构	TLR7 LEC ( $\mu\text{M}$ )	TLR8 LEC ( $\mu\text{M}$ )	PBMC LEC ( $\mu\text{M}$ )
45		19.9	> 25	0.74
46		0.83	> 25	0.17
47		17.5	> 25	1.79
48		0.05	> 25	0.03
49		22.43	> 25	2.34
50		1.01	> 25	0.13

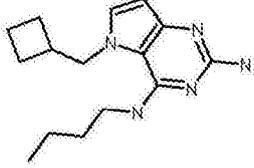
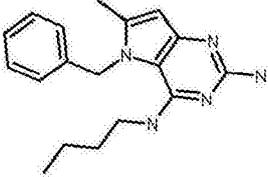
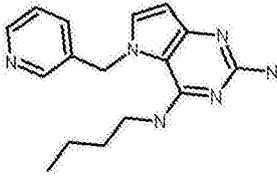
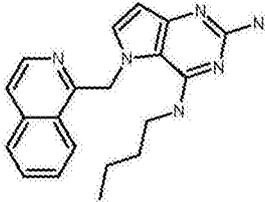
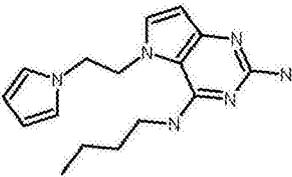
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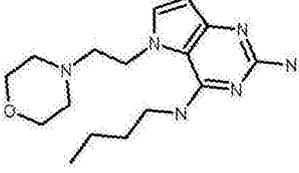
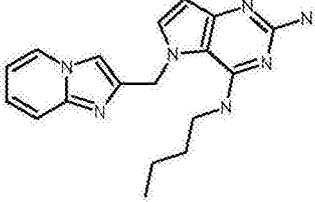
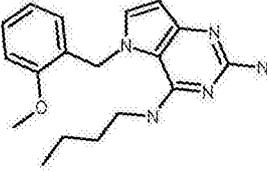
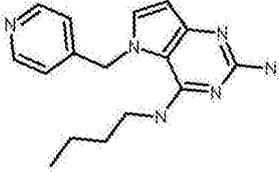
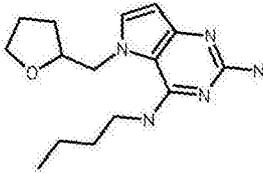
#	结构	TLR7 LEC ( $\mu\text{M}$ )	TLR8 LEC ( $\mu\text{M}$ )	PBMC LEC ( $\mu\text{M}$ )
51		5.14	> 25	0.59
52		0.12	> 25	0.09
53		0.38	2.78	0.07
54		1.68	> 25	0.90
55		0.08	0.81	0.06

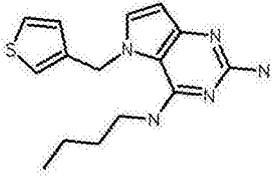
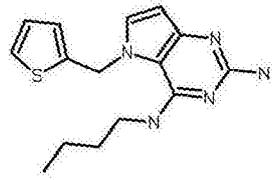
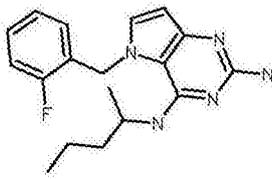
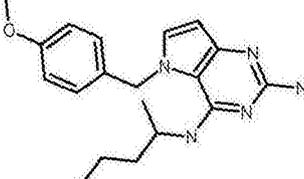
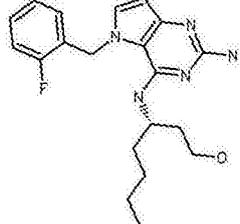
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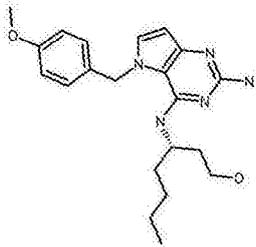
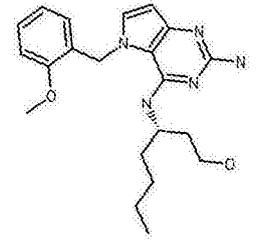
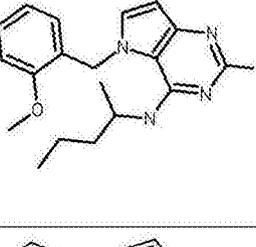
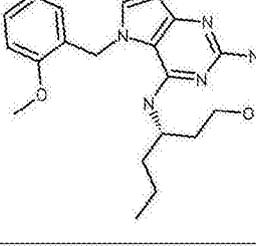
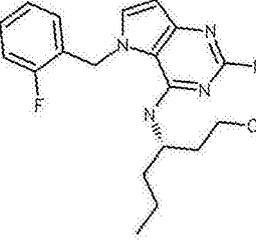
#	结构	TLR7 LEC ( $\mu\text{M}$ )	TLR8 LEC ( $\mu\text{M}$ )	PBMC LEC ( $\mu\text{M}$ )
56		0.99	17.5	0.07
57		0.33	> 25	0.28
58		0.24	> 25	0.90
59		0.37	> 25	0.22
60		0.39	> 25	0.33
61		1.01	> 25	1.95

[0269]

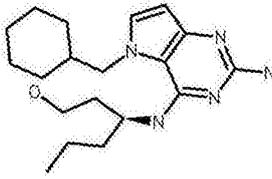
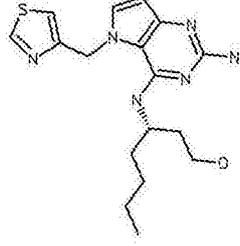
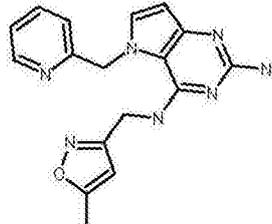
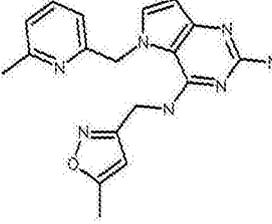
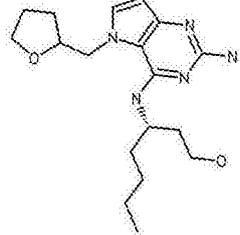
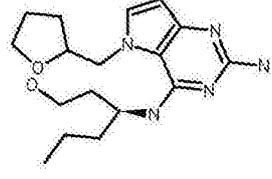
#	结构	TLR7 LEC ( $\mu\text{M}$ )	TLR8 LEC ( $\mu\text{M}$ )	PBMC LEC ( $\mu\text{M}$ )
62		0.06	0.9934	0.06
63		0.67	> 25	0.18
[0270] 64		1.36	> 25	0.26
65		0.1687	> 25	0.08
66		2.57	3.96	0.91

#	结构	TLR7 LEC ( $\mu\text{M}$ )	TLR8 LEC ( $\mu\text{M}$ )	PBMC LEC ( $\mu\text{M}$ )
67		0.056	6.71	0.04
68		0.19	> 25	0.04
[0271] 69		0.004	0.71	0.002
70		1.53	> 25	0.75
71		0.32	4.68	0.24

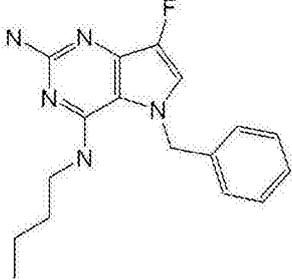
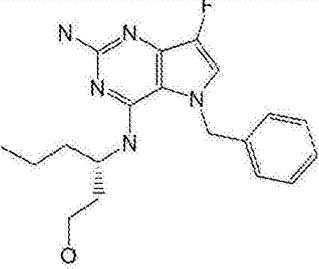
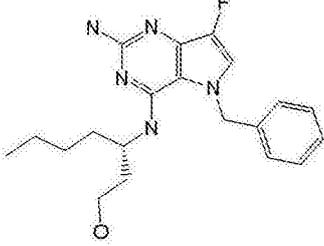
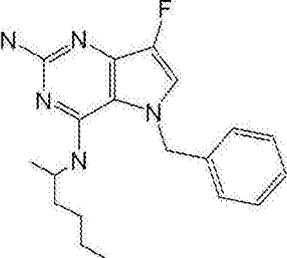
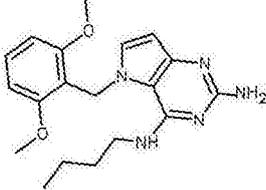
#	结构	TLR7 LEC ( $\mu\text{M}$ )	TLR8 LEC ( $\mu\text{M}$ )	PBMC LEC ( $\mu\text{M}$ )
72		0.13	> 25	0.04
73		0.28	> 25	0.13
[0272] 74		0.10	> 25	0.04
75		0.04	> 25	0.04
76		0.01	4.09	0.007

#	结构	TLR7 LEC ( $\mu\text{M}$ )	TLR8 LEC ( $\mu\text{M}$ )	PBMC LEC ( $\mu\text{M}$ )
77		0.008	2.62	0.002
78		0.0004	0.5577	< 0.0004
[0273] 79		0.004	0.94	0.001
80		< 0.0006	0.689	< 0.0004
81		0.01	22.02	0.002

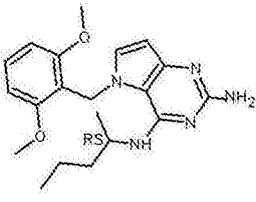
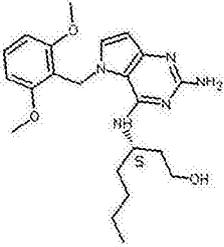
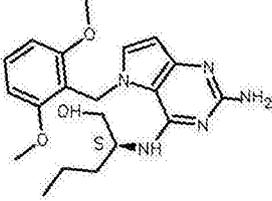
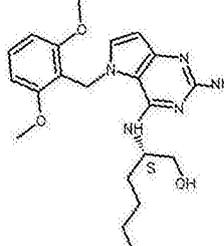
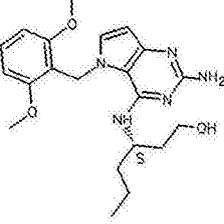
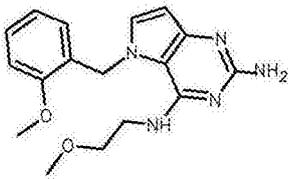
#	结构	TLR7 LEC ( $\mu\text{M}$ )	TLR8 LEC ( $\mu\text{M}$ )	PBMC LEC ( $\mu\text{M}$ )
82		0.07	0.57	0.01
83		1.57	> 25	2.3
[0274] 84		0.04	1.14	0.01
85		0.03	10.14	0.002
86		1.63	> 25	0.47

#	结构	TLR7 LEC ( $\mu\text{M}$ )	TLR8 LEC ( $\mu\text{M}$ )	PBMC LEC ( $\mu\text{M}$ )
87		0.01	> 25	0.008
88		0.01	2.46	0.0006
89		0.04	> 25	0.006
90		0.03	> 25	0.01
91		0.05	2.17	0.02
92		0.10	4.46	0.02

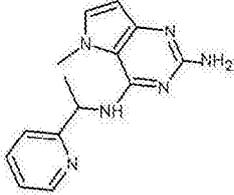
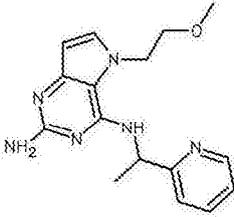
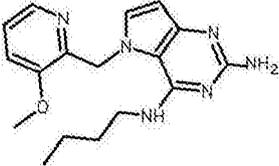
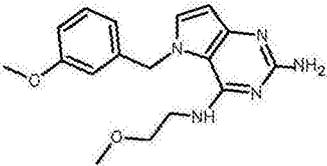
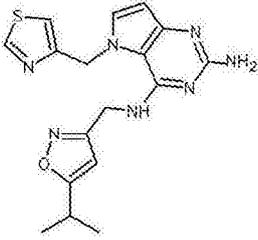
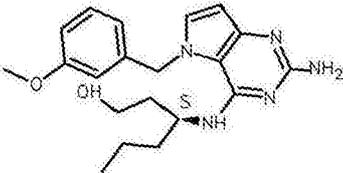
[0275]

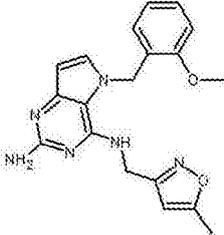
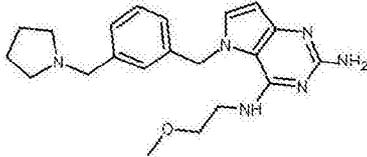
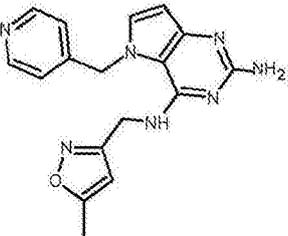
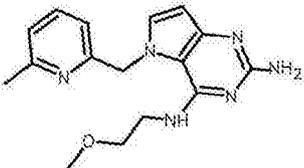
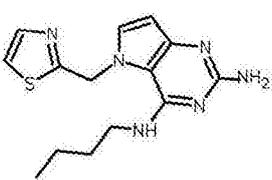
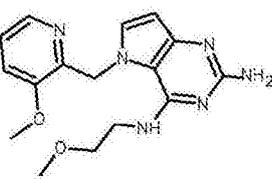
#	结构	TLR7 LEC ( $\mu\text{M}$ )	TLR8 LEC ( $\mu\text{M}$ )	PBMC LEC ( $\mu\text{M}$ )
93		0.26	> 25	0.12
94		0.01	> 25	0.01
95		0.01	3.26	0.007
96		0.05	> 25	0.04
97		< 0.01	0.23	0.001

[0276]

#	结构	TLR7 LEC ( $\mu\text{M}$ )	TLR8 LEC ( $\mu\text{M}$ )	PBMC LEC ( $\mu\text{M}$ )
98		< 0.01	0.22	0.001
99		< 0.01	0.1	< 0.001
100		< 0.01	0.04	< 0.001
101		< 0.01	0.08	< 0.001
102		< 0.01	0.14	< 0.001
103		0.032	> 25	0.018

[0277]

#	结构	TLR7 LEC ( $\mu\text{M}$ )	TLR8 LEC ( $\mu\text{M}$ )	PBMC LEC ( $\mu\text{M}$ )
104		11.960	> 25	1.980
105		0.827	> 25	0.194
[0278] 106		0.008	0.59	0.005
107		2.030	> 25	2.130
108		0.126	> 25	0.070
109		0.005	7.17	0.003

#	结构	TLR7 LEC ( $\mu\text{M}$ )	TLR8 LEC ( $\mu\text{M}$ )	PBMC LEC ( $\mu\text{M}$ )
110		0.002	> 25	0.001
111		0.637	> 25	0.293
112		0.741	> 25	0.209
113		1.320	> 25	0.807
114		0.186	2.27	0.133
115		0.241	7.93	0.079

[0279]

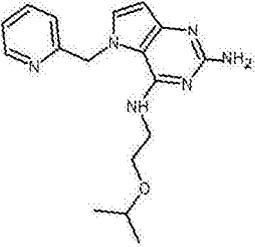
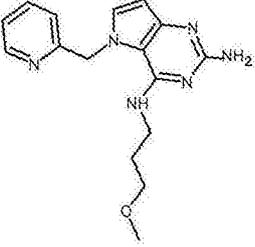
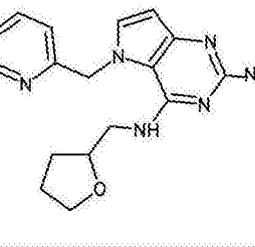
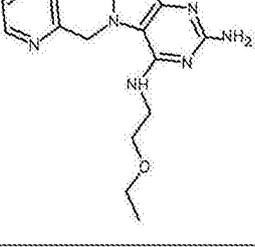
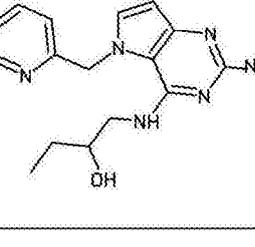
#	结构	TLR7 LEC ( $\mu\text{M}$ )	TLR8 LEC ( $\mu\text{M}$ )	PBMC LEC ( $\mu\text{M}$ )
116		0.049	> 25	0.022
117		2.950	> 22.7	1.430
118		1.650	> 25	3.010
119		1.810	> 25	2.180
120		3.220	> 25	2.160
121		0.172	> 25	0.046

[0280]

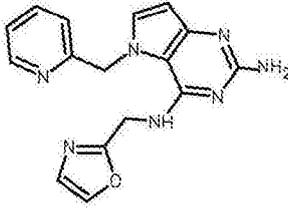
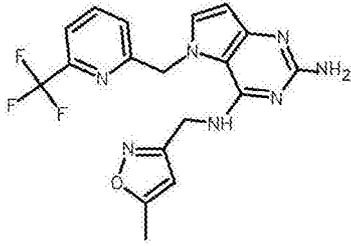
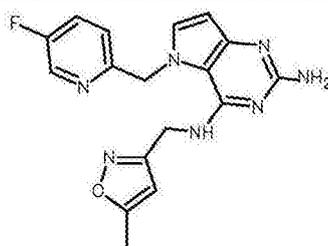
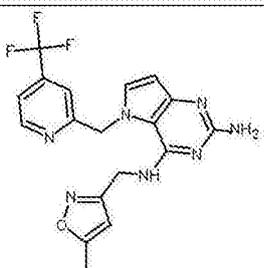
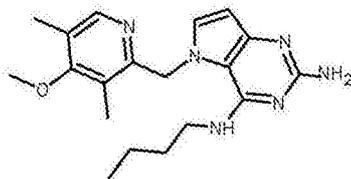
#	结构	TLR7 LEC ( $\mu\text{M}$ )	TLR8 LEC ( $\mu\text{M}$ )	PBMC LEC ( $\mu\text{M}$ )
122		0.050	> 25	0.030
123		0.026	> 25	0.002
[0281] 124		0.003	> 22	0.001
125		0.086	> 25	0.009
126		0.054	> 25	0.008

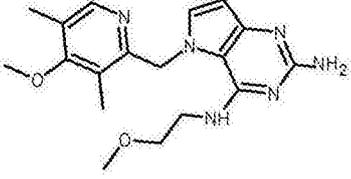
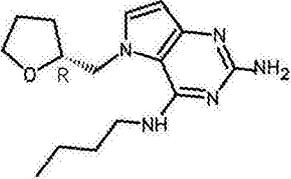
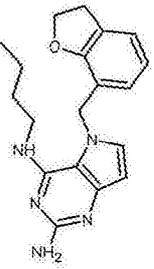
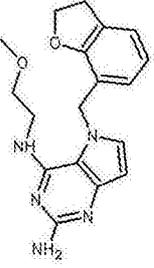
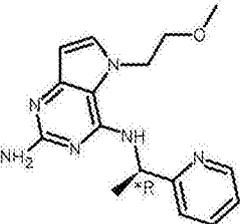
#	结构	TLR7 LEC ( $\mu\text{M}$ )	TLR8 LEC ( $\mu\text{M}$ )	PBMC LEC ( $\mu\text{M}$ )
127		0.337	> 25	0.019
128		0.342	> 25	0.062
[0282] 129		0.670	> 25	0.122
130		1.940	> 25	0.804
131		0.004	24.6	0.001

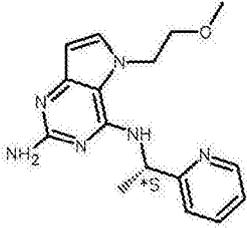
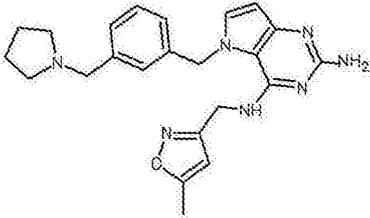
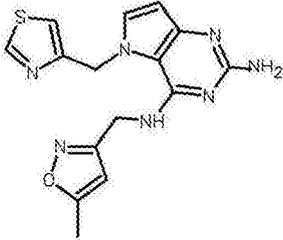
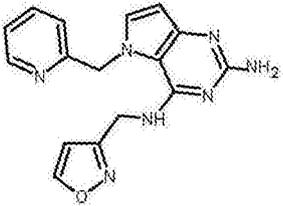
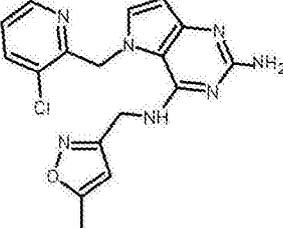
#	结构	TLR7 LEC ( $\mu\text{M}$ )	TLR8 LEC ( $\mu\text{M}$ )	PBMC LEC ( $\mu\text{M}$ )
132		5.99	> 25	0.879
133		0.07	> 25	0.023
[0283]				
134		1.20	> 25	0.104
135		12.5	> 25	4.050
136		3.04	> 25	0.559

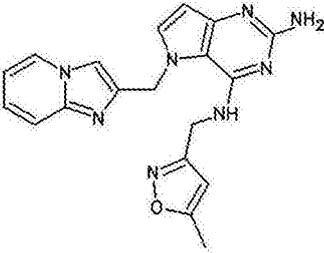
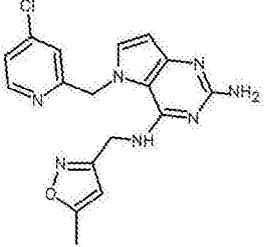
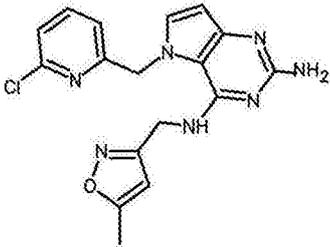
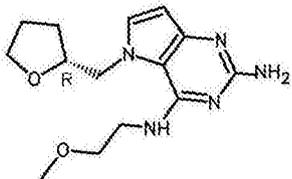
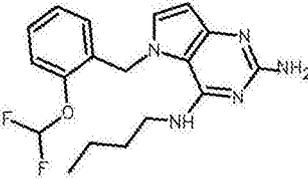
#	结构	TLR7 LEC ( $\mu\text{M}$ )	TLR8 LEC ( $\mu\text{M}$ )	PBMC LEC ( $\mu\text{M}$ )
137		13.8	> 25	2.030
138		4.45	> 25	0.502
139		1.41	> 25	0.588
140		1.24	> 25	0.513
141		0.43	> 25	0.048

[0284]

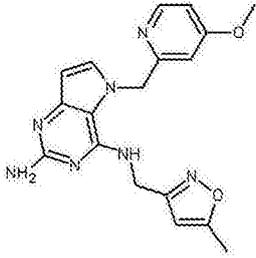
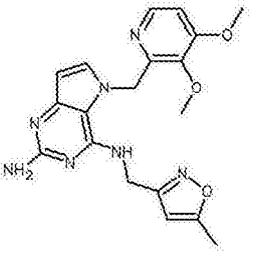
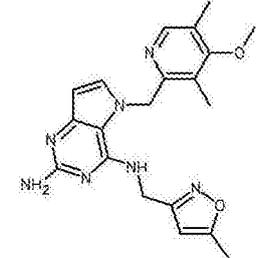
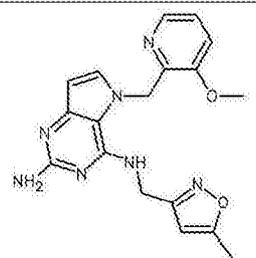
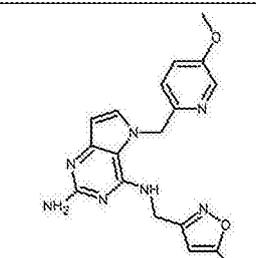
#	结构	TLR7 LEC ( $\mu\text{M}$ )	TLR8 LEC ( $\mu\text{M}$ )	PBMC LEC ( $\mu\text{M}$ )
142		0.52	> 25	0.134
143		0.10	> 25	0.016
[0285] 144		0.07	> 25	0.009
145		0.05	> 25	0.021
146		0.20	> 25	0.139

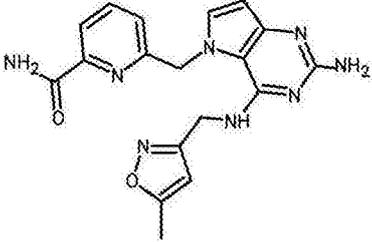
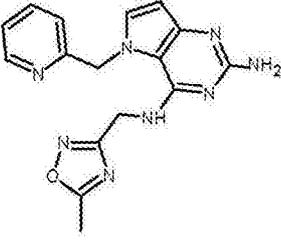
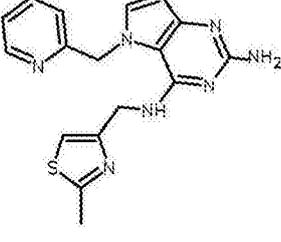
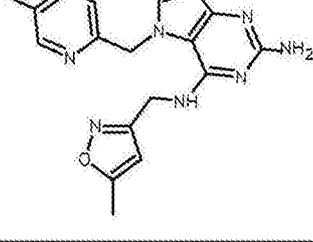
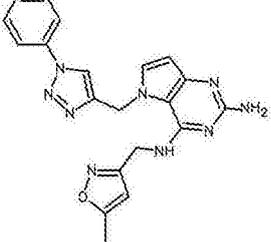
#	结构	TLR7 LEC ( $\mu\text{M}$ )	TLR8 LEC ( $\mu\text{M}$ )	PBMC LEC ( $\mu\text{M}$ )
147		4.49	> 25	2.020
148		0.16	3.93	0.056
[0286]				
149		0.02	> 25	0.006
150		0.25	> 25	0.054
151		12.8	> 25	2.580

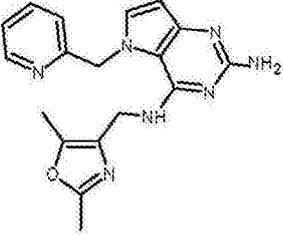
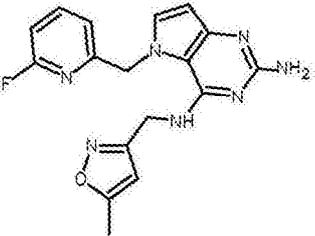
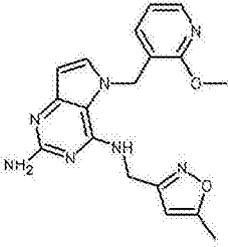
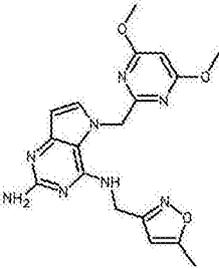
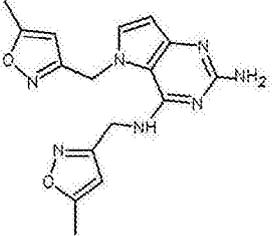
#	结构	TLR7 LEC ( $\mu\text{M}$ )	TLR8 LEC ( $\mu\text{M}$ )	PBMC LEC ( $\mu\text{M}$ )
152		0.73	> 25	0.142
153		0.05	> 25	0.002
[0287] 154		0.08	> 25	0.017
155		0.90	> 25	0.415
156		0.05	> 25	0.040

#	结构	TLR7 LEC ( $\mu\text{M}$ )	TLR8 LEC ( $\mu\text{M}$ )	PBMC LEC ( $\mu\text{M}$ )
157		0.03	> 25	0.003
158		0.05	> 25	0.020
[0288] 159		0.05	> 25	0.019
160		8.07	> 25	1.810
161		0.02	> 25	0.009

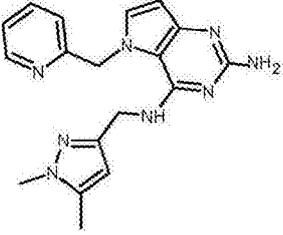
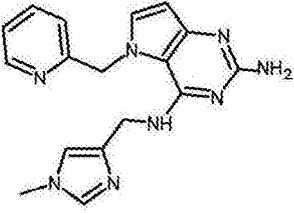
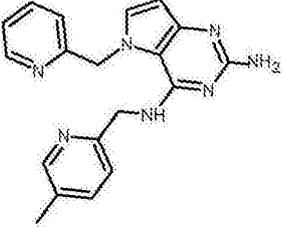
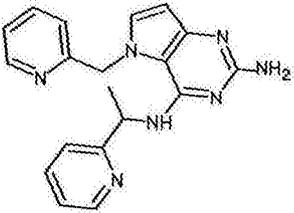
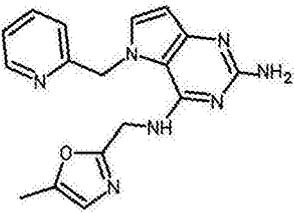
#	结构	TLR7 LEC ( $\mu\text{M}$ )	TLR8 LEC ( $\mu\text{M}$ )	PBMC LEC ( $\mu\text{M}$ )
162		0.32	> 25	0.128
163		< 0.01	0.75	0.001
[0289] 164		0.04	15.93	0.025
165		4.94	> 25	0.957
166		4.88	NA	NA

#	结构	TLR7 LEC ( $\mu\text{M}$ )	TLR8 LEC ( $\mu\text{M}$ )	PBMC LEC ( $\mu\text{M}$ )
167		0.09	> 25	0.008
168		0.09	> 25	0.011
[0290]				
169		0.04	> 25	0.011
170		0.01	> 25	0.002
171		0.02	> 25	NA

#	结构	TLR7 LEC ( $\mu\text{M}$ )	TLR8 LEC ( $\mu\text{M}$ )	PBMC LEC ( $\mu\text{M}$ )
172		1.40	> 25	0.017
173		0.53	> 25	0.066
[0291] 174		6.13	> 25	2.200
175		0.02	> 25	0.009
176		0.04	> 25	0.009

#	结构	TLR7 LEC ( $\mu\text{M}$ )	TLR8 LEC ( $\mu\text{M}$ )	PBMC LEC ( $\mu\text{M}$ )
177		8.67	> 25	3.930
178		0.15	> 25	0.014
[0292] 179		0.02	> 25	0.003
180		0.01	> 25	0.004
181		0.06	20.2	0.015

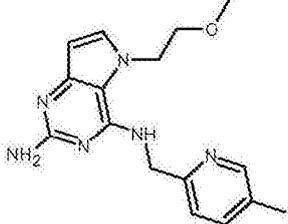
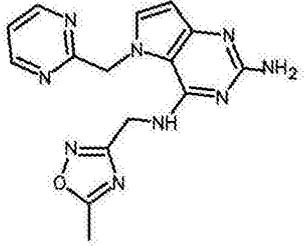
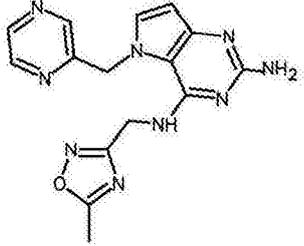
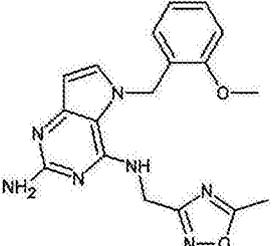
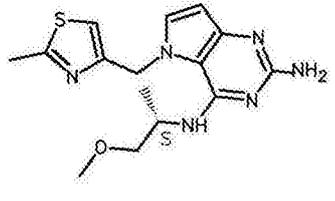
#	结构	TLR7 LEC ( $\mu\text{M}$ )	TLR8 LEC ( $\mu\text{M}$ )	PBMC LEC ( $\mu\text{M}$ )
182		0.05	> 25	0.018
183		0.59	> 25	0.009
[0293] 184		0.49	> 25	0.131
185		0.07	> 25	0.018
186		0.14	> 25	0.035

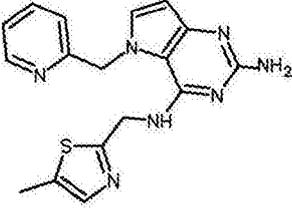
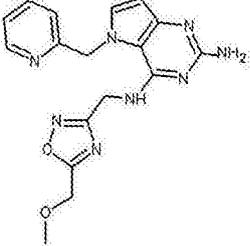
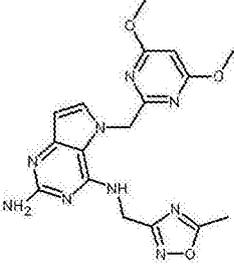
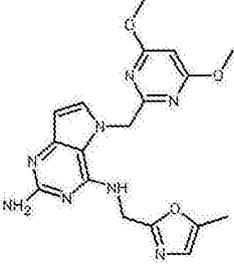
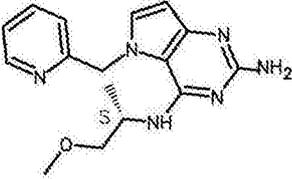
#	结构	TLR7 LEC ( $\mu\text{M}$ )	TLR8 LEC ( $\mu\text{M}$ )	PBMC LEC ( $\mu\text{M}$ )
187		4.78	> 25	0.520
188		7.62	> 25	0.047
189		0.40	> 25	0.074
190		0.26	> 25	0.038
191		0.06	> 24	0.006

[0294]

#	结构	TLR7 LEC ( $\mu\text{M}$ )	TLR8 LEC ( $\mu\text{M}$ )	PBMC LEC ( $\mu\text{M}$ )
192		0.07	> 25	0.030
193		11.3	> 25	0.447
[0295] 194		2.38	> 25	0.507
195		0.16	> 25	0.024
196		0.01	12.6	0.002

#	结构	TLR7 LEC ( $\mu\text{M}$ )	TLR8 LEC ( $\mu\text{M}$ )	PBMC LEC ( $\mu\text{M}$ )
197		0.39	> 25	0.040
198		8.76	> 25	0.617
[0296]				
199		0.60	23.5	0.032
200		0.17	11.4	0.035
201		7.30	> 25	0.978

#	结构	TLR7 LEC ( $\mu\text{M}$ )	TLR8 LEC ( $\mu\text{M}$ )	PBMC LEC ( $\mu\text{M}$ )
202		1.61	> 25	0.580
203		1.04	> 25	0.138
[0297] 204		1.78	> 25	0.188
205		< 0.01	7.7	0.001
206		0.74	15	0.129

#	结构	TLR7 LEC ( $\mu\text{M}$ )	TLR8 LEC ( $\mu\text{M}$ )	PBMC LEC ( $\mu\text{M}$ )
207		0.06	23	0.009
208		5.14	> 25	0.402
[0298] 209		0.04	> 25	0.008
210		0.02	> 25	0.003
211		6.94	22	0.470

#	结构	TLR7 LEC ( $\mu\text{M}$ )	TLR8 LEC ( $\mu\text{M}$ )	PBMC LEC ( $\mu\text{M}$ )
212		7.60	> 25	2.090
213		< 0.01	> 25	0.001
[0299] 214		1.16	> 25	0.151
215		< 0.01	> 25	0.001
216		1.24	> 25	0.091