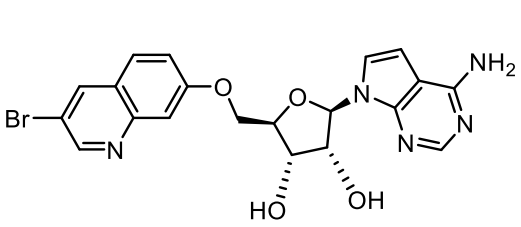
ileus during sepsis; gastroesophageal reflux disease (GORD, or its synonym GERD); eosinophilic esophagitis, gastroparesis such as diabetic gastroparesis; food intolerances and food allergies and other functional bowel disorders, such as non-ulcerative dyspepsia (NUD) and non-cardiac chest pain (NCCP, including costo-chondritis)).

[0037] In a particular example, a PRMT5 inhibitor may be useful in somatic cell reprogramming, such as reprogramming somatic cells into stem cells. In a particular example, a PRMT5 inhibitors may be useful in germ cell development, and are thus envisioned useful in the areas of reproductive technology and regenerative medicine.

[0038] Other diseases which may be treated or prevented, in particular treated, include, but are not limited to, ischemic injury associated myocardial infarctions, immunological diseases, stroke, arrhythmia, toxin-induced or alcohol related liver diseases, aspirin-sensitive rhinosinusitis, cystic fibrosis, cancer pain, and haematological diseases, for example chronic anemia and aplastic anemia.

[0038a] In one aspect, there is provided a method of identifying a patient that is likely to be responsive to treatment with a protein arginine N-methyltransferase 5 (PRMT5) inhibitor selected from



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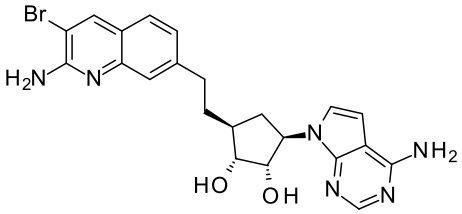

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the method comprising: evaluating a biological sample that had been obtained from the patient for the presence of a spliceosome alteration, wherein the spliceosome alteration comprises a mutation in a gene selected from the group consisting of U2AF1, RBM10 and KIAA1429, and wherein the presence of any said alteration indicates a higher likelihood for said patient to be responsive to treatment with said PRMT5 inhibitor than in the absence of any said alteration.

[0039] The present disclosure thus comprises a method of identifying a patient that is likely to be responsive to treatment with a protein arginine N-methyltransferase 5 (PRMT5) inhibitor comprising evaluating a biological sample from the patient for the presence of any of the following:

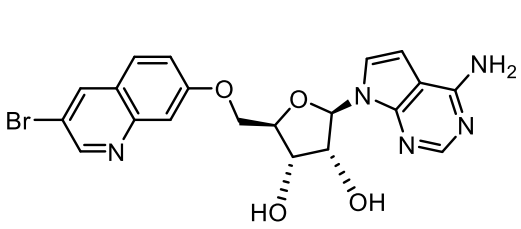
- a PIC3CA activating mutation,
- a spliceosome alteration,
- a cyclin D1 pathway amplicifation, and/or
- a WNT pathway alteration

wherein the presence of any said mutation or alteration indicates a higher likelihood for said patient to be responsive to treatment with said PRMT5 inhibitor than in the absence of any said mutation or alteration.

[0040] In an example, the spliceosome alteration comprises a mutation in a gene selected from the group consisting of U2AF1, RBM10 and KIAA1429. In a specific example, the gene is U2AF1 and the mutation is S34F. In another specific example, the gene is RBM10 and the mutation is selected from the group consisting of I696fs, I348N, G840fs. In yet another specific example, the gene is KIAA1429 and the mutation is selected from the group consisting of L837V, F1260L, D251if, T1333M, V1548L, G397A and Q962E. Other

What is claimed:

1. A method of identifying a patient that is likely to be responsive to treatment with a protein arginine N-methyltransferase 5 (PRMT5) inhibitor selected from



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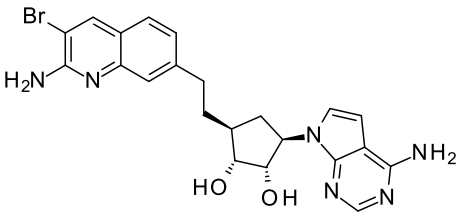

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the method comprising:

evaluating a biological sample that had been obtained from the patient for the presence of a spliceosome alteration, wherein the spliceosome alteration comprises a mutation in a gene selected from the group consisting of U2AF1, RBM10 and KIAA1429, and

wherein the presence of any said alteration indicates a higher likelihood for said patient to be responsive to treatment with said PRMT5 inhibitor than in the absence of any said alteration.

2. The method of claim 1, wherein the gene is U2AF1.

3. The method of claim 2, wherein the gene mutation results in an amino acid mutation S34F.

4. The method of claim 1, wherein the gene is RBM10 and the gene mutation results in an amino acid mutation selected from the group consisting of I696fs, I348N, G840fs.

5. The method of claim 1, wherein the gene is KIAA1429 and the gene mutation results in an amino acid mutation selected from the group consisting of L837V, F1260L, D251if, T1333M, V1548L, G397A and Q962E.

6. The method of any one of the previous claims 1-5, wherein the biological sample comprises a spliceosome alteration and the patient has NSCLC.