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(71) Applicant: SYROS PHARMACEUTICALS, INC. [US/US]; 620 Memorial Drive, Suite 300, Cambridge, Massachusetts 02139 (US).

(72) Inventors: MCKEOWN, Michael Robert; 74 Fenway, #54, Boston, Massachusetts 02115 (US). FIORE, Christopher; 620 Memorial Drive, Suite 300, Cambridge, Massachusetts 02139 (US). EATON, Matthew Lucas; 90 Putnam Avenue, #4, Cambridge, Massachusetts 02139 (US). LEE, Emily Payton; 1 Craigie Street, Apt. 35, Cambridge, Massachusetts 02138 (US). FRITZ, Christian; 620 Memorial Drive, Suite 300, Cambridge, Massachusetts 02139 (US).

(74) Agent: SHAIKH, Nishat A. et al.; Choate, Hall & Stewart LLP, Two International Place, Boston, Massachusetts 02110 (US).

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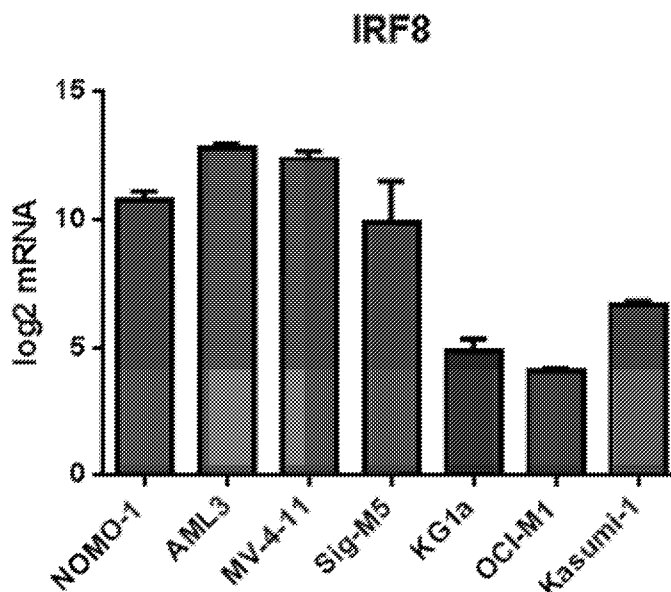


Figure 1

(57) Abstract: Described herein are methods that define cellular populations that are sensitive to RARA agonists and identify patient populations that will benefit from treatment with RARA agonists. The methods may comprise administering RARA agonists to patient populations.



SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR,  
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**AMENDED CLAIMS**  
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What is claimed is:

1. Tamibarotene for use in treating cancer in a subject, wherein the subject has a cancer that has been determined to have an *IRF8* enhancer strength equal to or above a pre-determined *IRF8* enhancer strength threshold or an *IRF8* mRNA level equal to or above a pre-determined *IRF8* mRNA threshold, or a combination thereof.
2. The tamibarotene for use of claim 1, wherein the subject has a cancer that has also been determined to have a *RARA* enhancer strength equal to or above a pre-determined *RARA* enhancer strength threshold, a *RARA* mRNA level equal to or above a pre-determined *RARA* mRNA threshold, or a combination thereof.
3. The tamibarotene for use of claim 1 or 2, wherein the subject has been selected by:
  - a. assaying a sample from the subject's cancer;
  - b. determining the strength of an *IRF8* enhancer or the level of *IRF8* mRNA, or a combination thereof, in the sample; and
  - c. selecting the subject if the *IRF8* enhancer strength is equal to or above a pre-determined *IRF8* enhancer strength threshold, or the *IRF8* mRNA level is equal to or above a pre-determined *IRF8* mRNA threshold, or a combination thereof.
4. The tamibarotene for use of claim 3, wherein the method by which the subject has been selected additionally comprises:
  - determining the strength of a *RARA* enhancer or a level of *RARA* mRNA, or a combination thereof, in the sample; and
  - selecting the subject if the *RARA* enhancer strength is equal to or above a pre-determined *RARA* enhancer strength threshold, or the *RARA* mRNA level is equal to or above a pre-determined *RARA* mRNA level threshold, or a combination thereof.
5. The tamibarotene for use of any one of claims 1-4, wherein the subject has non-APL AML or MDS.

6. The tamibarotene for use of claim 5, wherein the cancer sample is a PBMC or an enriched PBMC sample.
7. The tamibarotene for use of any one of claims 1-6, wherein the pre-determined IRF8 mRNA level threshold is a cutoff value.
8. The tamibarotene for use of claim 7, wherein the cutoff value is based on a pre-determined prevalence cutoff.
9. The tamibarotene for use of claim 8, wherein the pre-determined prevalence cutoff is between 20% and 45%.
10. The tamibarotene for use of any one of claims 2-9, wherein the pre-determined RARA mRNA level threshold is a cutoff value.
11. The tamibarotene for use of claim 10, wherein the cutoff value is set at a value that is equal to or up to 5% above the RARA mRNA level in the lowest responder in a population of test samples.
12. The tamibarotene for use of any one of claims 7-11, wherein one or both of the IRF8 mRNA level and the RARA mRNA level is determined using fluorescent hybridization, PCR, qPCR, qRT-PCR, RNA sequencing, RNA hybridization and signal amplification or northern blot.
13. The tamibarotene for use of claim 12, wherein one or both of the IRF8 mRNA level and the RARA mRNA level is determined using qPCR.