

**[1010]** As shown in FIG. 5A, a dose of 100 µg IP SMIP 28 protected guinea pigs that were infected intraperitoneally with guinea pig-adapted Ebola virus. SMIP 28 at 100 µg and at 1000 µg delayed mortality and resulted in increased survival in comparison to 10 µg IP SMIP 28 and vehicle.

**[1011]** As shown in FIG. 5B IP or IM SMIP 28 prolonged survival and resulted in an overall increase in survival. IP SMIP 28 at 100 µg delayed mortality and resulted in increased survival in comparison to R-848 and Poly I:C.

**[1012]** The data demonstrate that SMIP 28 administered intraperitoneally and intramuscularly is capable of protecting guinea pigs that have been challenged intraperitoneally and subcutaneously with guinea pig-adapted Ebola virus.

### Example 203

#### Benzonaphthyridine SMIPs Administered Intraperitoneally in Mice Induced an Immune Response

**[1013]** In the studies described below the effects of SMIPs as disclosed herein were tested. Mice were given SMIPs by intraperitoneal (IP) injection and peak cytokine concentration for particular cytokines was measured over a 24 hour period following SMIP treatment. Cytokine levels were measured for interferon gamma (IFN-γ), interleukin-10 (IL-10), the p40 (40 kDa) subunit of interleukin 12 (IL-12 p40), interleukin 1 beta (IL-1β), interleukin 5 (IL-5), interleukin 6 (IL-6), monocyte chemoattractant protein-1 (MCP-1), keratinocyte chemokine (KC), tumor necrosis factor alpha (TNF-α). To measure the ability of SMIPs to induce an immune response, groups of 3 mice were given vehicle (peanut oil) alone, SMIP 28 or R848. Peak cytokine concentration was measured over a 24-hr period.

**[1014]** As shown in FIG. 6 SMIP 28, compared to peanut oil-control, induced an immune response consisting of cytokine induction of IFN-γ, IL-12 p40, IL-1β, IL-6, MCP-1, mKC, and TNF-α. R-848 resulted in cytokine induction of IFN-γ, IL-10, IL-12 p40, IL-6, MCP-1, mKC, and TNF-α. Neither administration of SMIP 28 nor R-848, compared to peanut oil-control, resulted in a cytokine induction of IL-5. SMIP 28, compared to R-848, resulted in a significantly greater cytokine induction of IL-1β.

**[1015]** The data demonstrate that SMIP 28 is capable of stimulating cytokine production. SMIP 28 induced an immune response that induced a cytokine profile, comprising induction of IFN-γ, (IL-12 p40), IL-1β, IL-6, MCP-1, mKC, and TNF-α.

**[1016]** It is understood that the examples and aspects described herein are for illustrative purposes only and that various modifications or changes in light thereof will be suggested to persons skilled in the art and are to be included within the spirit and purview of this application and scope of the appended claims. All publications, patents, and patent applications cited herein are hereby incorporated by reference for all purposes.

1. A method of potentiating an immune response to a hemorrhagic fever virus, comprising administering to a subject a pharmaceutically effective amount of a composition comprising a benzonaphthyridine TLR7 agonist or salt, solvate, or derivative thereof.

2. A method of treating a subject who has been exposed to a hemorrhagic fever virus, comprising administering to said

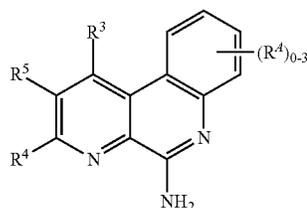
subject a pharmaceutically effective amount of a composition comprising a benzonaphthyridine TLR7 agonist or salt, solvate, or derivative thereof.

3. A method for inducing an immune response to a hemorrhagic fever virus, comprising administering to said subject an immunogenic composition comprising: (a) a benzonaphthyridine TLR7 agonist or salt, solvate, or derivative thereof, and (b) an antigen derived from a hemorrhagic fever virus.

4. (canceled)

5. (canceled)

6. The method of claim 1, wherein the benzonaphthyridine TLR7 agonist is a benzonaphthyridine compound of Formula (II) having the structure:



Formula (II)

wherein:

R<sup>3</sup> is H, halogen, C<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>2</sub>-C<sub>8</sub>alkene, C<sub>2</sub>-C<sub>8</sub>alkyne, C<sub>1</sub>-C<sub>6</sub>heteroalkyl, C<sub>1</sub>-C<sub>6</sub>haloalkyl, C<sub>1</sub>-C<sub>6</sub>alkoxy, C<sub>1</sub>-C<sub>6</sub>haloalkoxy, aryl, heteroaryl, C<sub>3</sub>-C<sub>8</sub>cycloalkyl, and

C<sub>3</sub>-C<sub>8</sub>heterocycloalkyl, wherein the C<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>1</sub>-C<sub>6</sub>heteroalkyl, C<sub>1</sub>-C<sub>6</sub>haloalkyl, C<sub>1</sub>-C<sub>6</sub>alkoxy, C<sub>1</sub>-C<sub>6</sub>haloalkoxy, C<sub>3</sub>-C<sub>8</sub>cycloalkyl, or C<sub>3</sub>-C<sub>8</sub>heterocycloalkyl groups of R<sup>3</sup> are each optionally substituted with 1 to 3 substituents independently selected from halogen, —CN, —R<sup>7</sup>, —OR<sup>8</sup>, —C(O)R<sup>8</sup>, —OC(O)R<sup>8</sup>, —C(O)OR<sup>8</sup>, —N(R<sup>9</sup>)<sub>2</sub>, —C(O)N(R<sup>9</sup>)<sub>2</sub>, —S(O)<sub>2</sub>R<sup>8</sup>, —S(O)<sub>2</sub>N(R<sup>9</sup>)<sub>2</sub> and —NR<sup>9</sup>S(O)<sub>2</sub>R<sup>8</sup>;

R<sup>4</sup> and R<sup>5</sup> are each independently selected from H, halogen, —C(O)OR<sup>7</sup>, —C(O)R<sup>7</sup>, —C(O)N(R<sup>11</sup>R<sup>12</sup>), —N(R<sup>11</sup>R<sup>12</sup>)<sub>2</sub>, —N(R<sup>9</sup>)<sub>2</sub>, —NHN(R<sup>9</sup>)<sub>2</sub>, —SR<sup>7</sup>, —(CH<sub>2</sub>)<sub>n</sub>OR<sup>7</sup>, —(CH<sub>2</sub>)<sub>n</sub>R<sup>7</sup>, —LR<sup>8</sup>, —LR<sup>10</sup>, —OLR<sup>8</sup>, —OLR<sup>10</sup>, C<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>1</sub>-C<sub>6</sub>heteroalkyl, C<sub>1</sub>-C<sub>6</sub>haloalkyl, C<sub>2</sub>-C<sub>8</sub>alkene, C<sub>2</sub>-C<sub>8</sub>alkyne, C<sub>1</sub>-C<sub>6</sub>alkoxy, C<sub>1</sub>-C<sub>6</sub>haloalkoxy, aryl, heteroaryl, C<sub>3</sub>-C<sub>8</sub>cycloalkyl, and C<sub>3</sub>-C<sub>8</sub>heterocycloalkyl, wherein the C<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>1</sub>-C<sub>6</sub>heteroalkyl, C<sub>1</sub>-C<sub>6</sub>haloalkyl, C<sub>2</sub>-C<sub>8</sub>alkene, C<sub>2</sub>-C<sub>8</sub>alkyne, C<sub>1</sub>-C<sub>6</sub>alkoxy, C<sub>1</sub>-C<sub>6</sub>haloalkoxy, aryl, heteroaryl, C<sub>3</sub>-C<sub>8</sub>cycloalkyl, and C<sub>3</sub>-C<sub>8</sub>heterocycloalkyl groups of R<sup>4</sup> and R<sup>5</sup> are each optionally substituted with 1 to 3 substituents independently selected from halogen, —CN, —NO<sub>2</sub>, —R<sup>7</sup>, —OR<sup>8</sup>, —C(O)R<sup>8</sup>, —OC(O)R<sup>8</sup>, —C(O)OR<sup>8</sup>, —N(R<sup>9</sup>)<sub>2</sub>, —P(O)(OR<sup>8</sup>)<sub>2</sub>, —OP(O)(OR<sup>8</sup>)<sub>2</sub>, —P(O)(OR<sup>10</sup>)<sub>2</sub>, —OP(O)(OR<sup>10</sup>)<sub>2</sub>, —C(O)N(R<sup>9</sup>)<sub>2</sub>, —S(O)<sub>2</sub>R<sup>8</sup>, —S(O)R<sup>8</sup>, —S(O)<sub>2</sub>N(R<sup>9</sup>)<sub>2</sub>, and —NR<sup>9</sup>S(O)<sub>2</sub>R<sup>8</sup>;

or R<sup>3</sup> and R<sup>4</sup>, or R<sup>4</sup> and R<sup>5</sup>, when present on adjacent ring atoms, can optionally be linked together to form a 5-6 membered ring, wherein the 5-6 membered ring is optionally substituted with R<sup>7</sup>;

each L is independently selected from a bond, —(O(CH<sub>2</sub>)<sub>m</sub>)—, C<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>2</sub>-C<sub>6</sub>alkenylene and