Summary

The present disclosure provides compositions which are useful as TB vaccines. The compositions provided herein comprise RNA for delivering *Mtb* antigens to a subject. The findings described herein demonstrate that RNA described herein, e.g., non-modified uridine containing mRNA (uRNA) or nucleoside modified mRNA (modRNA), expressing antigens of *Mycobacterium tuberculosis*, immunogenic variants or fragments thereof, is useful for preventing or treating tuberculosis. The RNA encoding antigens of *Mycobacterium tuberculosis*, immunogenic variants or fragments thereof is formulated and administered in a way that the antigens, variants or fragments can be produced and preferably secreted by patient cells to prevent or combat tuberculosis.

In particular, the present disclosure describes in some examples RNA components encoding antigen 85 A (Ag85A), antigen *Mtb* 72F (M72; a recombinant protein derived from two *Mtb* proteins, Mtb32A and Mtb39A; hereafter indicated as M72 only), 6 kilodalton early secretory antigenic target (ESAT6), resuscitation-promoting factor A (RpfA), resuscitation-promoting factor D (RpfD), hypoxic response protein 1 (Hrp1), virulence associated protein B47 (VapB47), and heparin-binding hemagglutinin A (HbhA). The present disclosure observes that immunization of mice with these RNA components induced strong antigen-specific T- and B-cell responses, whereby the immune response elicited by two i.m. doses given 21 days apart was higher than that elicited by a single subcutaneous immunization with BCG.

Mtb displays differential gene expression patterns during its active and dormant (non-dividing) phases (Andersen P, et al. Cold Spring Harb Perspect Med, 2014; 4(6):a018523). To prevent development of TB, there should be immunity against antigens specific for each of the various stages of *Mtb* infection. The TB vaccine candidate developed here comprising the RNA components described above is designed to induce protective immune responses against antigens specific for different stages of *Mtb* infection.

Unlike the attenuated vaccine BCG, this TB vaccine candidate does not carry the risks associated with infection and may therefore be given to people who cannot be administered live organism (such as pregnant women and immunocompromised persons).

In one aspect, the present disclosure provides for a composition or medical preparation comprising at least one RNA molecule, wherein the at least one RNA molecule encodes a set of *Mycobacterium tuberculosis* (Mtb) antigenic amino acid sequences, wherein the set of Mtb antigenic amino acid sequences comprises four or more, five or more, six or more, seven or more, or eight or more of the following: (i) an amino acid sequence comprising Ag85A, an immunogenic variant thereof, or an immunogenic fragment of the Ag85A or the immunogenic variant thereof; (ii) an amino acid sequence comprising ESAT6, an immunogenic variant thereof, or an immunogenic fragment of the ESAT6 or the immunogenic variant thereof; (iii) an amino acid sequence comprising VapB47, an immunogenic variant thereof, or an immunogenic fragment of the VapB47 or the immunogenic variant thereof; (iv) an amino acid sequence comprising Hrp1, an immunogenic variant thereof, or an immunogenic fragment of the Hrp1 or the immunogenic variant thereof; (v) an amino acid sequence comprising RpfA, an immunogenic variant thereof, or an immunogenic fragment of the RpfA or the immunogenic variant thereof; (vi) an amino acid sequence comprising RpfD, an immunogenic variant thereof, or an immunogenic fragment of the RpfD or the immunogenic variant thereof; (vii) an amino acid sequence comprising Mtb32a, an immunogenic variant thereof, or an immunogenic fragment of the Mtb32a or the immunogenic variant thereof; (viii) an amino acid sequence comprising Mtb39a, an immunogenic variant thereof, or an immunogenic fragment of the Mtb39a or the immunogenic variant thereof; and (ix) an amino acid sequence comprising HbhA, an immunogenic variant thereof, or an immunogenic fragment of the HbhA or the immunogenic variant thereof.

In one example, the disclosure provides a composition or medical preparation comprising at least one RNA molecule, wherein the at least one RNA molecule encodes a set of antigenic amino acid sequences, wherein the set of antigenic amino acid sequences comprises (i) at least one Mtb antigen from the acute phase of the Mtb life cycle, an immunogenic variant thereof, or an immunogenic fragment of the Mtb antigen or the immunogenic variant thereof, (ii) at least one Mtb antigen from the latent phase of the Mtb life cycle, an immunogenic variant thereof, or an immunogenic fragment of the Mtb antigen or the immunogenic variant thereof, and (iii) at least one Mtb antigen from the resuscitation phase of the Mtb life cycle, an immunogenic variant thereof, or an immunogenic fragment of the Mtb antigen or the immunogenic variant thereof.

In some examples, the at least one Mtb antigen from the acute phase of the Mtb life cycle, an immunogenic variant thereof, or an immunogenic fragment of the Mtb antigen or the immunogenic variant thereof comprises

(i) an amino acid sequence comprising Ag85A, an immunogenic variant thereof, or an immunogenic fragment of the Ag85A or the immunogenic variant thereof; and/or

(ii) an amino acid sequence comprising ESAT6, an immunogenic variant thereof, or an immunogenic fragment of the ESAT6 or the immunogenic variant thereof.

PepA (component of M72 fusion protein) has been reported to be expressed during the acute phase of Mtb infection. Accordingly, the at least one Mtb antigen from the acute phase of the Mtb life cycle, an immunogenic variant thereof, or an immunogenic fragment of the Mtb antigen or the immunogenic variant thereof comprises (optionally in addition to one or more of those described above) an amino acid sequence comprising M72, an immunogenic variant thereof, or an immunogenic fragment of the M72 or the immunogenic variant thereof.

In some examples, the at least one Mtb antigen from the latent phase of the Mtb life cycle, an immunogenic variant thereof, or an immunogenic fragment of the Mtb antigen or the immunogenic variant thereof comprises

(i) an amino acid sequence comprising VapB47, an immunogenic variant thereof, or an immunogenic fragment of the VapB47 or the immunogenic variant thereof; and/or

(iv) an amino acid sequence comprising Hrp1, an immunogenic variant thereof, or an immunogenic fragment of the Hrp1 or the immunogenic variant thereof.

In some examples, the at least one Mtb antigen from the resuscitation phase of the Mtb life cycle, an immunogenic variant thereof, or an immunogenic fragment of the Mtb antigen or the immunogenic variant thereof comprises

(i) an amino acid sequence comprising RpfA, an immunogenic variant thereof, or an immunogenic fragment of the RpfA or the immunogenic variant thereof; and/or

(vi) an amino acid sequence comprising RpfD, an immunogenic variant thereof, or an immunogenic fragment of the RpfD or the immunogenic variant thereof.

In one example, the disclosure provides a composition or medical preparation comprising at least one RNA molecule, wherein the at least one RNA molecule encodes a set of antigenic amino acid sequences, wherein each antigenic amino acid sequence comprises an Mtb antigen, an immunogenic variant thereof, or an immunogenic fragment of the Mtb antigen or the immunogenic variant thereof and each RNA molecule encodes at least two of the antigenic amino acid sequences as fusion molecule.

In some examples, each RNA molecule encodes two of the antigenic amino acid sequences as fusion molecule.

In some examples, the Mtb antigens, immunogenic variants, or immunogenic fragments in a fusion molecule are not linked by a linker comprising a sequence which is heterologous to the Mtb antigens, immunogenic variants, or immunogenic fragments.

In some examples, the set of antigenic amino acid sequences comprises two or more, three or more, four or more, five or more, six or more, seven or more, or eight or more or all of the following:

(i) an amino acid sequence comprising Ag85A, an immunogenic variant thereof, or an immunogenic fragment of the Ag85A or the immunogenic variant thereof;

(ii) an amino acid sequence comprising ESAT6, an immunogenic variant thereof, or an immunogenic fragment of the ESAT6 or the immunogenic variant thereof;

(iii) an amino acid sequence comprising VapB47, an immunogenic variant thereof, or an immunogenic fragment of the VapB47 or the immunogenic variant thereof;

(iv) an amino acid sequence comprising Hrp1, an immunogenic variant thereof, or an immunogenic fragment of the Hrp1 or the immunogenic variant thereof;

(v) an amino acid sequence comprising RpfA, an immunogenic variant thereof, or an immunogenic fragment of the RpfA or the immunogenic variant thereof;

(vi) an amino acid sequence comprising RpfD, an immunogenic variant thereof, or an immunogenic fragment of the RpfD or the immunogenic variant thereof;

(vii) an amino acid sequence comprising Mtb32a, an immunogenic variant thereof, or an immunogenic fragment of the Mtb32a or the immunogenic variant thereof;

(viii) an amino acid sequence comprising Mtb39a, an immunogenic variant thereof, or an immunogenic fragment of the Mtb39a or the immunogenic variant thereof; and

(ix) an amino acid sequence comprising HbhA, an immunogenic variant thereof, or an immunogenic fragment of the HbhA or the immunogenic variant thereof.

In one example, the disclosure provides a composition or medical preparation comprising at least one RNA molecule, wherein the at least one RNA molecule encodes at least one antigenic amino acid sequence comprising an Mtb antigen, an immunogenic variant thereof, or an immunogenic fragment of the Mtb antigen or the immunogenic variant thereof,

wherein the RNA encodes an amino acid sequence comprising a secretory signal peptide at the N-terminus of the encoded amino acid sequence and wherein the secretory signal peptide is not endogenous to the Mtb antigen. In some examples, the secretory signal peptide is of human origin. In some examples, the secretory signal peptide is not of human origin.

In some examples,

(i) the secretory signal peptide comprises the amino acid sequence of positions 1 to 26 of SEQ ID NO: 44, an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 1 to 26 of SEQ ID NO: 44, or a functional fragment of the amino acid sequence of positions 1 to 26 of SEQ ID NO: 44, or the amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 1 to 26 of SEQ ID NO: 44; and/or

(ii) the RNA sequence encoding the secretory signal peptide comprises the nucleotide sequence of positions 54 to 131 of SEQ ID NO: 43, a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 54 to 131 of SEQ ID NO: 43, or a fragment of the nucleotide sequence of positions 54 to 131 of SEQ ID NO: 43, or the nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 54 to 131 of SEQ ID NO: 43.

In some examples,

(i) the secretory signal peptide comprises the amino acid sequence of positions 1 to 25 of SEQ ID NO: 63, an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 1 to 25 of SEQ ID NO: 63, or a functional fragment of the amino acid sequence of positions 1 to 25 of SEQ ID NO: 63, or the amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 1 to 25 of SEQ ID NO: 63; and/or

(ii) the RNA sequence encoding the secretory signal peptide comprises the nucleotide sequence of positions 1 to 75 of SEQ ID NO: 62, a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 1 to 75 of SEQ ID NO: 62, or a fragment of the nucleotide sequence of positions 1 to 75 of SEQ ID NO: 62, or the nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 1 to 75 of SEQ ID NO: 62.

In some examples,

(i) the secretory signal peptide comprises the amino acid sequence of positions 1 to 13 of SEQ ID NO: 71, an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 1 to 13 of SEQ ID NO: 71, or a functional fragment of the amino acid sequence of positions 1 to 13 of SEQ ID NO: 71, or the amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 1 to 13 of SEQ ID NO: 71; and/or

(ii) the RNA sequence encoding the secretory signal peptide comprises the nucleotide sequence of positions 1 to 39 of SEQ ID NO: 70, a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 1 to 39 of SEQ ID NO: 70, or a fragment of the nucleotide sequence of positions 1 to 39 of SEQ ID NO: 70, or the nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 1 to 39 of SEQ ID NO: 70.

In one example, the disclosure provides a composition or medical preparation comprising at least one RNA molecule, wherein the at least one RNA molecule encodes at least one antigenic amino acid sequence comprising an Mtb antigen, an immunogenic variant thereof, or an immunogenic fragment of the Mtb antigen or the immunogenic variant thereof, wherein the RNA comprises modified uridines and/or is formulated in lipid nanoparticles.

In some examples, the at least one RNA molecule encodes two or more, three or more, four or more, five or more, six or more, seven or more, or eight or more of the following:

(i) an amino acid sequence comprising Ag85A, an immunogenic variant thereof, or an immunogenic fragment of the Ag85A or the immunogenic variant thereof;

(ii) an amino acid sequence comprising ESAT6, an immunogenic variant thereof, or an immunogenic fragment of the ESAT6 or the immunogenic variant thereof;

(iii) an amino acid sequence comprising VapB47, an immunogenic variant thereof, or an immunogenic fragment of the VapB47 or the immunogenic variant thereof;

(iv) an amino acid sequence comprising Hrp1, an immunogenic variant thereof, or an immunogenic fragment of the Hrp1 or the immunogenic variant thereof;

(v) an amino acid sequence comprising RpfA, an immunogenic variant thereof, or an immunogenic fragment of the RpfA or the immunogenic variant thereof;

(vi) an amino acid sequence comprising RpfD, an immunogenic variant thereof, or an immunogenic fragment of the RpfD or the immunogenic variant thereof;

(vii) an amino acid sequence comprising Mtb32a, an immunogenic variant thereof, or an immunogenic fragment of the Mtb32a or the immunogenic variant thereof;

(viii) an amino acid sequence comprising Mtb39a, an immunogenic variant thereof, or an immunogenic fragment of the Mtb39a or the immunogenic variant thereof; and

(ix) an amino acid sequence comprising HbhA, an immunogenic variant thereof, or an immunogenic fragment of the HbhA or the immunogenic variant thereof.

In some examples, the at least one RNA molecule encodes the following amino acid sequences:

(i) an amino acid sequence comprising Ag85A, an immunogenic variant thereof, or an immunogenic fragment of the Ag85A or the immunogenic variant thereof;

(ii) an amino acid sequence comprising ESAT6, an immunogenic variant thereof, or an immunogenic fragment of the ESAT6 or the immunogenic variant thereof;

(iii) an amino acid sequence comprising VapB47, an immunogenic variant thereof, or an immunogenic fragment of the VapB47 or the immunogenic variant thereof;

(iv) an amino acid sequence comprising Hrp1, an immunogenic variant thereof, or an immunogenic fragment of the Hrp1 or the immunogenic variant thereof;

(v) an amino acid sequence comprising RpfA, an immunogenic variant thereof, or an immunogenic fragment of the RpfA or the immunogenic variant thereof;

(vi) an amino acid sequence comprising RpfD, an immunogenic variant thereof, or an immunogenic fragment of the RpfD or the immunogenic variant thereof;

(vii) an amino acid sequence comprising Mtb32a, an immunogenic variant thereof, or an immunogenic fragment of the Mtb32a or the immunogenic variant thereof;

(viii) an amino acid sequence comprising Mtb39a, an immunogenic variant thereof, or an immunogenic fragment of the Mtb39a or the immunogenic variant thereof; and

(ix) an amino acid sequence comprising HbhA, an immunogenic variant thereof, or an immunogenic fragment of the HbhA or the immunogenic variant thereof.

In one example, the disclosure provides a composition or medical preparation comprising at least one RNA molecule, wherein the at least one RNA molecule encodes two or more, three or more, four or more, five or more, six or more, seven or more, eight or more, or all of the following amino acid sequences:

(i) an amino acid sequence comprising Ag85A, an immunogenic variant thereof, or an immunogenic fragment of the Ag85A or the immunogenic variant thereof;

(ii) an amino acid sequence comprising ESAT6, an immunogenic variant thereof, or an immunogenic fragment of the ESAT6 or the immunogenic variant thereof;

(iii) an amino acid sequence comprising VapB47, an immunogenic variant thereof, or an immunogenic fragment of the VapB47 or the immunogenic variant thereof;

(iv) an amino acid sequence comprising Hrp1, an immunogenic variant thereof, or an immunogenic fragment of the Hrp1 or the immunogenic variant thereof;

(v) an amino acid sequence comprising RpfA, an immunogenic variant thereof, or an immunogenic fragment of the RpfA or the immunogenic variant thereof;

(vi) an amino acid sequence comprising RpfD, an immunogenic variant thereof, or an immunogenic fragment of the RpfD or the immunogenic variant thereof;

(vii) an amino acid sequence comprising Mtb32a, an immunogenic variant thereof, or an immunogenic fragment of the Mtb32a or the immunogenic variant thereof;

(viii) an amino acid sequence comprising Mtb39a, an immunogenic variant thereof, or an immunogenic fragment of the Mtb39a or the immunogenic variant thereof; and

(ix) an amino acid sequence comprising HbhA, an immunogenic variant thereof, or an immunogenic fragment of the HbhA or the immunogenic variant thereof.

In some examples, the amino acid sequence comprising Mtb32a, an immunogenic variant thereof, or an immunogenic fragment of the Mtb32a or the immunogenic variant thereof and the amino acid sequence comprising Mtb39a, an immunogenic variant thereof, or an immunogenic fragment of the Mtb39a or the immunogenic variant thereof are present as a fusion protein.

In some examples, the fusion protein comprises an amino acid sequence comprising M72, an immunogenic variant thereof, or an immunogenic fragment of the M72 or the immunogenic variant thereof.

In some examples, the at least one RNA molecule encodes two or more, three or more, four or more, five or more, six or more, seven or more, or all of the following amino acid sequences:

(i) an amino acid sequence comprising Ag85A, an immunogenic variant thereof, or an immunogenic fragment of the Ag85A or the immunogenic variant thereof;

(ii) an amino acid sequence comprising ESAT6, an immunogenic variant thereof, or an immunogenic fragment of the ESAT6 or the immunogenic variant thereof;

(iii) an amino acid sequence comprising VapB47, an immunogenic variant thereof, or an immunogenic fragment of the VapB47 or the immunogenic variant thereof;

(iv) an amino acid sequence comprising Hrp1, an immunogenic variant thereof, or an immunogenic fragment of the Hrp1 or the immunogenic variant thereof;

(v) an amino acid sequence comprising RpfA, an immunogenic variant thereof, or an immunogenic fragment of the RpfA or the immunogenic variant thereof;

(vi) an amino acid sequence comprising RpfD, an immunogenic variant thereof, or an immunogenic fragment of the RpfD or the immunogenic variant thereof;

(vii) an amino acid sequence comprising M72, an immunogenic variant thereof, or an immunogenic fragment of the M72 or the immunogenic variant thereof; and

(viii) an amino acid sequence comprising HbhA, an immunogenic variant thereof, or an immunogenic fragment of the HbhA or the immunogenic variant thereof.

In one example, the disclosure provides a composition or medical preparation comprising at least one RNA molecule, wherein the at least one RNA molecule encodes two or more, three or more, four or more, five or more, six or more, seven or more, or all of the following amino acid sequences:

(i) an amino acid sequence comprising Ag85A, an immunogenic variant thereof, or an immunogenic fragment of the Ag85A or the immunogenic variant thereof;

(ii) an amino acid sequence comprising ESAT6, an immunogenic variant thereof, or an immunogenic fragment of the ESAT6 or the immunogenic variant thereof;

(iii) an amino acid sequence comprising VapB47, an immunogenic variant thereof, or an immunogenic fragment of the VapB47 or the immunogenic variant thereof;

(iv) an amino acid sequence comprising Hrp1, an immunogenic variant thereof, or an immunogenic fragment of the Hrp1 or the immunogenic variant thereof;

(v) an amino acid sequence comprising RpfA, an immunogenic variant thereof, or an immunogenic fragment of the RpfA or the immunogenic variant thereof;

(vi) an amino acid sequence comprising RpfD, an immunogenic variant thereof, or an immunogenic fragment of the RpfD or the immunogenic variant thereof;

(vii) an amino acid sequence comprising M72, an immunogenic variant thereof, or an immunogenic fragment of the M72 or the immunogenic variant thereof; and

(viii) an amino acid sequence comprising HbhA, an immunogenic variant thereof, or an immunogenic fragment of the HbhA or the immunogenic variant thereof.

In some examples,

(i) the amino acid sequence comprising Ag85A, an immunogenic variant thereof, or an immunogenic fragment of the Ag85A or the immunogenic variant thereof comprises the amino acid sequence of positions 2 to 298 of SEQ ID NO: 20, an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 2 to 298 of SEQ ID NO: 20, or an immunogenic fragment of the amino acid sequence of positions 2 to 298 of SEQ ID NO: 20, or the amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 2 to 298 of SEQ ID NO: 20; and/or

(ii) the RNA sequence encoding the amino acid sequence comprising Ag85A, an immunogenic variant thereof, or an immunogenic fragment of the Ag85A or the immunogenic variant thereof comprises the nucleotide sequence of positions 4 to 894 of SEQ ID NO: 19, a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 4 to 894 of SEQ ID NO: 19, or a fragment of the nucleotide sequence of positions 4 to 894 of SEQ ID NO: 19, or the nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 4 to 894 of SEQ ID NO: 19.

In some examples,

(i) the amino acid sequence comprising Ag85A, an immunogenic variant thereof, or an immunogenic fragment of the Ag85A or the immunogenic variant thereof comprises the amino acid sequence of positions 27 to 323 of SEQ ID NO: 44, an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 27 to 323 of SEQ ID NO: 44, or an immunogenic fragment of the amino acid sequence of positions 27 to 323 of SEQ ID NO: 44, or the amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 27 to 323 of SEQ ID NO: 44; and/or

(ii) the RNA sequence encoding the amino acid sequence comprising Ag85A, an immunogenic variant thereof, or an immunogenic fragment of the Ag85A or the immunogenic variant thereof comprises the nucleotide sequence of positions 132 to 1022 of SEQ ID NO: 43, a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 132 to 1022 of SEQ ID NO: 43, or a fragment of the nucleotide sequence of positions 132 to 1022 of SEQ ID NO: 43, or the nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 132 to 1022 of SEQ ID NO: 43.

In some examples,

(i) the amino acid sequence comprising ESAT6, an immunogenic variant thereof, or an immunogenic fragment of the ESAT6 or the immunogenic variant thereof comprises the amino acid sequence of positions 2 to 95 of SEQ ID NO: 4, an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino

acid sequence of positions 2 to 95 of SEQ ID NO: 4, or an immunogenic fragment of the amino acid sequence of positions 2 to 95 of SEQ ID NO: 4, or the amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 2 to 95 of SEQ ID NO: 4; and/or

(ii) the RNA sequence encoding the amino acid sequence comprising ESAT6, an immunogenic variant thereof, or an immunogenic fragment of the ESAT6 or the immunogenic variant thereof comprises the nucleotide sequence of positions 4 to 285 of SEQ ID NO: 21, a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 4 to 285 of SEQ ID NO: 21, or a fragment of the nucleotide sequence of positions 4 to 285 of SEQ ID NO: 21, or the nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 4 to 285 of SEQ ID NO: 21.

In some examples,

(i) the amino acid sequence comprising ESAT6, an immunogenic variant thereof, or an immunogenic fragment of the ESAT6 or the immunogenic variant thereof comprises the amino acid sequence of positions 27 to 120 of SEQ ID NO: 46, an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 27 to 120 of SEQ ID NO: 46, or an immunogenic fragment of the amino acid sequence of positions 27 to 120 of SEQ ID NO: 46, or the amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 27 to 120 of SEQ ID NO: 46; and/or

(ii) the RNA sequence encoding the amino acid sequence comprising ESAT6, an immunogenic variant thereof, or an immunogenic fragment of the ESAT6 or the immunogenic variant thereof comprises the nucleotide sequence of positions 132 to 413 of SEQ ID NO: 45, a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 132 to 413 of SEQ ID NO: 45, or a fragment of the nucleotide sequence of positions 132 to 413 of SEQ ID NO: 45, or the nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 132 to 413 of SEQ ID NO: 45.

In some examples,

(i) the amino acid sequence comprising VapB47, an immunogenic variant thereof, or an immunogenic fragment of the VapB47 or the immunogenic variant thereof comprises the amino acid sequence of positions 2 to 99 of SEQ ID NO: 6, an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 2 to 99 of SEQ ID NO: 6, or an immunogenic fragment of the amino acid sequence of positions 2 to 99 of SEQ ID NO: 6, or the amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 2 to 99 of SEQ ID NO: 6; and/or

(ii) the RNA sequence encoding the amino acid sequence comprising VapB47, an immunogenic variant thereof, or an immunogenic fragment of the VapB47 or the immunogenic variant thereof comprises the nucleotide sequence of positions 4 to 297 of SEQ ID NO: 22, a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 4 to 297 of SEQ ID NO: 22, or a fragment of the nucleotide sequence of positions 4 to 297 of SEQ ID NO: 22, or the nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 4 to 297 of SEQ ID NO: 22.

In some examples,

(i) the amino acid sequence comprising VapB47, an immunogenic variant thereof, or an immunogenic fragment of the VapB47 or the immunogenic variant thereof comprises the amino acid sequence of positions 749 to 846 of SEQ ID NO: 52, an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 749 to 846 of SEQ ID NO: 52, or an immunogenic fragment of the amino acid sequence of positions 749 to 846 of SEQ ID NO: 52, or the amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 749 to 846 of SEQ ID NO: 52; and/or

(ii) the RNA sequence encoding the amino acid sequence comprising VapB47, an immunogenic variant thereof, or an immunogenic fragment of the VapB47 or the immunogenic variant thereof comprises the nucleotide sequence of

positions 2298 to 2591 of SEQ ID NO: 51, a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 2298 to 2591 of SEQ ID NO: 51, or a fragment of the nucleotide sequence of positions 2298 to 2591 of SEQ ID NO: 51, or the nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 2298 to 2591 of SEQ ID NO: 51.

In some examples,

(i) the amino acid sequence comprising Hrp1, an immunogenic variant thereof, or an immunogenic fragment of the Hrp1 or the immunogenic variant thereof comprises the amino acid sequence of positions 2 to 143 of SEQ ID NO: 8, an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 2 to 143 of SEQ ID NO: 8, or an immunogenic fragment of the amino acid sequence of positions 2 to 143 of SEQ ID NO: 8, or the amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 2 to 143 of SEQ ID NO: 8; and/or

(ii) the RNA sequence encoding the amino acid sequence comprising Hrp1, an immunogenic variant thereof, or an immunogenic fragment of the Hrp1 or the immunogenic variant thereof comprises the nucleotide sequence of positions 4 to 429 of SEQ ID NO: 23, a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 4 to 429 of SEQ ID NO: 23, or a fragment of the nucleotide sequence of positions 4 to 429 of SEQ ID NO: 23, or the nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 4 to 429 of SEQ ID NO: 23.

In some examples,

(i) the amino acid sequence comprising Hrp1, an immunogenic variant thereof, or an immunogenic fragment of the Hrp1 or the immunogenic variant thereof comprises the amino acid sequence of positions 324 to 465 of SEQ ID NO: 44, an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 324 to 465 of SEQ ID NO: 44, or an immunogenic fragment of the amino acid sequence of positions 324 to 465 of SEQ ID NO: 44, or the amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 324 to 465 of SEQ ID NO: 44; and/or

(ii) the RNA sequence encoding the amino acid sequence comprising Hrp1, an immunogenic variant thereof, or an immunogenic fragment of the Hrp1 or the immunogenic variant thereof comprises the nucleotide sequence of positions 1023 to 1448 of SEQ ID NO: 43, a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 1023 to 1448 of SEQ ID NO: 43, or a fragment of the nucleotide sequence of positions 1023 to 1448 of SEQ ID NO: 43, or the nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 1023 to 1448 of SEQ ID NO: 43.

In some examples,

(i) the amino acid sequence comprising RpfA, an immunogenic variant thereof, or an immunogenic fragment of the RpfA or the immunogenic variant thereof comprises the amino acid sequence of positions 2 to 407 of SEQ ID NO: 10, an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 2 to 407 of SEQ ID NO: 10, or an immunogenic fragment of the amino acid sequence of positions 2 to 407 of SEQ ID NO: 10, or the amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 2 to 407 of SEQ ID NO: 10; and/or

(ii) the RNA sequence encoding the amino acid sequence comprising RpfA, an immunogenic variant thereof, or an immunogenic fragment of the RpfA or the immunogenic variant thereof comprises the nucleotide sequence of positions 4 to 1221 of SEQ ID NO: 24, a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 4 to 1221 of SEQ ID NO: 24, or a fragment of the nucleotide

sequence of positions 4 to 1221 of SEQ ID NO: 24, or the nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 4 to 1221 of SEQ ID NO: 24.

In some examples,

(i) the amino acid sequence comprising RpfA, an immunogenic variant thereof, or an immunogenic fragment of the RpfA or the immunogenic variant thereof comprises the amino acid sequence of positions 27 to 432 of SEQ ID NO: 48, an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 27 to 432 of SEQ ID NO: 48, or an immunogenic fragment of the amino acid sequence of positions 27 to 432 of SEQ ID NO: 48, or the amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 27 to 432 of SEQ ID NO: 48; and/or

(ii) the RNA sequence encoding the amino acid sequence comprising RpfA, an immunogenic variant thereof, or an immunogenic fragment of the RpfA or the immunogenic variant thereof comprises the nucleotide sequence of positions 132 to 1349 of SEQ ID NO: 47, a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 132 to 1349 of SEQ ID NO: 47, or a fragment of the nucleotide sequence of positions 132 to 1349 of SEQ ID NO: 47, or the nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 132 to 1349 of SEQ ID NO: 47.

In some examples,

(i) the amino acid sequence comprising RpfD, an immunogenic variant thereof, or an immunogenic fragment of the RpfD or the immunogenic variant thereof comprises the amino acid sequence of positions 2 to 154 of SEQ ID NO: 12, an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 2 to 154 of SEQ ID NO: 12, or an immunogenic fragment of the amino acid sequence of positions 2 to 154 of SEQ ID NO: 12, or the amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 2 to 154 of SEQ ID NO: 12; and/or

(ii) the RNA sequence encoding the amino acid sequence comprising RpfD, an immunogenic variant thereof, or an immunogenic fragment of the RpfD or the immunogenic variant thereof comprises the nucleotide sequence of positions 4 to 462 of SEQ ID NO: 25, a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 4 to 462 of SEQ ID NO: 25, or a fragment of the nucleotide sequence of positions 4 to 462 of SEQ ID NO: 25, or the nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 4 to 462 of SEQ ID NO: 25.

In some examples,

(i) the amino acid sequence comprising RpfD, an immunogenic variant thereof, or an immunogenic fragment of the RpfD or the immunogenic variant thereof comprises the amino acid sequence of positions 121 to 273 of SEQ ID NO: 46, an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 121 to 273 of SEQ ID NO: 46, or an immunogenic fragment of the amino acid sequence of positions 121 to 273 of SEQ ID NO: 46, or the amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 121 to 273 of SEQ ID NO: 46; and/or

(ii) the RNA sequence encoding the amino acid sequence comprising RpfD, an immunogenic variant thereof, or an immunogenic fragment of the RpfD or the immunogenic variant thereof comprises the nucleotide sequence of positions 414 to 872 of SEQ ID NO: 45, a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 414 to 872 of SEQ ID NO: 45, or a fragment of the nucleotide sequence of positions 414 to 872 of SEQ ID NO: 45, or the nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 414 to 872 of SEQ ID NO: 45.

In some examples,

(i) the amino acid sequence comprising M72, an immunogenic variant thereof, or an immunogenic fragment of the M72 or the immunogenic variant thereof comprises the amino acid sequence of positions 2 to 723 of SEQ ID NO:

29, an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 2 to 723 of SEQ ID NO: 29, or an immunogenic fragment of the amino acid sequence of positions 2 to 723 of SEQ ID NO: 29, or the amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 2 to 723 of SEQ ID NO: 29; and/or

(ii) the RNA sequence encoding the amino acid sequence comprising M72, an immunogenic variant thereof, or an immunogenic fragment of the M72 or the immunogenic variant thereof comprises the nucleotide sequence of positions 4 to 2169 of SEQ ID NO: 28, a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 4 to 2169 of SEQ ID NO: 28, or a fragment of the nucleotide sequence of positions 4 to 2169 of SEQ ID NO: 28, or the nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 4 to 2169 of SEQ ID NO: 28.

In some examples,

(i) the amino acid sequence comprising M72, an immunogenic variant thereof, or an immunogenic fragment of the M72 or the immunogenic variant thereof comprises the amino acid sequence of positions 27 to 748 of SEQ ID NO: 52, an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 27 to 748 of SEQ ID NO: 52, or an immunogenic fragment of the amino acid sequence of positions 27 to 748 of SEQ ID NO: 52, or the amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 27 to 748 of SEQ ID NO: 52; and/or

(ii) the RNA sequence encoding the amino acid sequence comprising M72, an immunogenic variant thereof, or an immunogenic fragment of the M72 or the immunogenic variant thereof comprises the nucleotide sequence of positions 132 to 2297 of SEQ ID NO: 51, a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 132 to 2297 of SEQ ID NO: 51, or a fragment of the nucleotide sequence of positions 132 to 2297 of SEQ ID NO: 51, or the nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 132 to 2297 of SEQ ID NO: 51.

In some examples,

(i) the amino acid sequence comprising HbhA, an immunogenic variant thereof, or an immunogenic fragment of the HbhA or the immunogenic variant thereof comprises the amino acid sequence of positions 2 to 199 of SEQ ID NO: 18, an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 2 to 199 of SEQ ID NO: 18, or an immunogenic fragment of the amino acid sequence of positions 2 to 199 of SEQ ID NO: 18, or the amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 2 to 199 of SEQ ID NO: 18; and/or

(ii) the RNA sequence encoding the amino acid sequence comprising HbhA, an immunogenic variant thereof, or an immunogenic fragment of the HbhA or the immunogenic variant thereof comprises the nucleotide sequence of positions 4 to 597 of SEQ ID NO: 30, a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 4 to 597 of SEQ ID NO: 30, or a fragment of the nucleotide sequence of positions 4 to 597 of SEQ ID NO: 30, or the nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 4 to 597 of SEQ ID NO: 30.

In some examples,

(i) the amino acid sequence comprising HbhA, an immunogenic variant thereof, or an immunogenic fragment of the HbhA or the immunogenic variant thereof comprises the amino acid sequence of positions 433 to 630 of SEQ ID NO: 48, an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 433 to 630 of SEQ ID NO: 48, or an immunogenic fragment of the amino acid sequence of positions 433 to 630 of SEQ ID NO: 48, or the amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 433 to 630 of SEQ ID NO: 48; and/or

(ii) the RNA sequence encoding the amino acid sequence comprising HbhA, an immunogenic variant thereof, or an immunogenic fragment of the HbhA or the immunogenic variant thereof comprises the nucleotide sequence of positions 1350 to 1943 of SEQ ID NO: 47, a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 1350 to 1943 of SEQ ID NO: 47, or a fragment of the nucleotide sequence of positions 1350 to 1943 of SEQ ID NO: 47, or the nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 1350 to 1943 of SEQ ID NO: 47.

In some examples, the composition or medical preparation comprises:

(i) an RNA molecule encoding an amino acid sequence comprising Ag85A, an immunogenic variant thereof, or an immunogenic fragment of the Ag85A or the immunogenic variant thereof and Hrp1, an immunogenic variant thereof, or an immunogenic fragment of the Hrp1 or the immunogenic variant thereof;

(ii) an RNA molecule encoding an amino acid sequence comprising ESAT6, an immunogenic variant thereof, or an immunogenic fragment of the ESAT6 or the immunogenic variant thereof and RpfD, an immunogenic variant thereof, or an immunogenic fragment of the RpfD or the immunogenic variant thereof;

(iii) an RNA molecule encoding an amino acid sequence comprising RpfA, an immunogenic variant thereof, or an immunogenic fragment of the RpfA or the immunogenic variant thereof and HbhA, an immunogenic variant thereof, or an immunogenic fragment of the HbhA or the immunogenic variant thereof; and

(iv) an RNA molecule encoding an amino acid sequence comprising M72, an immunogenic variant thereof, or an immunogenic fragment of the M72 or the immunogenic variant thereof and VapB47, an immunogenic variant thereof, or an immunogenic fragment of the VapB47 or the immunogenic variant thereof.

In some examples,

(i) the amino acid sequence comprising Ag85A, an immunogenic variant thereof, or an immunogenic fragment of the Ag85A or the immunogenic variant thereof and Hrp1, an immunogenic variant thereof, or an immunogenic fragment of the Hrp1 or the immunogenic variant thereof comprises the amino acid sequence of positions 27 to 465 of SEQ ID NO: 44, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 27 to 465 of SEQ ID NO: 44; and/or

(ii) the RNA sequence encoding the amino acid sequence comprising Ag85A, an immunogenic variant thereof, or an immunogenic fragment of the Ag85A or the immunogenic variant thereof and Hrp1, an immunogenic variant thereof, or an immunogenic fragment of the Hrp1 or the immunogenic variant thereof comprises the nucleotide sequence of positions 132 to 1448 of SEQ ID NO: 43, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 132 to 1448 of SEQ ID NO: 43.

In some examples,

(i) the amino acid sequence comprising ESAT6, an immunogenic variant thereof, or an immunogenic fragment of the ESAT6 or the immunogenic variant thereof and RpfD, an immunogenic variant thereof, or an immunogenic fragment of the RpfD or the immunogenic variant thereof comprises the amino acid sequence of positions 27 to 273 of SEQ ID NO: 46, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 27 to 273 of SEQ ID NO: 46; and/or

(ii) the RNA sequence encoding the amino acid sequence comprising ESAT6, an immunogenic variant thereof, or an immunogenic fragment of the ESAT6 or the immunogenic variant thereof and RpfD, an immunogenic variant thereof, or an immunogenic fragment of the RpfD or the immunogenic variant thereof comprises the nucleotide sequence of positions 132 to 872 of SEQ ID NO: 45, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 132 to 872 of SEQ ID NO: 45.

In some examples,

(i) the amino acid sequence comprising RpfA, an immunogenic variant thereof, or an immunogenic fragment of the RpfA or the immunogenic variant thereof and HbhA, an immunogenic variant thereof, or an immunogenic fragment of the HbhA or the immunogenic variant thereof comprises the amino acid sequence of positions 27 to 630 of SEQ ID NO: 48, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 27 to 630 of SEQ ID NO: 48; and/or

(ii) the RNA sequence encoding the amino acid sequence comprising RpfA, an immunogenic variant thereof, or an immunogenic fragment of the RpfA or the immunogenic variant thereof and HbhA, an immunogenic variant thereof, or an immunogenic fragment of the HbhA or the immunogenic variant thereof comprises the nucleotide sequence of positions 132 to 1943 of SEQ ID NO: 47, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 132 to 1943 of SEQ ID NO: 47.

In some examples,

(i) the amino acid sequence comprising M72, an immunogenic variant thereof, or an immunogenic fragment of the M72 or the immunogenic variant thereof and VapB47, an immunogenic variant thereof, or an immunogenic fragment of the VapB47 or the immunogenic variant thereof comprises the amino acid sequence of positions 27 to 846 of SEQ ID NO: 52, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 27 to 846 of SEQ ID NO: 52; and/or

(ii) the RNA sequence encoding the amino acid sequence comprising M72, an immunogenic variant thereof, or an immunogenic fragment of the M72 or the immunogenic variant thereof and VapB47, an immunogenic variant thereof, or an immunogenic fragment of the VapB47 or the immunogenic variant thereof comprises the nucleotide sequence of positions 132 to 2591 of SEQ ID NO: 51, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 132 to 2591 of SEQ ID NO: 51.

In some examples,

(i) the amino acid sequence comprising Ag85A, an immunogenic variant thereof, or an immunogenic fragment of the Ag85A or the immunogenic variant thereof and Hrp1, an immunogenic variant thereof, or an immunogenic fragment of the Hrp1 or the immunogenic variant thereof comprises the amino acid sequence of SEQ ID NO: 44, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 44; and/or

(ii) (a) the RNA sequence encoding the amino acid sequence comprising Ag85A, an immunogenic variant thereof, or an immunogenic fragment of the Ag85A or the immunogenic variant thereof and Hrp1, an immunogenic variant thereof, or an immunogenic fragment of the Hrp1 or the immunogenic variant thereof comprises the nucleotide sequence of positions 54 to 1448 of SEQ ID NO: 43, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 54 to 1448 of SEQ ID NO: 43; or

(b) the RNA sequence encoding the amino acid sequence comprising Ag85A, an immunogenic variant thereof, or an immunogenic fragment of the Ag85A or the immunogenic variant thereof and Hrp1, an immunogenic variant thereof, or an immunogenic fragment of the Hrp1 or the immunogenic variant thereof comprises the nucleotide sequence of SEQ ID NO: 43, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 43.

In some examples,

(i) the amino acid sequence comprising ESAT6, an immunogenic variant thereof, or an immunogenic fragment of the ESAT6 or the immunogenic variant thereof and RpfD, an immunogenic variant thereof, or an immunogenic fragment of the RpfD or the immunogenic variant thereof comprises the amino acid sequence of SEQ ID NO: 46, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 46; and/or

(ii) (a) the RNA sequence encoding the amino acid sequence comprising ESAT6, an immunogenic variant thereof, or an immunogenic fragment of the ESAT6 or the immunogenic variant thereof and RpfD, an immunogenic variant thereof, or an immunogenic fragment of the RpfD or the immunogenic variant thereof comprises the nucleotide sequence of positions 54 to 872 of SEQ ID NO: 45, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 54 to 872 of SEQ ID NO: 45; or

(b) the RNA sequence encoding the amino acid sequence comprising ESAT6, an immunogenic variant thereof, or an immunogenic fragment of the ESAT6 or the immunogenic variant thereof and RpfD, an immunogenic variant thereof, or an immunogenic fragment of the RpfD or the immunogenic variant thereof comprises the nucleotide sequence of SEQ ID NO: 45, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 45.

In some examples,

(i) the amino acid sequence comprising RpfA, an immunogenic variant thereof, or an immunogenic fragment of the RpfA or the immunogenic variant thereof and HbhA, an immunogenic variant thereof, or an immunogenic fragment of the HbhA or the immunogenic variant thereof comprises the amino acid sequence of SEQ ID NO: 48, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 48; and/or

(ii) (a) the RNA sequence encoding the amino acid sequence comprising RpfA, an immunogenic variant thereof, or an immunogenic fragment of the RpfA or the immunogenic variant thereof and HbhA, an immunogenic variant thereof, or an immunogenic fragment of the HbhA or the immunogenic variant thereof comprises the nucleotide sequence of positions 54 to 1943 of SEQ ID NO: 47, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 54 to 1943 of SEQ ID NO: 47; or

(b) the RNA sequence encoding the amino acid sequence comprising RpfA, an immunogenic variant thereof, or an immunogenic fragment of the RpfA or the immunogenic variant thereof and HbhA, an immunogenic variant thereof, or an immunogenic fragment of the HbhA or the immunogenic variant thereof comprises the nucleotide sequence of SEQ ID NO: 47, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 47.

In some examples,

(i) the amino acid sequence comprising M72, an immunogenic variant thereof, or an immunogenic fragment of the M72 or the immunogenic variant thereof and VapB47, an immunogenic variant thereof, or an immunogenic fragment of the VapB47 or the immunogenic variant thereof comprises the amino acid sequence of SEQ ID NO: 52, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 52; and/or

(ii) (a) the RNA sequence encoding the amino acid sequence comprising M72, an immunogenic variant thereof, or an immunogenic fragment of the M72 or the immunogenic variant thereof and VapB47, an immunogenic variant thereof, or an immunogenic fragment of the VapB47 or the immunogenic variant thereof comprises the nucleotide sequence of positions 54 to 2591 of SEQ ID NO: 51, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 54 to 2591 of SEQ ID NO: 51; or

(b) the RNA sequence encoding the amino acid sequence comprising M72, an immunogenic variant thereof, or an immunogenic fragment of the M72 or the immunogenic variant thereof and VapB47, an immunogenic variant thereof, or an immunogenic fragment of the VapB47 or the immunogenic variant thereof comprises the nucleotide sequence of SEQ ID NO: 51, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 51.

In some examples,

(i) the amino acid sequence comprising Ag85A, an immunogenic variant thereof, or an immunogenic fragment of the Ag85A or the immunogenic variant thereof and Hrp1, an immunogenic variant thereof, or an immunogenic fragment of the Hrp1 or the immunogenic variant thereof comprises the amino acid sequence of SEQ ID NO: 63, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 63; and/or

(ii) the RNA sequence encoding the amino acid sequence comprising Ag85A, an immunogenic variant thereof, or an immunogenic fragment of the Ag85A or the immunogenic variant thereof and Hrp1, an immunogenic variant thereof, or an immunogenic fragment of the Hrp1 or the immunogenic variant thereof comprises the nucleotide sequence of SEQ ID NO: 62, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 62.

In some examples,

(i) the amino acid sequence comprising ESAT6, an immunogenic variant thereof, or an immunogenic fragment of the ESAT6 or the immunogenic variant thereof and RpfD, an immunogenic variant thereof, or an immunogenic fragment of the RpfD or the immunogenic variant thereof comprises the amino acid sequence of SEQ ID NO: 65, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 65; and/or

(ii) the RNA sequence encoding the amino acid sequence comprising ESAT6, an immunogenic variant thereof, or an immunogenic fragment of the ESAT6 or the immunogenic variant thereof and RpfD, an immunogenic variant thereof, or an immunogenic fragment of the RpfD or the immunogenic variant thereof comprises the nucleotide sequence of SEQ ID NO: 64, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 64.

In some examples,

(i) the amino acid sequence comprising RpfA, an immunogenic variant thereof, or an immunogenic fragment of the RpfA or the immunogenic variant thereof and HbhA, an immunogenic variant thereof, or an immunogenic fragment of the HbhA or the immunogenic variant thereof comprises the amino acid sequence of SEQ ID NO: 67, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 67; and/or

(ii) the RNA sequence encoding the amino acid sequence comprising RpfA, an immunogenic variant thereof, or an immunogenic fragment of the RpfA or the immunogenic variant thereof and HbhA, an immunogenic variant thereof, or an immunogenic fragment of the HbhA or the immunogenic variant thereof comprises the nucleotide sequence of SEQ ID NO: 66, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 66.

In some examples,

(i) the amino acid sequence comprising M72, an immunogenic variant thereof, or an immunogenic fragment of the M72 or the immunogenic variant thereof and VapB47, an immunogenic variant thereof, or an immunogenic fragment of the VapB47 or the immunogenic variant thereof comprises the amino acid sequence of SEQ ID NO: 69, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 69; and/or

(ii) the RNA sequence encoding the amino acid sequence comprising M72, an immunogenic variant thereof, or an immunogenic fragment of the M72 or the immunogenic variant thereof and VapB47, an immunogenic variant thereof, or an immunogenic fragment of the VapB47 or the immunogenic variant thereof comprises the nucleotide sequence of SEQ ID NO: 68, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 68.

In some examples,

(i) the amino acid sequence comprising Ag85A, an immunogenic variant thereof, or an immunogenic fragment of the Ag85A or the immunogenic variant thereof and Hrp1, an immunogenic variant thereof, or an immunogenic fragment of the Hrp1 or the immunogenic variant thereof comprises the amino acid sequence of SEQ ID NO: 71, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 71; and/or

(ii) the RNA sequence encoding the amino acid sequence comprising Ag85A, an immunogenic variant thereof, or an immunogenic fragment of the Ag85A or the immunogenic variant thereof and Hrp1, an immunogenic variant thereof, or an immunogenic fragment of the Hrp1 or the immunogenic variant thereof comprises the nucleotide sequence of SEQ ID NO: 70, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 70.

In some examples,

(i) the amino acid sequence comprising ESAT6, an immunogenic variant thereof, or an immunogenic fragment of the ESAT6 or the immunogenic variant thereof and RpfD, an immunogenic variant thereof, or an immunogenic fragment of the RpfD or the immunogenic variant thereof comprises the amino acid sequence of SEQ ID NO: 73, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 73; and/or

(ii) the RNA sequence encoding the amino acid sequence comprising ESAT6, an immunogenic variant thereof, or an immunogenic fragment of the ESAT6 or the immunogenic variant thereof and RpfD, an immunogenic variant thereof, or an immunogenic fragment of the RpfD or the immunogenic variant thereof comprises the nucleotide sequence of SEQ ID NO: 72, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 72.

In some examples,

(i) the amino acid sequence comprising RpfA, an immunogenic variant thereof, or an immunogenic fragment of the RpfA or the immunogenic variant thereof and HbhA, an immunogenic variant thereof, or an immunogenic fragment of the HbhA or the immunogenic variant thereof comprises the amino acid sequence of SEQ ID NO: 75, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 75; and/or

(ii) the RNA sequence encoding the amino acid sequence comprising RpfA, an immunogenic variant thereof, or an immunogenic fragment of the RpfA or the immunogenic variant thereof and HbhA, an immunogenic variant thereof, or an immunogenic fragment of the HbhA or the immunogenic variant thereof comprises the nucleotide sequence of SEQ ID NO: 74, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 74.

In some examples,

(i) the amino acid sequence comprising M72, an immunogenic variant thereof, or an immunogenic fragment of the M72 or the immunogenic variant thereof and VapB47, an immunogenic variant thereof, or an immunogenic fragment of the VapB47 or the immunogenic variant thereof comprises the amino acid sequence of SEQ ID NO: 77, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 77; and/or

(ii) the RNA sequence encoding the amino acid sequence comprising M72, an immunogenic variant thereof, or an immunogenic fragment of the M72 or the immunogenic variant thereof and VapB47, an immunogenic variant thereof, or an immunogenic fragment of the VapB47 or the immunogenic variant thereof comprises the nucleotide sequence of SEQ ID NO: 76, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 76.

In some examples, the RNA encodes an amino acid sequence comprising a secretory signal peptide.

In some examples, the secretory signal peptide is fused, preferably N-terminally, to the amino acid sequence.

In some examples, the secretory signal peptide is not endogenous to the Mtb antigen. In some examples, the secretory signal peptide is of human origin. In some examples, the secretory signal peptide is not of human origin.

In some examples,

(i) the secretory signal peptide comprises the amino acid sequence of positions 1 to 26 of SEQ ID NO: 44, an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 1 to 26 of SEQ ID NO: 44, or a functional fragment of the amino acid sequence of positions 1 to 26 of SEQ ID NO: 44, or the amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 1 to 26 of SEQ ID NO: 44; and/or

(ii) the RNA sequence encoding the secretory signal peptide comprises the nucleotide sequence of positions 54 to 131 of SEQ ID NO: 43, a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 54 to 131 of SEQ ID NO: 43, or a fragment of the nucleotide sequence of positions 54 to 131 of SEQ ID NO: 43, or the nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 54 to 131 of SEQ ID NO: 43.

In some examples,

(i) the secretory signal peptide comprises the amino acid sequence of positions 1 to 25 of SEQ ID NO: 63, an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 1 to 25 of SEQ ID NO: 63, or a functional fragment of the amino acid sequence of positions 1 to 25 of SEQ ID NO: 63, or the amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 1 to 25 of SEQ ID NO: 63; and/or

(ii) the RNA sequence encoding the secretory signal peptide comprises the nucleotide sequence of positions 1 to 75 of SEQ ID NO: 62, a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 1 to 75 of SEQ ID NO: 62, or a fragment of the nucleotide sequence of positions 1 to 75 of SEQ ID NO: 62, or the nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 1 to 75 of SEQ ID NO: 62.

In some examples,

(i) the secretory signal peptide comprises the amino acid sequence of positions 1 to 13 of SEQ ID NO: 71, an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 1 to 13 of SEQ ID NO: 71, or a functional fragment of the amino acid sequence of positions 1 to 13 of SEQ ID NO: 71, or the amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 1 to 13 of SEQ ID NO: 71; and/or

(ii) the RNA sequence encoding the secretory signal peptide comprises the nucleotide sequence of positions 1 to 39 of SEQ ID NO: 70, a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 1 to 39 of SEQ ID NO: 70, or a fragment of the nucleotide sequence of positions 1 to 39 of SEQ ID NO: 70, or the nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 1 to 39 of SEQ ID NO: 70.

In some examples, the composition or medical preparation comprises:

(i) RNA comprising the nucleotide sequence of SEQ ID NO: 43, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 43;

(ii) RNA comprising the nucleotide sequence of SEQ ID NO: 45, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 45;

(iii) RNA comprising the nucleotide sequence of SEQ ID NO: 47, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 47; and

(iv) RNA comprising the nucleotide sequence of SEQ ID NO: 51, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 51.

In some examples, the composition or medical preparation comprises:

(i) RNA comprising the nucleotide sequence of SEQ ID NO: 43;

(ii) RNA comprising the nucleotide sequence of SEQ ID NO: 45;

(iii) RNA comprising the nucleotide sequence of SEQ ID NO: 47; and

(iv) RNA comprising the nucleotide sequence of SEQ ID NO: 51.

In some examples, the composition or medical preparation comprises:

(i) RNA comprising a nucleotide sequence encoding the amino acid sequence of SEQ ID NO: 44, or a nucleotide sequence encoding an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 44;

(ii) RNA comprising a nucleotide sequence encoding the amino acid sequence of SEQ ID NO: 46, or a nucleotide sequence encoding an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 46;

(iii) RNA comprising a nucleotide sequence encoding the amino acid sequence of SEQ ID NO: 48, or a nucleotide sequence encoding an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 48; and

(iv) RNA comprising a nucleotide sequence encoding the amino acid sequence of SEQ ID NO: 52, or a nucleotide sequence encoding an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 52.

In some examples, the composition or medical preparation comprises:

(i) RNA comprising a nucleotide sequence encoding the amino acid sequence of SEQ ID NO: 44;

(ii) RNA comprising a nucleotide sequence encoding the amino acid sequence of SEQ ID NO: 46;

(iii) RNA comprising a nucleotide sequence encoding the amino acid sequence of SEQ ID NO: 48; and

(iv) RNA comprising a nucleotide sequence encoding the amino acid sequence of SEQ ID NO: 52.

In some examples, the composition or medical preparation comprises:

(i) RNA comprising the nucleotide sequence of SEQ ID NO: 62, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 62;

(ii) RNA comprising the nucleotide sequence of SEQ ID NO: 64, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 64;

(iii) RNA comprising the nucleotide sequence of SEQ ID NO: 66, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 66; and

(iv) RNA comprising the nucleotide sequence of SEQ ID NO: 68, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 68.

In some examples, the composition or medical preparation comprises:

(i) RNA comprising the nucleotide sequence of SEQ ID NO: 62;

(ii) RNA comprising the nucleotide sequence of SEQ ID NO: 64;

(iii) RNA comprising the nucleotide sequence of SEQ ID NO: 66; and

(iv) RNA comprising the nucleotide sequence of SEQ ID NO: 68.

In some examples, the composition or medical preparation comprises:

(i) RNA comprising a nucleotide sequence encoding the amino acid sequence of SEQ ID NO: 63, or a nucleotide sequence encoding an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 63;

(ii) RNA comprising a nucleotide sequence encoding the amino acid sequence of SEQ ID NO: 65, or a nucleotide sequence encoding an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 65;

(iii) RNA comprising a nucleotide sequence encoding the amino acid sequence of SEQ ID NO: 67, or a nucleotide sequence encoding an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 67; and

(iv) RNA comprising a nucleotide sequence encoding the amino acid sequence of SEQ ID NO: 69, or a nucleotide sequence encoding an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 69.

In some examples, the composition or medical preparation comprises:

(i) RNA comprising a nucleotide sequence encoding the amino acid sequence of SEQ ID NO: 63;

(ii) RNA comprising a nucleotide sequence encoding the amino acid sequence of SEQ ID NO: 65;

(iii) RNA comprising a nucleotide sequence encoding the amino acid sequence of SEQ ID NO: 67; and

(iv) RNA comprising a nucleotide sequence encoding the amino acid sequence of SEQ ID NO: 69.

In some examples, the composition or medical preparation comprises:

(i) RNA comprising the nucleotide sequence of SEQ ID NO: 70, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 70;

(ii) RNA comprising the nucleotide sequence of SEQ ID NO: 72, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 72;

(iii) RNA comprising the nucleotide sequence of SEQ ID NO: 74, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 74; and

(iv) RNA comprising the nucleotide sequence of SEQ ID NO: 76, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 76.

In some examples, the composition or medical preparation comprises:

(i) RNA comprising the nucleotide sequence of SEQ ID NO: 70;

(ii) RNA comprising the nucleotide sequence of SEQ ID NO: 72;

(iii) RNA comprising the nucleotide sequence of SEQ ID NO: 74; and

(iv) RNA comprising the nucleotide sequence of SEQ ID NO: 76.

In some examples, the composition or medical preparation comprises:

(i) RNA comprising a nucleotide sequence encoding the amino acid sequence of SEQ ID NO: 71, or a nucleotide sequence encoding an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 71;

(ii) RNA comprising a nucleotide sequence encoding the amino acid sequence of SEQ ID NO: 73, or a nucleotide sequence encoding an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 73;

(iii) RNA comprising a nucleotide sequence encoding the amino acid sequence of SEQ ID NO: 75, or a nucleotide sequence encoding an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 75; and

(iv) RNA comprising a nucleotide sequence encoding the amino acid sequence of SEQ ID NO: 77, or a nucleotide sequence encoding an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 77.

In some examples, the composition or medical preparation comprises:

(i) RNA comprising a nucleotide sequence encoding the amino acid sequence of SEQ ID NO: 71;

(ii) RNA comprising a nucleotide sequence encoding the amino acid sequence of SEQ ID NO: 73;

(iii) RNA comprising a nucleotide sequence encoding the amino acid sequence of SEQ ID NO: 75; and

(iv) RNA comprising a nucleotide sequence encoding the amino acid sequence of SEQ ID NO: 77.

In some examples, the RNA is formulated in lipid nanoparticles.

In some examples, the lipid nanoparticles comprise each of:

(i) a cationically ionizable lipid;

(ii) a steroid;

(iii) a neutral lipid; and

(iv) a polymer-conjugated lipid.

In some examples, the cationically ionizable lipid is present in a concentration ranging from about 40 to about 60 mol percent of the total lipids.

In some examples, the steroid is present in a concentration ranging from about 30 to about 50 mol percent of the total lipids.

In some examples, the neutral lipid is present in a concentration ranging from about 5 to about 15 mol percent of the total lipids.

In some examples, the polymer-conjugated lipid is present in a concentration ranging from about 1 to about 10 mol percent of the total lipids.

In some examples, the cationically ionizable lipid is within a range of about 40 to about 60 mole percent, the steroid is within a range of about 30 to about 50 mole percent, the neutral lipid is within a range of about 5 to about 15 mole percent, and the polymer-conjugated lipid is within a range of about 1 to about 10 mole percent.

In some examples, the cationically ionizable lipid is or comprises ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate).

In some examples, the steroid is or comprises cholesterol.

In some examples, the neutral lipid is or comprises a phospholipid.

In some examples, the phospholipid is or comprises distearoylphosphatidylcholine (DSPC).

In some examples, the polymer-conjugated lipid is or comprises a polyethylene glycol (PEG)-lipid.

In some examples, the PEG-lipid is or comprises 2-[(polyethylene glycol)-2000]-*N,N*-ditetradecylacetamide.

In some examples, the lipid nanoparticles comprise:

(a) ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate);

(b) cholesterol;

(c) distearoylphosphatidylcholine (DSPC); and

(d) 2-[(polyethylene glycol)-2000]-*N,N*-ditetradecylacetamide.

In some examples, ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate) is within a range of about 40 to about 60 mole percent, cholesterol is within a range of about 30 to about 50 mole percent, distearoylphosphatidylcholine (DSPC) is within a range of about 5 to about 15 mole percent, and 2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide is within a range of about 1 to about 10 mole percent.

In some examples, the RNA comprises a 5′-cap.

In some examples, the 5′ cap is or comprises a cap1 structure.

In some examples, the 5′-cap is or comprises $m_2^{7,3'}$-OGppp($m_1^{2'\text{-}O}$)ApG.

In some examples, the RNA comprises a 5′-UTR.

In some examples, the 5′-UTR is or comprises a modified human alpha-globin 5′-UTR.

In some examples, the 5′-UTR is or comprises the nucleotide sequence of SEQ ID NO: 56, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 56.

In some examples, the 5′-UTR is or comprises the nucleotide sequence of SEQ ID NO: 57, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 57.

In some examples, the RNA comprises a 3′-UTR.

In some examples, the 3′-UTR is or comprises a first sequence from the amino terminal enhancer of split (AES) messenger RNA and a second sequence from the mitochondrial encoded 12S ribosomal RNA.

In some examples, the 3′-UTR is or comprises the nucleotide sequence of SEQ ID NO: 58, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 58.

In some examples, the RNA comprises a polyA sequence.

In some examples, the polyA sequence is an interrupted sequence of A nucleotides.

In some examples, the polyA sequence comprises 30 adenine nucleotides followed by 70 adenine nucleotides, wherein the 30 adenine nucleotides and 70 adenine nucleotides are separated by a linker sequence of 10 nucleotides.

In some examples, the polyA sequence is or comprises the nucleotide sequence of SEQ ID NO: 59, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 59.

In some examples, the sequence downstream from the open reading frame, i.e., 3′-UTR and polyA sequence, is or comprises the nucleotide sequence of SEQ ID NO: 60, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 60.

In some examples, the RNA comprises a 5′-cap, a 5′-UTR, a 3′-UTR, and a polyA sequence.

In some examples, the RNA comprises modified uridines.

In some examples, the RNA comprises modified uridines in place of all uridines.

In some examples, the modified uridines are N1-methyl-pseudouridine.

In some examples, the coding sequence of the RNA is codon-optimized and/or is characterized in that its G/C content is increased compared to the parental sequence.

In some examples, the RNA is in a liquid formulation.

In some examples, the RNA is in a frozen formulation.

In some examples, the RNA is in a lyophilized formulation.

In some examples, the RNA is formulated for injection.

In some examples, the RNA is formulated for intramuscular administration.

In some examples, the composition or medical preparation is a pharmaceutical composition.

In some examples, the pharmaceutical composition further comprises one or more pharmaceutically acceptable carriers, diluents and/or excipients.

In some examples, the composition or medical preparation is a vaccine.

In some examples, the composition or medical preparation is a kit.

In some examples, different RNA molecules are in separate vials.

In some examples, the composition or medical preparation further comprises instructions for use of the composition or medical preparation for treating or preventing tuberculosis.

In some examples, the composition or medical preparation is for pharmaceutical use.

In some examples, the pharmaceutical use comprises a therapeutic or prophylactic treatment of a disease or disorder.

In some examples, the therapeutic or prophylactic treatment of a disease or disorder comprises treating or preventing tuberculosis.

In some examples, the composition or medical preparation is for administration to a human.

In one aspect, the present disclosure provides for the composition or medical preparation as disclosed herein for pharmaceutical use. In another aspect, the present disclosure provides for a use of the composition or medical preparation as disclosed herein in the manufacture of a medicament for a therapeutic or prophylactic treatment of tuberculosis in a human subject.

In one example, the disclosure provides a method of vaccinating a subject comprising administering the composition described herein to the subject.

In some examples, the vaccination is for preventing tuberculosis.

In some examples, administration is by intramuscular administration.

In some examples, the method comprises administering to the subject at least one dose of the composition.

In some examples, the method comprises administering to the subject at least two doses of the composition.

In some examples, an amount of the RNA of at least 10 µg per dose is administered.

In some examples, the subject is a human.

In further examples, the disclosure provides the following:

A nucleic acid, e.g., RNA, encoding an amino acid sequence comprising Ag85A, an immunogenic variant thereof, or an immunogenic fragment of the Ag85A or the immunogenic variant thereof and comprising the nucleotide sequence of positions 4 to 894 of SEQ ID NO: 19, a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 4 to 894 of SEQ ID NO: 19, or a fragment of the nucleotide sequence of positions 4 to 894 of SEQ ID NO: 19, or the nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 4 to 894 of SEQ ID NO: 19.

A nucleic acid, e.g., RNA, encoding an amino acid sequence comprising ESAT6, an immunogenic variant thereof, or an immunogenic fragment of the ESAT6 or the immunogenic variant thereof and comprising the nucleotide sequence of positions 4 to 285 of SEQ ID NO: 21, a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 4 to 285 of SEQ ID NO: 21, or a fragment of the nucleotide sequence of positions 4 to 285 of SEQ ID NO: 21, or the nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 4 to 285 of SEQ ID NO: 21.

A nucleic acid, e.g., RNA, encoding an amino acid sequence comprising VapB47, an immunogenic variant thereof, or an immunogenic fragment of the VapB47 or the immunogenic variant thereof and comprising the nucleotide sequence of positions 4 to 297 of SEQ ID NO: 22, a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 4 to 297 of SEQ ID NO: 22, or a fragment of the nucleotide sequence of positions 4 to 297 of SEQ ID NO: 22, or the nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 4 to 297 of SEQ ID NO: 22.

A nucleic acid, e.g., RNA, encoding an amino acid sequence comprising Hrp1, an immunogenic variant thereof, or an immunogenic fragment of the Hrp1 or the immunogenic variant thereof and comprising the nucleotide sequence of positions 4 to 429 of SEQ ID NO: 23, a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 4 to 429 of SEQ ID NO: 23, or a fragment of the nucleotide sequence of positions 4 to 429 of SEQ ID NO: 23, or the nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 4 to 429 of SEQ ID NO: 23.

A nucleic acid, e.g., RNA, encoding an amino acid sequence comprising RpfA, an immunogenic variant thereof, or an immunogenic fragment of the RpfA or the immunogenic variant thereof and comprising the nucleotide sequence of positions 4 to 1221 of SEQ ID NO: 24, a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 4 to 1221 of SEQ ID NO: 24, or a fragment of the nucleotide sequence of positions 4 to 1221 of SEQ ID NO: 24, or the nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 4 to 1221 of SEQ ID NO: 24.

A nucleic acid, e.g., RNA, encoding an amino acid sequence comprising RpfD, an immunogenic variant thereof, or an immunogenic fragment of the RpfD or the immunogenic variant thereof and comprising the nucleotide sequence of positions 4 to 462 of SEQ ID NO: 25, a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 4 to 462 of SEQ ID NO: 25, or a fragment of the nucleotide

sequence of positions 4 to 462 of SEQ ID NO: 25, or the nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 4 to 462 of SEQ ID NO: 25.

A nucleic acid, e.g., RNA, encoding an amino acid sequence comprising M72, an immunogenic variant thereof, or an immunogenic fragment of the M72 or the immunogenic variant thereof and comprising the nucleotide sequence of positions 4 to 2169 of SEQ ID NO: 28, a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 4 to 2169 of SEQ ID NO: 28, or a fragment of the nucleotide sequence of positions 4 to 2169 of SEQ ID NO: 28, or the nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 4 to 2169 of SEQ ID NO: 28.

A nucleic acid, e.g., RNA, encoding an amino acid sequence comprising HbhA, an immunogenic variant thereof, or an immunogenic fragment of the HbhA or the immunogenic variant thereof and comprising the nucleotide sequence of positions 4 to 597 of SEQ ID NO: 30, a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 4 to 597 of SEQ ID NO: 30, or a fragment of the nucleotide sequence of positions 4 to 597 of SEQ ID NO: 30, or the nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 4 to 597 of SEQ ID NO: 30.

A polypeptide comprising an amino acid sequence comprising Ag85A, an immunogenic variant thereof, or an immunogenic fragment of the Ag85A or the immunogenic variant thereof and Hrp1, an immunogenic variant thereof, or an immunogenic fragment of the Hrp1 or the immunogenic variant thereof.

A nucleic acid, e.g., RNA, encoding an amino acid sequence comprising Ag85A, an immunogenic variant thereof, or an immunogenic fragment of the Ag85A or the immunogenic variant thereof and Hrp1, an immunogenic variant thereof, or an immunogenic fragment of the Hrp1 or the immunogenic variant thereof.

A polypeptide comprising an amino acid sequence comprising ESAT6, an immunogenic variant thereof, or an immunogenic fragment of the ESAT6 or the immunogenic variant thereof and RpfD, an immunogenic variant thereof, or an immunogenic fragment of the RpfD or the immunogenic variant thereof.

A nucleic acid, e.g., RNA, encoding an amino acid sequence comprising ESAT6, an immunogenic variant thereof, or an immunogenic fragment of the ESAT6 or the immunogenic variant thereof and RpfD, an immunogenic variant thereof, or an immunogenic fragment of the RpfD or the immunogenic variant thereof.

A polypeptide comprising an amino acid sequence comprising RpfA, an immunogenic variant thereof, or an immunogenic fragment of the RpfA or the immunogenic variant thereof and HbhA, an immunogenic variant thereof, or an immunogenic fragment of the HbhA or the immunogenic variant thereof.

A nucleic acid, e.g., RNA, encoding an amino acid sequence comprising RpfA, an immunogenic variant thereof, or an immunogenic fragment of the RpfA or the immunogenic variant thereof and HbhA, an immunogenic variant thereof, or an immunogenic fragment of the HbhA or the immunogenic variant thereof.

A polypeptide comprising an amino acid sequence comprising M72, an immunogenic variant thereof, or an immunogenic fragment of the M72 or the immunogenic variant thereof and VapB47, an immunogenic variant thereof, or an immunogenic fragment of the VapB47 or the immunogenic variant thereof.

A nucleic acid, e.g., RNA, encoding an amino acid sequence comprising M72, an immunogenic variant thereof, or an immunogenic fragment of the M72 or the immunogenic variant thereof and VapB47, an immunogenic variant thereof, or an immunogenic fragment of the VapB47 or the immunogenic variant thereof.

In some examples,

(i) a polypeptide comprising an amino acid sequence comprising Ag85A, an immunogenic variant thereof, or an immunogenic fragment of the Ag85A or the immunogenic variant thereof and Hrp1, an immunogenic variant thereof, or an immunogenic fragment of the Hrp1 or the immunogenic variant thereof comprises the amino acid sequence of positions 27 to 465 of SEQ ID NO: 44, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 27 to 465 of SEQ ID NO: 44; and/or

(ii) a nucleic acid, e.g., RNA, encoding an amino acid sequence comprising Ag85A, an immunogenic variant thereof, or an immunogenic fragment of the Ag85A or the immunogenic variant thereof and Hrp1, an immunogenic variant thereof, or an immunogenic fragment of the Hrp1 or the immunogenic variant thereof comprises the nucleotide sequence of positions 132 to 1448 of SEQ ID NO: 43, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 132 to 1448 of SEQ ID NO: 43.

In some examples,

(i) a polypeptide comprising an amino acid sequence comprising ESAT6, an immunogenic variant thereof, or an immunogenic fragment of the ESAT6 or the immunogenic variant thereof and RpfD, an immunogenic variant thereof, or an immunogenic fragment of the RpfD or the immunogenic variant thereof comprises the amino acid sequence of positions 27 to 273 of SEQ ID NO: 46, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 27 to 273 of SEQ ID NO: 46; and/or

(ii) a nucleic acid, e.g., RNA, encoding an amino acid sequence comprising ESAT6, an immunogenic variant thereof, or an immunogenic fragment of the ESAT6 or the immunogenic variant thereof and RpfD, an immunogenic variant thereof, or an immunogenic fragment of the RpfD or the immunogenic variant thereof comprises the nucleotide sequence of positions 132 to 872 of SEQ ID NO: 45, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 132 to 872 of SEQ ID NO: 45.

In some examples,

(i) a polypeptide comprising an amino acid sequence comprising RpfA, an immunogenic variant thereof, or an immunogenic fragment of the RpfA or the immunogenic variant thereof and HbhA, an immunogenic variant thereof, or an immunogenic fragment of the HbhA or the immunogenic variant thereof comprises the amino acid sequence of positions 27 to 630 of SEQ ID NO: 48, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 27 to 630 of SEQ ID NO: 48; and/or

(ii) a nucleic acid, e.g., RNA, encoding an amino acid sequence comprising RpfA, an immunogenic variant thereof, or an immunogenic fragment of the RpfA or the immunogenic variant thereof and HbhA, an immunogenic variant thereof, or an immunogenic fragment of the HbhA or the immunogenic variant thereof comprises the nucleotide sequence of positions 132 to 1943 of SEQ ID NO: 47, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 132 to 1943 of SEQ ID NO: 47.

In some examples,

(i) a polypeptide comprising an amino acid sequence comprising M72, an immunogenic variant thereof, or an immunogenic fragment of the M72 or the immunogenic variant thereof and VapB47, an immunogenic variant thereof, or an immunogenic fragment of the VapB47 or the immunogenic variant thereof comprises the amino acid sequence of positions 27 to 846 of SEQ ID NO: 52, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 27 to 846 of SEQ ID NO: 52; and/or

(ii) a nucleic acid, e.g., RNA, encoding an amino acid sequence comprising M72, an immunogenic variant thereof, or an immunogenic fragment of the M72 or the immunogenic variant thereof and VapB47, an immunogenic variant thereof, or an immunogenic fragment of the VapB47 or the immunogenic variant thereof comprises the nucleotide sequence of positions 132 to 2591 of SEQ ID NO: 51, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 132 to 2591 of SEQ ID NO: 51.

In some examples,

(i) a polypeptide comprising an amino acid sequence comprising Ag85A, an immunogenic variant thereof, or an immunogenic fragment of the Ag85A or the immunogenic variant thereof and Hrp1, an immunogenic variant thereof, or an immunogenic fragment of the Hrp1 or the immunogenic variant thereof comprises the amino acid sequence of SEQ ID NO: 44, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 44; and/or

(ii) (a) a nucleic acid, e.g., RNA, encoding an amino acid sequence comprising Ag85A, an immunogenic variant thereof, or an immunogenic fragment of the Ag85A or the immunogenic variant thereof and Hrp1, an immunogenic variant thereof, or an immunogenic fragment of the Hrp1 or the immunogenic variant thereof comprises the nucleotide sequence of positions 54 to 1448 of SEQ ID NO: 43, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 54 to 1448 of SEQ ID NO: 43; or

(b) a nucleic acid, e.g., RNA, encoding an amino acid sequence comprising Ag85A, an immunogenic variant thereof, or an immunogenic fragment of the Ag85A or the immunogenic variant thereof and Hrp1, an immunogenic variant thereof, or an immunogenic fragment of the Hrp1 or the immunogenic variant thereof comprises the nucleotide sequence of SEQ ID NO: 43, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 43.

In some examples,

(i) a polypeptide comprising an amino acid sequence comprising ESAT6, an immunogenic variant thereof, or an immunogenic fragment of the ESAT6 or the immunogenic variant thereof and RpfD, an immunogenic variant thereof, or an immunogenic fragment of the RpfD or the immunogenic variant thereof comprises the amino acid sequence of SEQ ID NO: 46, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 46; and/or

(ii) (a) a nucleic acid, e.g., RNA, encoding an amino acid sequence comprising ESAT6, an immunogenic variant thereof, or an immunogenic fragment of the ESAT6 or the immunogenic variant thereof and RpfD, an immunogenic variant thereof, or an immunogenic fragment of the RpfD or the immunogenic variant thereof comprises the nucleotide sequence of positions 54 to 872 of SEQ ID NO: 45, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 54 to 872 of SEQ ID NO: 45; or

(b) a nucleic acid, e.g., RNA, encoding an amino acid sequence comprising ESAT6, an immunogenic variant thereof, or an immunogenic fragment of the ESAT6 or the immunogenic variant thereof and RpfD, an immunogenic variant thereof, or an immunogenic fragment of the RpfD or the immunogenic variant thereof comprises the nucleotide sequence of SEQ ID NO: 45, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 45.

In some examples,

(i) a polypeptide comprising an amino acid sequence comprising RpfA, an immunogenic variant thereof, or an immunogenic fragment of the RpfA or the immunogenic variant thereof and HbhA, an immunogenic variant thereof, or an immunogenic fragment of the HbhA or the immunogenic variant thereof comprises the amino acid sequence of SEQ ID NO: 48, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 48; and/or

(ii) (a) a nucleic acid, e.g., RNA, encoding an amino acid sequence comprising RpfA, an immunogenic variant thereof, or an immunogenic fragment of the RpfA or the immunogenic variant thereof and HbhA, an immunogenic variant thereof, or an immunogenic fragment of the HbhA or the immunogenic variant thereof comprises the nucleotide sequence of positions 54 to 1943 of SEQ ID NO: 47, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 54 to 1943 of SEQ ID NO: 47; or

(b) a nucleic acid, e.g., RNA, encoding an amino acid sequence comprising RpfA, an immunogenic variant thereof, or an immunogenic fragment of the RpfA or the immunogenic variant thereof and HbhA, an immunogenic variant thereof, or an immunogenic fragment of the HbhA or the immunogenic variant thereof comprises the nucleotide sequence of SEQ ID NO: 47, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 47.

In some examples,

(i) a polypeptide comprising an amino acid sequence comprising M72, an immunogenic variant thereof, or an immunogenic fragment of the M72 or the immunogenic variant thereof and VapB47, an immunogenic variant thereof, or an immunogenic fragment of the VapB47 or the immunogenic variant thereof comprises the amino acid sequence of SEQ ID NO: 52, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 52; and/or

(ii) (a) a nucleic acid, e.g., RNA, encoding an amino acid sequence comprising M72, an immunogenic variant thereof, or an immunogenic fragment of the M72 or the immunogenic variant thereof and VapB47, an immunogenic variant thereof, or an immunogenic fragment of the VapB47 or the immunogenic variant thereof comprises the nucleotide sequence of positions 54 to 2591 of SEQ ID NO: 51, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 54 to 2591 of SEQ ID NO: 51; or

(b) a nucleic acid, e.g., RNA, encoding an amino acid sequence comprising M72, an immunogenic variant thereof, or an immunogenic fragment of the M72 or the immunogenic variant thereof and VapB47, an immunogenic variant thereof, or an immunogenic fragment of the VapB47 or the immunogenic variant thereof comprises the nucleotide sequence of SEQ ID NO: 51, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 51.

In some examples,

(i) a polypeptide comprising an amino acid sequence comprising Ag85A, an immunogenic variant thereof, or an immunogenic fragment of the Ag85A or the immunogenic variant thereof and Hrp1, an immunogenic variant thereof, or an immunogenic fragment of the Hrp1 or the immunogenic variant thereof comprises the amino acid sequence of SEQ ID NO: 63, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 63; and/or

(ii) a nucleic acid, e.g., RNA, encoding an amino acid sequence comprising Ag85A, an immunogenic variant thereof, or an immunogenic fragment of the Ag85A or the immunogenic variant thereof and Hrp1, an immunogenic variant thereof, or an immunogenic fragment of the Hrp1 or the immunogenic variant thereof comprises the nucleotide sequence of SEQ ID NO: 62, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 62.

In some examples,

(i) a polypeptide comprising an amino acid sequence comprising ESAT6, an immunogenic variant thereof, or an immunogenic fragment of the ESAT6 or the immunogenic variant thereof and RpfD, an immunogenic variant thereof, or an immunogenic fragment of the RpfD or the immunogenic variant thereof comprises the amino acid sequence of SEQ ID NO: 65, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 65; and/or

(ii) a nucleic acid, e.g., RNA, encoding an amino acid sequence comprising ESAT6, an immunogenic variant thereof, or an immunogenic fragment of the ESAT6 or the immunogenic variant thereof and RpfD, an immunogenic variant thereof, or an immunogenic fragment of the RpfD or the immunogenic variant thereof comprises the nucleotide sequence of SEQ ID NO: 64, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 64.

In some examples,

(i) a polypeptide comprising an amino acid sequence comprising RpfA, an immunogenic variant thereof, or an immunogenic fragment of the RpfA or the immunogenic variant thereof and HbhA, an immunogenic variant thereof, or an immunogenic fragment of the HbhA or the immunogenic variant thereof comprises the amino acid sequence of SEQ ID NO: 67, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 67; and/or

(ii) a nucleic acid, e.g., RNA, encoding an amino acid sequence comprising RpfA, an immunogenic variant thereof, or an immunogenic fragment of the RpfA or the immunogenic variant thereof and HbhA, an immunogenic variant thereof, or an immunogenic fragment of the HbhA or the immunogenic variant thereof comprises the nucleotide sequence of SEQ ID NO: 66, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 66.

In some examples,

(i) a polypeptide comprising an amino acid sequence comprising M72, an immunogenic variant thereof, or an immunogenic fragment of the M72 or the immunogenic variant thereof and VapB47, an immunogenic variant thereof, or an immunogenic fragment of the VapB47 or the immunogenic variant thereof comprises the amino acid sequence of SEQ ID NO: 69, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 69; and/or

(ii) a nucleic acid, e.g., RNA, encoding an amino acid sequence comprising M72, an immunogenic variant thereof, or an immunogenic fragment of the M72 or the immunogenic variant thereof and VapB47, an immunogenic variant thereof, or an immunogenic fragment of the VapB47 or the immunogenic variant thereof comprises the nucleotide sequence of SEQ ID NO: 68, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 68.

In some examples,

(i) a polypeptide comprising an amino acid sequence comprising Ag85A, an immunogenic variant thereof, or an immunogenic fragment of the Ag85A or the immunogenic variant thereof and Hrp1, an immunogenic variant thereof, or an immunogenic fragment of the Hrp1 or the immunogenic variant thereof comprises the amino acid sequence of SEQ ID NO: 71, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 71; and/or

(ii) a nucleic acid, e.g., RNA, encoding an amino acid sequence comprising Ag85A, an immunogenic variant thereof, or an immunogenic fragment of the Ag85A or the immunogenic variant thereof and Hrp1, an immunogenic variant thereof, or an immunogenic fragment of the Hrp1 or the immunogenic variant thereof comprises the nucleotide sequence of SEQ ID NO: 70, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 70.

In some examples,

(i) a polypeptide comprising an amino acid sequence comprising ESAT6, an immunogenic variant thereof, or an immunogenic fragment of the ESAT6 or the immunogenic variant thereof and RpfD, an immunogenic variant thereof, or an immunogenic fragment of the RpfD or the immunogenic variant thereof comprises the amino acid sequence of SEQ ID NO: 73, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 73; and/or

(ii) a nucleic acid, e.g., RNA, encoding an amino acid sequence comprising ESAT6, an immunogenic variant thereof, or an immunogenic fragment of the ESAT6 or the immunogenic variant thereof and RpfD, an immunogenic variant thereof, or an immunogenic fragment of the RpfD or the immunogenic variant thereof comprises the nucleotide sequence of SEQ ID NO: 72, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 72.

In some examples,

(i) a polypeptide comprising an amino acid sequence comprising RpfA, an immunogenic variant thereof, or an immunogenic fragment of the RpfA or the immunogenic variant thereof and HbhA, an immunogenic variant thereof, or an immunogenic fragment of the HbhA or the immunogenic variant thereof comprises the amino acid sequence of SEQ ID NO: 75, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 75; and/or

(ii) a nucleic acid, e.g., RNA, encoding an amino acid sequence comprising RpfA, an immunogenic variant thereof, or an immunogenic fragment of the RpfA or the immunogenic variant thereof and HbhA, an immunogenic variant thereof, or an immunogenic fragment of the HbhA or the immunogenic variant thereof comprises the nucleotide sequence of SEQ ID NO: 74, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 74.

In some examples,

(i) a polypeptide comprising an amino acid sequence comprising M72, an immunogenic variant thereof, or an immunogenic fragment of the M72 or the immunogenic variant thereof and VapB47, an immunogenic variant thereof, or an immunogenic fragment of the VapB47 or the immunogenic variant thereof comprises the amino acid sequence of SEQ ID NO: 77, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 77; and/or

(ii) a nucleic acid, e.g., RNA, encoding an amino acid sequence comprising M72, an immunogenic variant thereof, or an immunogenic fragment of the M72 or the immunogenic variant thereof and VapB47, an immunogenic variant thereof, or an immunogenic fragment of the VapB47 or the immunogenic variant thereof comprises the nucleotide sequence of SEQ ID NO: 76, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 76.

Brief description of the Figures

Figure 1: RNA mixes of four modRNAs encoding 4 (RNA mix 1), 6 (RNA mix 2), or 8 (RNA mix 3) *Mtb* antigens. *Top* General mRNA construct structure with 5'-cap, 5'- and 3'-untranslated regions (UTR), the open reading frame (ORF), and a poly-adenosine tail. *Bottom*, RNA mixes 1 to 3 comprising 4 to 8 *Mtb* antigens sequences tested. All antigen-encoding sequences were fused on the N-terminus to a major histocompatibility complex (MHC) class I signal peptide fragment (sec) that mediates translocation into the endoplasmic reticulum. **A**) The modRNA constructs in RNA mix 1 encode *Mycobacterium tuberculosis* (*Mtb*) antigens Ag85A(Δ1-41), M72, ESAT6, and HbhA separately. **B**) The modRNA constructs in RNA mix 2 encode antigens Ag85A(Δ1-41), and M72 separately and 2 fusion-antigens: Hrp1-ESAT6 and RpfD-HbhA. **C**) The modRNA constructs in RNA mix 3 encode four fusion-antigens: ESAT6-RpfD, Ag85A(Δ1-41)-Hrp1, RpfA-HbhA, and M72-vapB47. The modRNAs mixtures were formulated with lipid nanoparticles 315 (LNP-315). UTR: untranslated region, poly(A): poly-adenosine tail.

Figure 2: Immunization schedule for *in vivo* mouse immunogenicity studies. Mice received **A**) two intramuscular (i.m.) injections (on days 0 and 21) or **B**) three intravenous (i.v.) injections (on days 0, 7, and 21). Arrowheads indicate injection days. Blood samples (indicated by the arrows) were collected for serum analysis of antigen-specific IgG antibodies on day 14, 28, and 42 after the first injection. On the last experimental day (day 42) mice spleens were dissected for isolation of splenocytes, for subsequent analysis of T-cell responses to antigen-specific peptides.

Figure 3: Scheme of the mRNA constructs used to determine the most immunogenic mRNA platform and Mtb antigens. *Top* General mRNA construct structure with 5'-cap, 5'- and 3'-untranslated regions (UTR), the open reading frame (ORF), and a poly-adenosine tail. *Bottom*, **A**-**E**) The antigen-encoding mRNA constructs included in the ORF. All antigen-encoding sequences were fused to an N-terminal major histocompatibility complex (MHC) class I signal peptide fragment (sec) that mediates translocation into the endoplasmic reticulum. One construct (B) contained a C-terminal MHC class I transmembrane and cytoplasmic domain (MITD), a cell trafficking-signal for cell membrane anchoring. *Mycobacterium tuberculosis* antigens tested: Ag85A, ESAT6, HbhA, Hrp1, M72, RpfA, RpfD, vapB47.

Claims

1. A composition or medical preparation comprising at least one RNA molecule, wherein the at least one RNA molecule encodes a set of *Mycobacterium tuberculosis* (Mtb) antigenic amino acid sequences, wherein the set of Mtb antigenic amino acid sequences comprises four or more, five or more, six or more, seven or more, or eight or more of the following:

(i) an amino acid sequence comprising Ag85A, an immunogenic variant thereof, or an immunogenic fragment of the Ag85A or the immunogenic variant thereof;

(ii) an amino acid sequence comprising ESAT6, an immunogenic variant thereof, or an immunogenic fragment of the ESAT6 or the immunogenic variant thereof;

(iii) an amino acid sequence comprising VapB47, an immunogenic variant thereof, or an immunogenic fragment of the VapB47 or the immunogenic variant thereof;

(iv) an amino acid sequence comprising Hrp1, an immunogenic variant thereof, or an immunogenic fragment of the Hrp1 or the immunogenic variant thereof;

(v) an amino acid sequence comprising RpfA, an immunogenic variant thereof, or an immunogenic fragment of the RpfA or the immunogenic variant thereof;

(vi) an amino acid sequence comprising RpfD, an immunogenic variant thereof, or an immunogenic fragment of the RpfD or the immunogenic variant thereof;

(vii) an amino acid sequence comprising Mtb32a, an immunogenic variant thereof, or an immunogenic fragment of the Mtb32a or the immunogenic variant thereof;

(viii) an amino acid sequence comprising Mtb39a, an immunogenic variant thereof, or an immunogenic fragment of the Mtb39a or the immunogenic variant thereof; and

(ix) an amino acid sequence comprising HbhA, an immunogenic variant thereof, or an immunogenic fragment of the HbhA or the immunogenic variant thereof.

2. The composition or medical preparation of claim 1, wherein the amino acid sequence comprising Mtb32a, an immunogenic variant thereof, or an immunogenic fragment of the Mtb32a or the immunogenic variant thereof and the amino acid sequence comprising Mtb39a, an immunogenic variant thereof, or an immunogenic fragment of the Mtb39a or the immunogenic variant thereof are present as a fusion protein, wherein optionally the fusion protein comprises an amino acid sequence comprising M72, an immunogenic variant thereof, or an immunogenic fragment of the M72 or the immunogenic variant thereof.

3. The composition or medical preparation of claim 1 or 2, wherein

(i) the amino acid sequence comprising Ag85A, an immunogenic variant thereof, or an immunogenic fragment of the Ag85A or the immunogenic variant thereof comprises the amino acid sequence of positions 27 to 323 of SEQ ID NO: 44, an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 27 to 323 of SEQ ID NO: 44, or an immunogenic fragment of the amino acid sequence of positions 27 to 323 of SEQ ID NO: 44, or the amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 27 to 323 of SEQ ID NO: 44; and/or

(ii) the RNA sequence encoding the amino acid sequence comprising Ag85A, an immunogenic variant thereof, or an immunogenic fragment of the Ag85A or the immunogenic variant thereof comprises the nucleotide sequence of positions 132 to 1022 of SEQ ID NO: 43, a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 132 to 1022 of SEQ ID NO: 43, or a fragment

of the nucleotide sequence of positions 132 to 1022 of SEQ ID NO: 43, or the nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 132 to 1022 of SEQ ID NO: 43; and/or

(iii) the amino acid sequence comprising ESAT6, an immunogenic variant thereof, or an immunogenic fragment of the ESAT6 or the immunogenic variant thereof comprises the amino acid sequence of positions 27 to 120 of SEQ ID NO: 46, an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 27 to 120 of SEQ ID NO: 46, or an immunogenic fragment of the amino acid sequence of positions 27 to 120 of SEQ ID NO: 46, or the amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 27 to 120 of SEQ ID NO: 46; and/or

(iv) the RNA sequence encoding the amino acid sequence comprising ESAT6, an immunogenic variant thereof, or an immunogenic fragment of the ESAT6 or the immunogenic variant thereof comprises the nucleotide sequence of positions 132 to 413 of SEQ ID NO: 45, a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 132 to 413 of SEQ ID NO: 45, or a fragment of the nucleotide sequence of positions 132 to 413 of SEQ ID NO: 45, or the nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 132 to 413 of SEQ ID NO: 45; and/or

(v) the amino acid sequence comprising VapB47, an immunogenic variant thereof, or an immunogenic fragment of the VapB47 or the immunogenic variant thereof comprises the amino acid sequence of positions 749 to 846 of SEQ ID NO: 52, an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 749 to 846 of SEQ ID NO: 52, or an immunogenic fragment of the amino acid sequence of positions 749 to 846 of SEQ ID NO: 52, or the amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 749 to 846 of SEQ ID NO: 52; and/or

(vi) the RNA sequence encoding the amino acid sequence comprising VapB47, an immunogenic variant thereof, or an immunogenic fragment of the VapB47 or the immunogenic variant thereof comprises the nucleotide sequence of positions 2298 to 2591 of SEQ ID NO: 51, a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 2298 to 2591 of SEQ ID NO: 51, or a fragment of the nucleotide sequence of positions 2298 to 2591 of SEQ ID NO: 51, or the nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 2298 to 2591 of SEQ ID NO: 51; and/or

(vii) the amino acid sequence comprising Hrp1, an immunogenic variant thereof, or an immunogenic fragment of the Hrp1 or the immunogenic variant thereof comprises the amino acid sequence of positions 324 to 465 of SEQ ID NO: 44, an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 324 to 465 of SEQ ID NO: 44, or an immunogenic fragment of the amino acid sequence of positions 324 to 465 of SEQ ID NO: 44, or the amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 324 to 465 of SEQ ID NO: 44; and/or

(viii) the RNA sequence encoding the amino acid sequence comprising Hrp1, an immunogenic variant thereof, or an immunogenic fragment of the Hrp1 or the immunogenic variant thereof comprises the nucleotide sequence of positions 1023 to 1448 of SEQ ID NO: 43, a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 1023 to 1448 of SEQ ID NO: 43, or a fragment of the nucleotide sequence of positions 1023 to 1448 of SEQ ID NO: 43, or the nucleotide sequence having at least

99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 1023 to 1448 of SEQ ID NO: 43; and/or

(ix) the amino acid sequence comprising RpfA, an immunogenic variant thereof, or an immunogenic fragment of the RpfA or the immunogenic variant thereof comprises the amino acid sequence of positions 27 to 432 of SEQ ID NO: 48, an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 27 to 432 of SEQ ID NO: 48, or an immunogenic fragment of the amino acid sequence of positions 27 to 432 of SEQ ID NO: 48, or the amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 27 to 432 of SEQ ID NO: 48; and/or

(x) the RNA sequence encoding the amino acid sequence comprising RpfA, an immunogenic variant thereof, or an immunogenic fragment of the RpfA or the immunogenic variant thereof comprises the nucleotide sequence of positions 132 to 1349 of SEQ ID NO: 47, a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 132 to 1349 of SEQ ID NO: 47, or a fragment of the nucleotide sequence of positions 132 to 1349 of SEQ ID NO: 47, or the nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 132 to 1349 of SEQ ID NO: 47; and/or

(xi) the amino acid sequence comprising RpfD, an immunogenic variant thereof, or an immunogenic fragment of the RpfD or the immunogenic variant thereof comprises the amino acid sequence of positions 121 to 273 of SEQ ID NO: 46, an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 121 to 273 of SEQ ID NO: 46, or an immunogenic fragment of the amino acid sequence of positions 121 to 273 of SEQ ID NO: 46, or the amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 121 to 273 of SEQ ID NO: 46; and/or

(xii) the RNA sequence encoding the amino acid sequence comprising RpfD, an immunogenic variant thereof, or an immunogenic fragment of the RpfD or the immunogenic variant thereof comprises the nucleotide sequence of positions 414 to 872 of SEQ ID NO: 45, a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 414 to 872 of SEQ ID NO: 45, or a fragment of the nucleotide sequence of positions 414 to 872 of SEQ ID NO: 45, or the nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 414 to 872 of SEQ ID NO: 45; and/or

(xiii) the amino acid sequence comprising Mtb32a, an immunogenic variant thereof, or an immunogenic fragment of the Mtb32a or the immunogenic variant thereof comprises the amino acid sequence of SEQ ID NO: 14, an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 14, or an immunogenic fragment of the amino acid sequence of SEQ ID NO: 14, or the amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 14; and/or

(xiv) the RNA sequence encoding the amino acid sequence comprising Mtb32a, an immunogenic variant thereof, or an immunogenic fragment of the Mtb32a or the immunogenic variant thereof comprises the nucleotide sequence of SEQ ID NO: 13, a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 13, or a fragment of the nucleotide sequence of SEQ ID NO: 13, or the nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 13; and/or

(xv) the amino acid sequence comprising Mtb39a, an immunogenic variant thereof, or an immunogenic fragment of the Mtb39a or the immunogenic variant thereof comprises the amino acid sequence of SEQ ID NO: 16,

an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 16, or an immunogenic fragment of the amino acid sequence of SEQ ID NO: 16, or the amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 16; and/or

(xvi) the RNA sequence encoding the amino acid sequence comprising Mtb39a, an immunogenic variant thereof, or an immunogenic fragment of the Mtb39a or the immunogenic variant thereof comprises the nucleotide sequence of SEQ ID NO: 15, a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 15, or a fragment of the nucleotide sequence of SEQ ID NO: 15, or the nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 15; and/or

(xvii) the amino acid sequence comprising M72, an immunogenic variant thereof, or an immunogenic fragment of the M72 or the immunogenic variant thereof comprises the amino acid sequence of positions 27 to 748 of SEQ ID NO: 52, an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 27 to 748 of SEQ ID NO: 52, or an immunogenic fragment of the amino acid sequence of positions 27 to 748 of SEQ ID NO: 52, or the amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 27 to 748 of SEQ ID NO: 52; and/or

(xviii) the RNA sequence encoding the amino acid sequence comprising M72, an immunogenic variant thereof, or an immunogenic fragment of the M72 or the immunogenic variant thereof comprises the nucleotide sequence of positions 132 to 2297 of SEQ ID NO: 51, a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 132 to 2297 of SEQ ID NO: 51, or a fragment of the nucleotide sequence of positions 132 to 2297 of SEQ ID NO: 51, or the nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 132 to 2297 of SEQ ID NO: 51; and/or

(xix) the amino acid sequence comprising HbhA, an immunogenic variant thereof, or an immunogenic fragment of the HbhA or the immunogenic variant thereof comprises the amino acid sequence of positions 433 to 630 of SEQ ID NO: 48, an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 433 to 630 of SEQ ID NO: 48, or an immunogenic fragment of the amino acid sequence of positions 433 to 630 of SEQ ID NO: 48, or the amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 433 to 630 of SEQ ID NO: 48; and/or

(xx) the RNA sequence encoding the amino acid sequence comprising HbhA, an immunogenic variant thereof, or an immunogenic fragment of the HbhA or the immunogenic variant thereof comprises the nucleotide sequence of positions 1350 to 1943 of SEQ ID NO: 47, a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 1350 to 1943 of SEQ ID NO: 47, or a fragment of the nucleotide sequence of positions 1350 to 1943 of SEQ ID NO: 47, or the nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 1350 to 1943 of SEQ ID NO: 47.

4. The composition or medical preparation of any one of claims 1 to 3, which comprises:

(i) an RNA molecule encoding an amino acid sequence comprising Ag85A, an immunogenic variant thereof, or an immunogenic fragment of the Ag85A or the immunogenic variant thereof and Hrp1, an immunogenic variant thereof, or an immunogenic fragment of the Hrp1 or the immunogenic variant thereof;

(ii) an RNA molecule encoding an amino acid sequence comprising ESAT6, an immunogenic variant thereof, or an immunogenic fragment of the ESAT6 or the immunogenic variant thereof and RpfD, an immunogenic variant thereof, or an immunogenic fragment of the RpfD or the immunogenic variant thereof;
(iii) an RNA molecule encoding an amino acid sequence comprising RpfA, an immunogenic variant thereof, or an immunogenic fragment of the RpfA or the immunogenic variant thereof and HbhA, an immunogenic variant thereof, or an immunogenic fragment of the HbhA or the immunogenic variant thereof; and/or
(iv) an RNA molecule encoding an amino acid sequence comprising M72, an immunogenic variant thereof, or an immunogenic fragment of the M72 or the immunogenic variant thereof and VapB47, an immunogenic variant thereof, or an immunogenic fragment of the VapB47 or the immunogenic variant thereof.

5. The composition or medical preparation of claim 4, wherein
(i) the amino acid sequence comprising Ag85A, an immunogenic variant thereof, or an immunogenic fragment of the Ag85A or the immunogenic variant thereof and Hrp1, an immunogenic variant thereof, or an immunogenic fragment of the Hrp1 or the immunogenic variant thereof comprises the amino acid sequence of positions 27 to 465 of SEQ ID NO: 44, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 27 to 465 of SEQ ID NO: 44; and/or
(ii) the RNA sequence encoding the amino acid sequence comprising Ag85A, an immunogenic variant thereof, or an immunogenic fragment of the Ag85A or the immunogenic variant thereof and Hrp1, an immunogenic variant thereof, or an immunogenic fragment of the Hrp1 or the immunogenic variant thereof comprises the nucleotide sequence of positions 132 to 1448 of SEQ ID NO: 43, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 132 to 1448 of SEQ ID NO: 43; and/or
(iii) the amino acid sequence comprising ESAT6, an immunogenic variant thereof, or an immunogenic fragment of the ESAT6 or the immunogenic variant thereof and RpfD, an immunogenic variant thereof, or an immunogenic fragment of the RpfD or the immunogenic variant thereof comprises the amino acid sequence of positions 27 to 273 of SEQ ID NO: 46, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 27 to 273 of SEQ ID NO: 46; and/or
(iv) the RNA sequence encoding the amino acid sequence comprising ESAT6, an immunogenic variant thereof, or an immunogenic fragment of the ESAT6 or the immunogenic variant thereof and RpfD, an immunogenic variant thereof, or an immunogenic fragment of the RpfD or the immunogenic variant thereof comprises the nucleotide sequence of positions 132 to 872 of SEQ ID NO: 45, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 132 to 872 of SEQ ID NO: 45; and/or
(v) the amino acid sequence comprising RpfA, an immunogenic variant thereof, or an immunogenic fragment of the RpfA or the immunogenic variant thereof and HbhA, an immunogenic variant thereof, or an immunogenic fragment of the HbhA or the immunogenic variant thereof comprises the amino acid sequence of positions 27 to 630 of SEQ ID NO: 48, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 27 to 630 of SEQ ID NO: 48; and/or
(vi) the RNA sequence encoding the amino acid sequence comprising RpfA, an immunogenic variant thereof, or an immunogenic fragment of the RpfA or the immunogenic variant thereof and HbhA, an immunogenic variant thereof, or an immunogenic fragment of the HbhA or the immunogenic variant thereof comprises the nucleotide sequence of positions 132 to 1943 of SEQ ID NO: 47, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 132 to 1943 of SEQ ID NO: 47; and/or

(vii) the amino acid sequence comprising M72, an immunogenic variant thereof, or an immunogenic fragment of the M72 or the immunogenic variant thereof and VapB47, an immunogenic variant thereof, or an immunogenic fragment of the VapB47 or the immunogenic variant thereof comprises the amino acid sequence of positions 27 to 846 of SEQ ID NO: 52, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 27 to 846 of SEQ ID NO: 52; and/or

(viii) the RNA sequence encoding the amino acid sequence comprising M72, an immunogenic variant thereof, or an immunogenic fragment of the M72 or the immunogenic variant thereof and VapB47, an immunogenic variant thereof, or an immunogenic fragment of the VapB47 or the immunogenic variant thereof comprises the nucleotide sequence of positions 132 to 2591 of SEQ ID NO: 51, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 132 to 2591 of SEQ ID NO: 51.

6. The composition or medical preparation of any one of claims 1 to 5, wherein the RNA encodes an amino acid sequence comprising a secretory signal peptide, wherein optionally the secretory signal peptide is fused N-terminally to the amino acid sequence; and wherein further optionally

(i) the secretory signal peptide comprises the amino acid sequence of positions 1 to 26 of SEQ ID NO: 44, an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 1 to 26 of SEQ ID NO: 44, or a functional fragment of the amino acid sequence of positions 1 to 26 of SEQ ID NO: 44, or the amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of positions 1 to 26 of SEQ ID NO: 44; and/or

(ii) the RNA sequence encoding the secretory signal peptide comprises the nucleotide sequence of positions 54 to 131 of SEQ ID NO: 43, a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 54 to 131 of SEQ ID NO: 43, or a fragment of the nucleotide sequence of positions 54 to 131 of SEQ ID NO: 43, or the nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of positions 54 to 131 of SEQ ID NO: 43.

7. The composition or medical preparation of any one of claims 1 to 6, which comprises:

(i) RNA comprising the nucleotide sequence of SEQ ID NO: 43, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 43;

(ii) RNA comprising the nucleotide sequence of SEQ ID NO: 45, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 45;

(iii) RNA comprising the nucleotide sequence of SEQ ID NO: 47, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 47; and

(iv) RNA comprising the nucleotide sequence of SEQ ID NO: 51, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 51,.

8. The composition or medical preparation of any one of claims 1 to 7, wherein the RNA is formulated in lipid nanoparticles comprising each of:

(i) a cationically ionizable lipid;

(ii) a steroid;

(iii) a neutral lipid; and

(iv) a polymer-conjugated lipid.

9. The composition or medical preparation of claim 8, wherein the cationically ionizable lipid is present in a concentration ranging from about 40 to about 60 mol percent of the total lipids; and/or wherein the steroid is

present in a concentration ranging from about 30 to about 50 mol percent of the total lipids; and/or wherein the neutral lipid is present in a concentration ranging from about 5 to about 15 mol percent of the total lipids; and/or wherein the polymer-conjugated lipid is present in a concentration ranging from about 1 to about 10 mol percent of the total lipids.

10. The composition or medical preparation of claim 8 or 9, wherein

(i) the cationically ionizable lipid is or comprises ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate); and/or

(ii) the steroid is or comprises cholesterol; and/or

(iii) the neutral lipid is or comprises a phospholipid, optionally being or comprising distearoylphosphatidylcholine (DSPC); and/or

(iv) the polymer-conjugated lipid is or comprises a polyethylene glycol (PEG)-lipid, optionally being or comprising 2-[(polyethylene glycol)-2000]-*N,N*-ditetradecylacetamide.

11. The composition or medical preparation of any one of claims 1 to 10, wherein

(i) the RNA comprises a 5′-cap, wherein optionally the 5′ cap is or comprises a cap1 structure, wherein further optionally the 5′-cap is or comprises $m_2^{7,3'}$-OGppp($m_1^{2'-O}$)ApG; and/or

(ii) the RNA comprises a 5′-UTR, wherein optionally the 5′-UTR is or comprises a modified human alpha-globin 5′-UTR, wherein further optionally the 5′-UTR is or comprises the nucleotide sequence of SEQ ID NO: 56, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 56; and/or

(iii) the RNA comprises a 3′-UTR, wherein optionally the 3′-UTR is or comprises a first sequence from the amino terminal enhancer of split (AES) messenger RNA and a second sequence from the mitochondrial encoded 12S ribosomal RNA, wherein further optionally the 3′-UTR is or comprises the nucleotide sequence of SEQ ID NO: 58, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 58; and/or

(iv) the RNA comprises a polyA sequence, wherein optionally the polyA sequence is an interrupted sequence of A nucleotides., wherein further optionally the polyA sequence comprises 30 adenine nucleotides followed by 70 adenine nucleotides, wherein the 30 adenine nucleotides and 70 adenine nucleotides are separated by a linker sequence of 10 nucleotides, and wherein still further optionally the polyA sequence is or comprises the nucleotide sequence of SEQ ID NO: 59, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 59; and/or

(v) the RNA comprises modified uridines, wherein optionally the RNA comprises modified uridines in place of all uridines, wherein further optionally the modified uridines are N1-methyl-pseudouridine; and/or

(vi) the coding sequence of the RNA is codon-optimized and/or is characterized in that its G/C content is increased compared to the parental sequence.

12. The composition or medical preparation of any one of claims 1 to 11, wherein the RNA is in a liquid formulation, a frozen formulation or a lyophilized formulation.

13. The composition or medical preparation of any one of claims 1 to 12, wherein the RNA is formulated for injection, wherein optionally the RNA is formulated for intramuscular administration.

14. The composition or medical preparation of any one of claims 1 to 13, which is a pharmaceutical composition, wherein the pharmaceutical composition optionally further comprises one or more pharmaceutically acceptable carriers, diluents and/or excipients.

15. The composition or medical preparation of any one of claims 1 to 14, which is a vaccine.

16. The composition or medical preparation of any one of claims 1 to 13, which is a kit, wherein optionally different RNA molecules are in separate vials, the kit further optionally comprising instructions for use of the composition or medical preparation for treating or preventing tuberculosis.

17. The composition or medical preparation of any one of claims 1 to 16 for pharmaceutical use.

18. Use of the composition or medical preparation of any one of claims 1 to 16 in the manufacture of a medicament for a therapeutic or prophylactic treatment of tuberculosis in a human subject.

19. The use of claim 18, wherein the medicament is to be administered to the subject for vaccinating the subject, optionally by intramuscular administration.

20. The use of claim 18 or 19, wherein the subject is to be administered at least one dose or at least two doses of the composition, wherein optionally an amount of the RNA of at least 10 µg per dose is to be administered.