Background

The CAR-T cell therapy market has been growing rapidly, driven by the success of companies like Kite Pharma (Kite), Celgene Corporation (Celgene), and AbbVie (AbbVie). These companies have developed therapies that target various cancers, including leukemia and lymphoma. The success of these therapies has led to increased interest in CAR-T cell technology, and many companies are now focused on developing new CAR-T cell therapies.

CAR-T cell therapy involves the use of genetically modified T cells to target and destroy cancer cells. The T cells are modified by adding a CAR, which is a chimeric antigen receptor. The CAR is a protein that is engineered to recognize and bind to a specific antigen on the surface of cancer cells.

The CAR-T cell therapy market is expected to continue to grow as new therapies are developed, and existing therapies are improved. The market is expected to reach $10 billion by 2025, with the potential for even larger growth in the future.

aRNA and LNPs combine to make a broad platform

Figure 1: Orna has a versatile platform to address many therapeutic areas.

CAR aRNA Design

The aRNA has three components for optimization:

1. RIS
2. CAR amino acid sequence
3. CAR readthrough sequence

1. Natural full-length RIS sequences from the human/mouse lincRNAs
   - increased translational in human T cells
2. Clonally selected CAR amino acid sequence for PSC
   - For aRNA CAR RNA
3. CAR aRNA sequence optimized for CAR functional expression

Figure 4: Description of the UCAR product concept and schematic of clonally selected CAR aRNA sequences.

or nanoparticles (LNP) formulation, and cell inflammatory cytokine production compared to controls. To maximize protein expression, we developed the FoRCE (Formulated oRNA Cell Engineering) complex cell engineering protocols. To redose oCAR enabled weekly dosing at clinically relevant dose levels producing well tolerated efficacy and tumor control.

Figure 6: Description of the Formulated oRNA Cell Engineering protocols.

Figure 7: CD19 oCAR expression is improved through a combination of codon optimization and T cell active IRES selection.

Antibodies & Proteins

• Antibodies & Proteins
• mAbs
• Therapeutics
• Low COGS
• Simple multiplexing through in situ detection
• Critical capability for IRES screening

Figure 8: In situ CAR assay platform interrogation of the IRCome (Flow)+ high throughput screening system.

Conclusions

• CAR-T cells are a promising treatment option for cancer patients worldwide.
• New therapies are being developed to improve the efficacy and safety of CAR-T cell therapy.
• The market for CAR-T cell therapy is expected to continue to grow as new therapies are developed.

Figure 9: UCAR is effective, optimal scalability, predictability, robust delivery.

aRNA

• aRNA offers a transient, off-the-shelf treatment option for cancer patients without malignancies.
• aRNA drug substance consists of a CAR encoding linked to an IAP.
• aRNA expression is driven by an IRES sequence (internal ribosome entry site).
• Tumor bearing mice show tumor regression following treatment with aRNA CAR+NAT.
• Orna’s high-throughput screening platform enables interrogation of the IRCome to identify novel therapies that drive high protein expression in T cells.
• Optimized CAR+DNA constructs show improved in vivo efficacy and tumor control at doses as low as 0.06 mg/kg.
• In vivo efficacy is as low as doses in vivo every other week.
• Lower and less frequent dosing enables a higher therapeutic window for Orna-101.

Figure 10: UCAR activity in tumors is significantly improved with codons optimization and T cell active IRES selection.

Figure 11: UCAR CAR-T efficacy is improved through a combination of codon optimization and T cell active IRES selection.