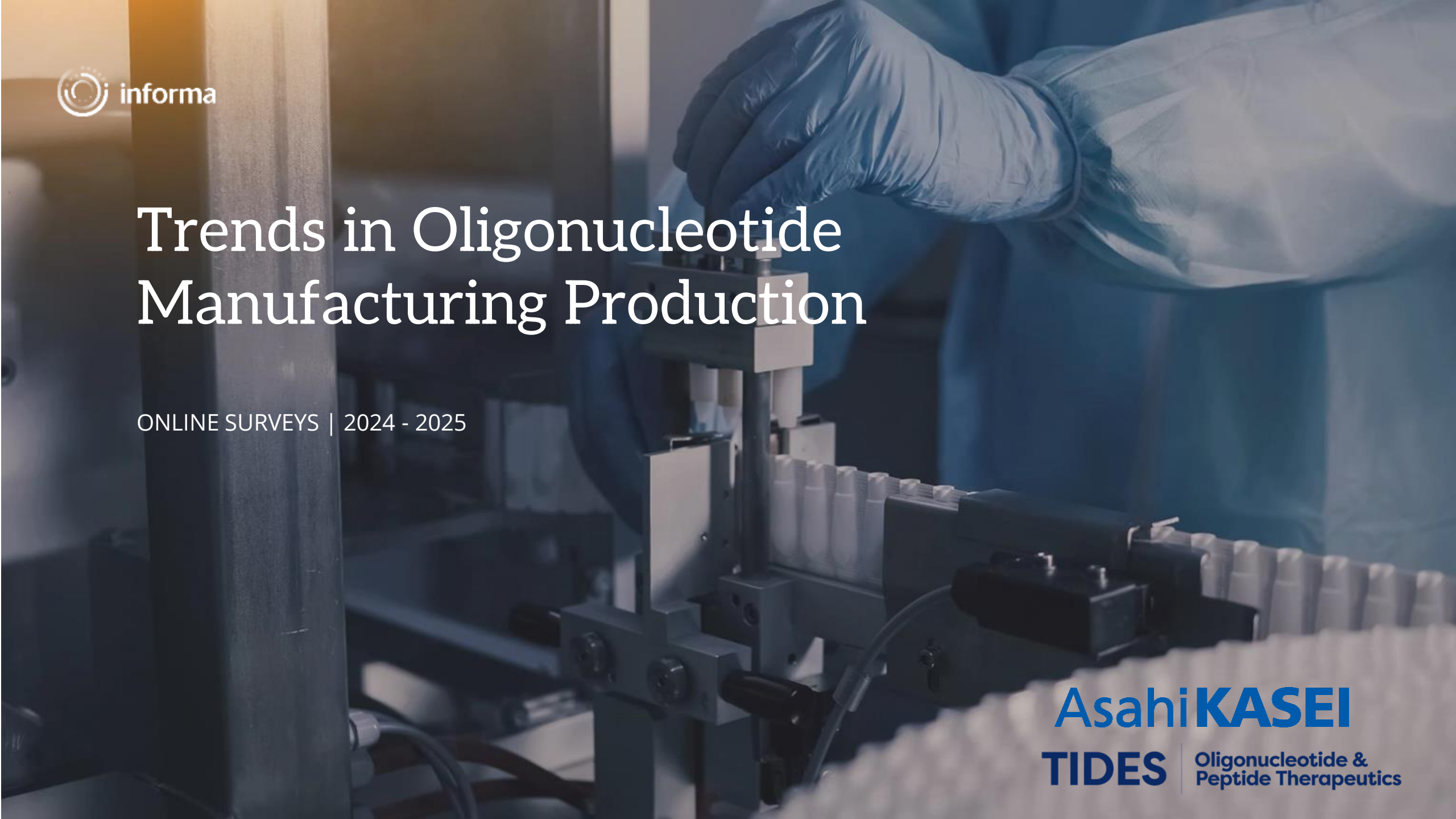


informa

Trends in Oligonucleotide Manufacturing Production

ONLINE SURVEYS | 2024 - 2025

AsahiKASEI

TIDES | Oligonucleotide & Peptide Therapeutics

Table of Contents

Section 1.
Introduction

informa

Overview

Methodology, data collection and analysis by TIDES in cooperation with Asahi Kasei. Data collected August 6 - 22, 2025. Methodology conforms to accepted marketing research methods, practices and procedures.

Methodology

Beginning on August 6, 2025, TIDES sent emailed invitations to participate in an online survey to active users. By August 22, 2025, TIDES com had received 102 qualified respondents - employed in a role involving the development and/or manufacture of oligonucleotide therapeutics.

Comparative data collected July 31 – August 14, 2024.

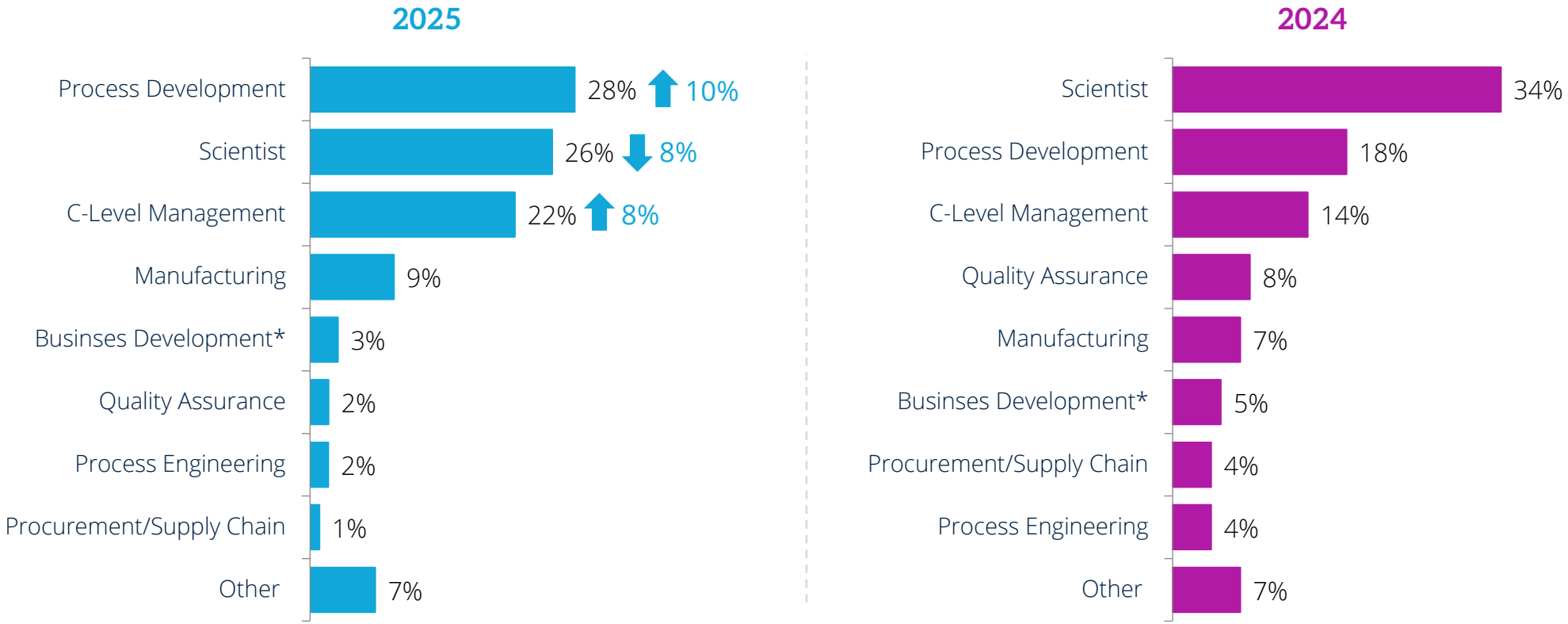
Response Motivation

To encourage prompt response and increase the response rate overall, email invitations and survey materials were branded with the TIDES name and logo to capitalize on user affinity.

Each respondent was afforded the opportunity to enter a drawing for one of two $/£/€200 Amazon gift cards

Primary Job Function

The primary job functions held by respondents remained stable over time, despite variation in specific incidences: Process Development, Scientist and C-Level Management.



Question: Which of the following BEST describes your primary job function?
Base: All respondents (2025 n=102; 2024 n=102). *Response option added due to a large number of "other" write-ins.

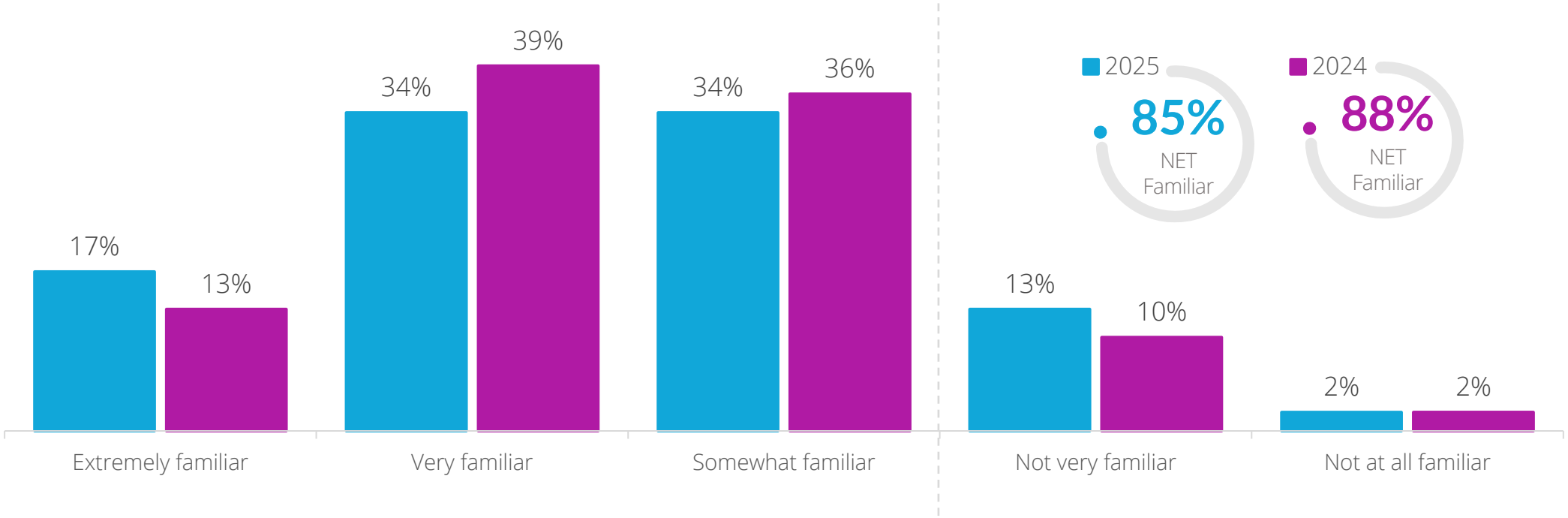
Section 2.

Production Scale-Up in Oligonucleotide Manufacturing

informa

Familiarity with the Topic of Scaling Up Production in Oligonucleotide Manufacturing Specifically

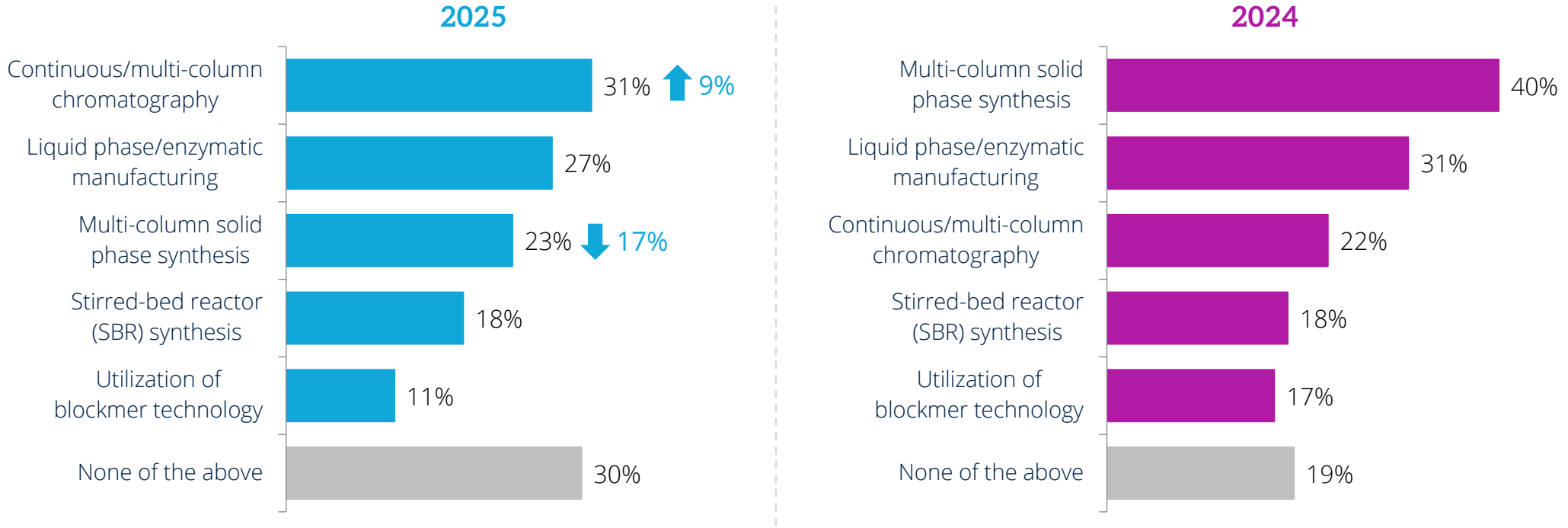
Familiarity with the topic of scaling up production in oligonucleotide manufacturing has remained stable over time.



Question: How familiar are you with the topic of scaling up production when it comes to oligonucleotide manufacturing specifically?
Base: All respondents (2025 n=102; 2024 n=102).

Scale-up Practices Adopted in Oligonucleotide Manufacturing

The adoption of two scale-up practices in oligonucleotide manufacturing changed notably in 2025: multi-column solid phase synthesis decreased 17%, and continuous/multi-column solid phase synthesis increased 9%.



Question: Which of the following scale-up practices, if any, has your organization adopted in your oligonucleotide manufacturing processes? (Select all that apply.)
Base: All respondents; multiple answers permitted (2025 n=102; 2024 n=102).

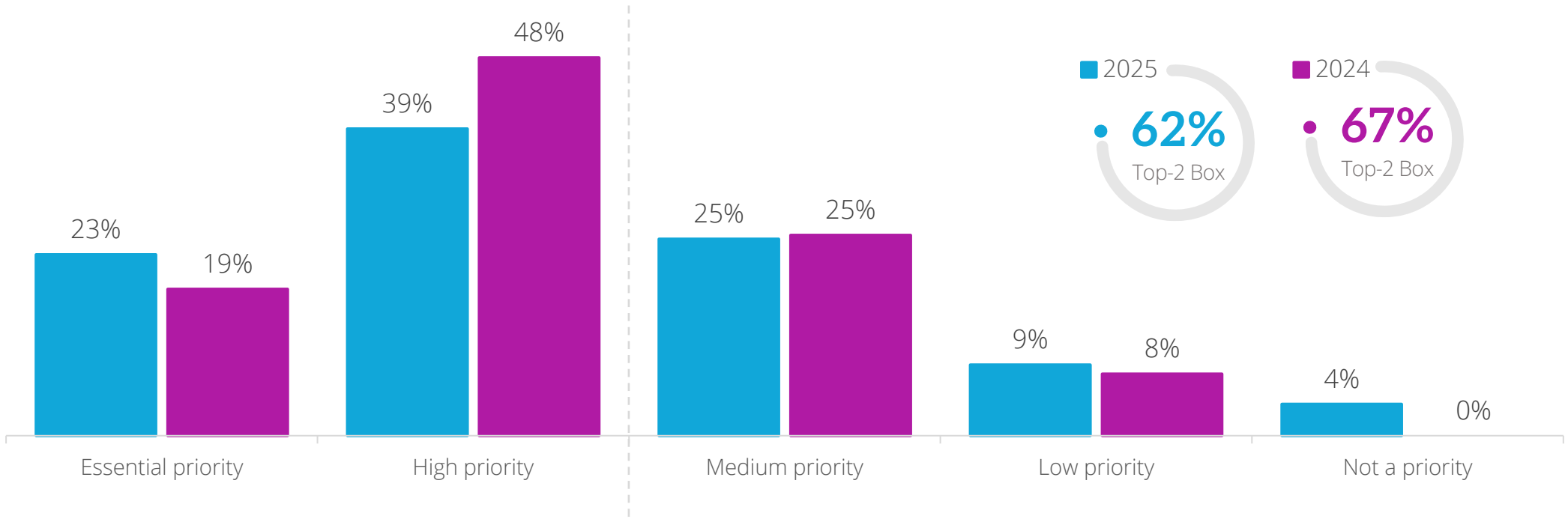
Section 3.

Technology & Scale-Up Solutions

informa

Priority Placed on Seeking Solutions to Scale Manufacturing

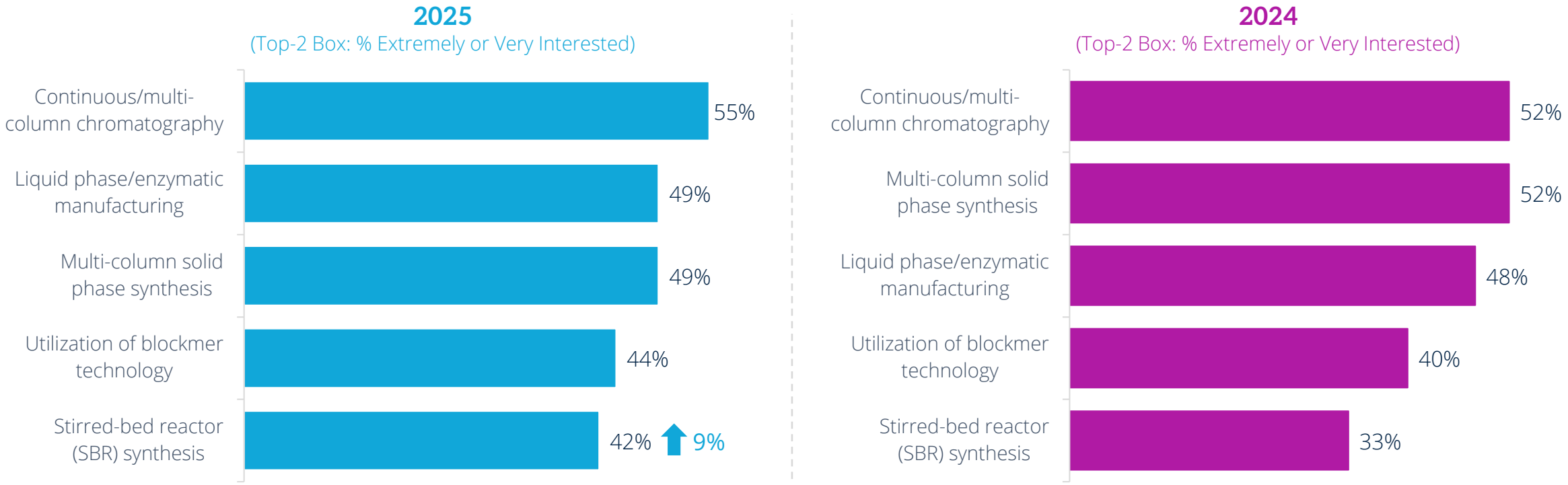
As in 2024, most 2025 respondents report their organizations consider seeking solutions to scale manufacturing processes a “high” or “essential” priority.



Question: How much of a priority does your organization place on seeking solutions to scale its manufacturing processes?
Base: All respondents (2025 n=102; 2024 n=102).

Top-2 Box Summary: Interest in Oligonucleotide Manufacturing Scale Up Solutions

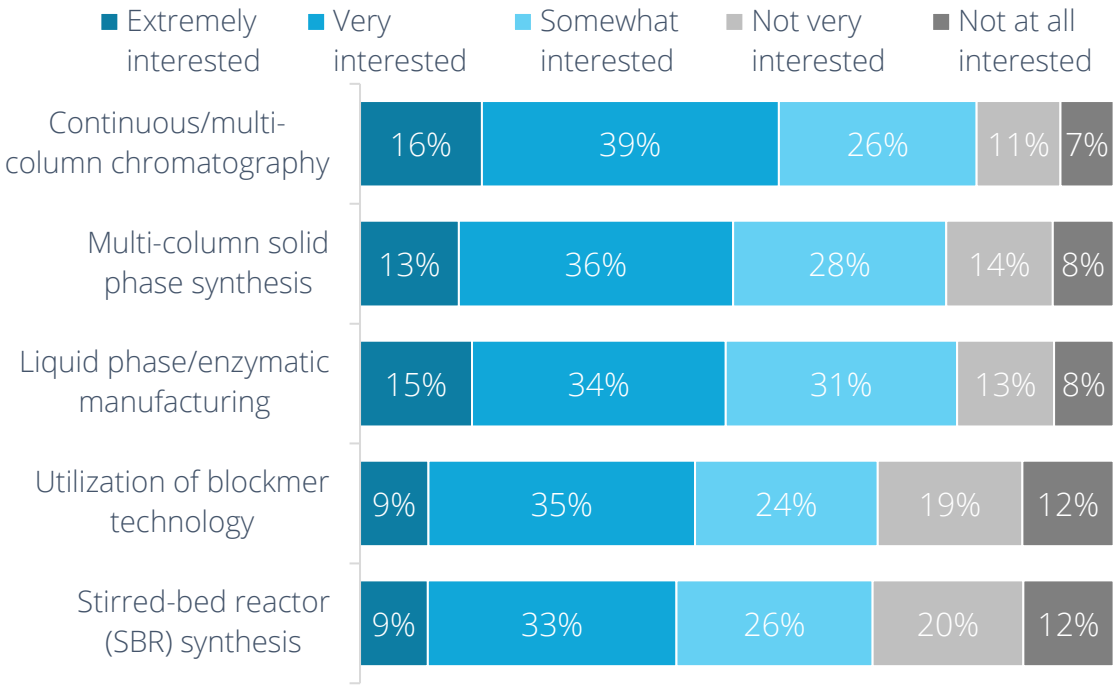
Interest in oligonucleotide manufacturing scale-up solutions remained largely stable over time with one exception. Interest in stirred-bed reactor (SBR) synthesis increased 9% in 2025.

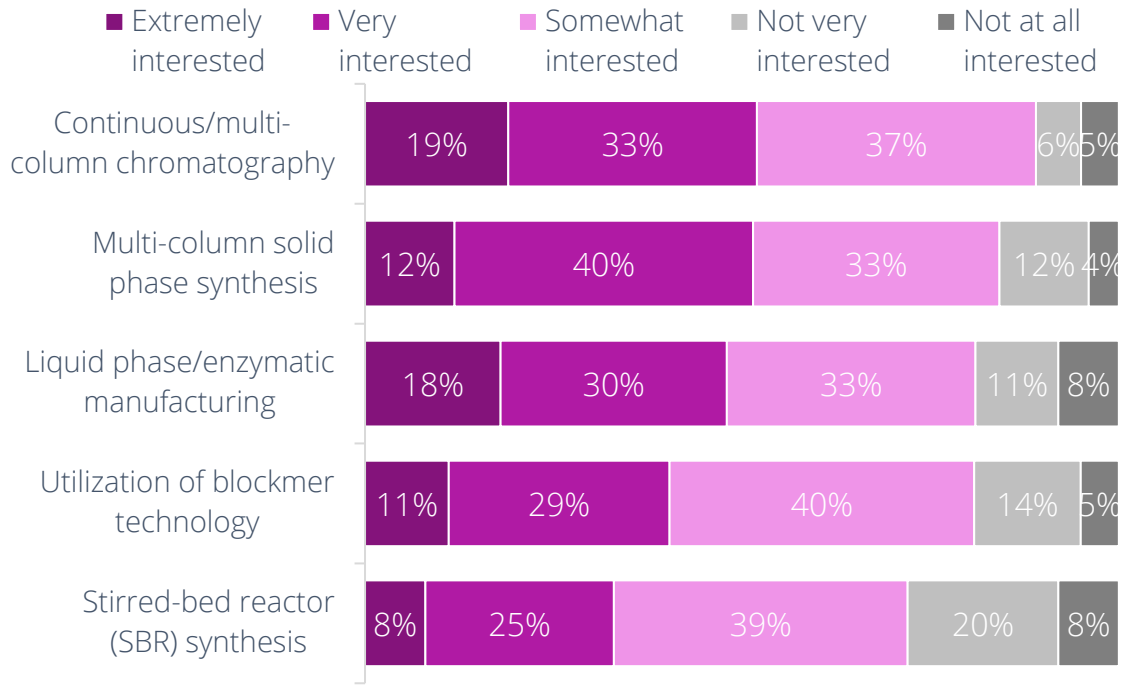


Question: Please rate your interest in the following oligonucleotide manufacturing scale-up solutions.
Base: All respondents (2025 n=102; 2024 n=102).

Full Detail: Interest in Oligonucleotide Manufacturing Scale Up Solutions

Interest in oligonucleotide manufacturing scale-up solutions remained largely stable over time with one notable exception. Interest in SBR synthesis increased 9% in 2025.

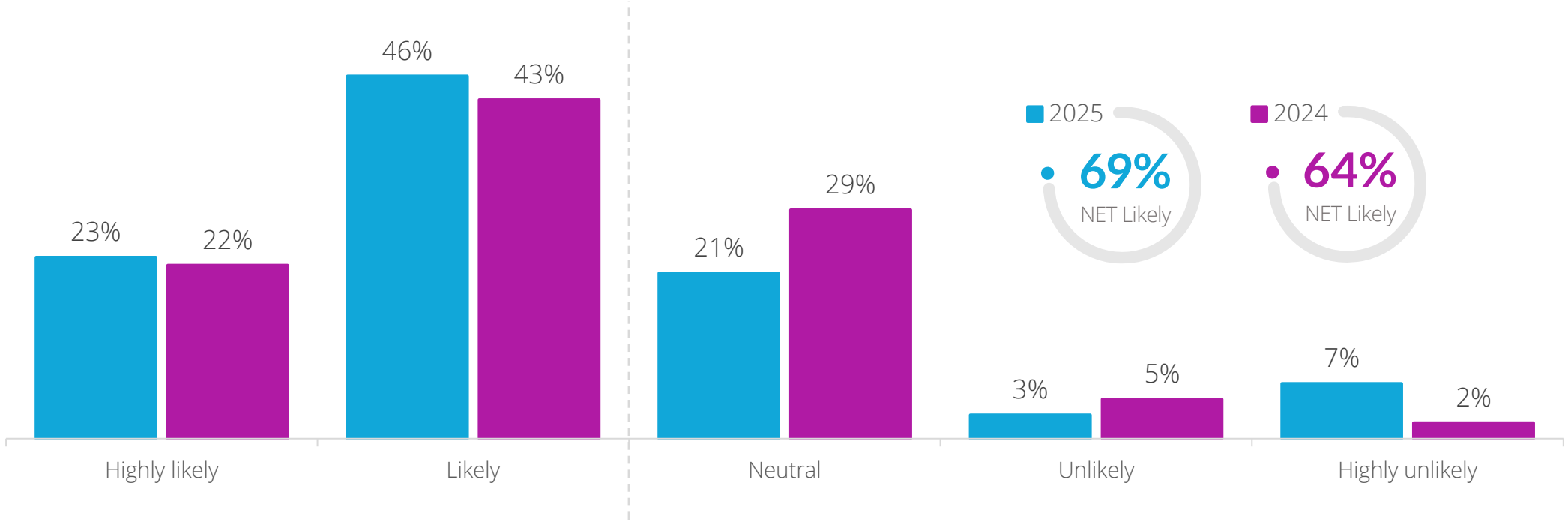




Question: Please rate your interest in the following oligonucleotide manufacturing scale-up solutions.
Base: All respondents (2025 n=102; 2024 n=102).

Investment Likelihood: Technologies to Increase Productivity

As in 2024, most 2025 respondents report their organizations are likely to invest in technologies that would increase overall productivity of their manufacturing.



Question: How likely is your organization to invest in technologies that would increase the overall productivity of your manufacturing?
Base: All respondents (2025 n=102; 2024 n=102).

Potential Oligonucleotide Manufacturing Scale-up Solutions

When asked to freely mention what other oligonucleotide manufacturing scale-up solutions could be considered, four clear focus areas emerged from the 2025 sample:

1. **Synthesis approaches** are evolving beyond traditional methods toward enzymatic and liquid-phase alternatives, continuous flow technology with non-protected monomers, and improved solid-phase techniques.
2. **Purification innovations** center on advanced chromatography with better resins and RP-HPLC replacing IEX, alongside non-chromatographic methods like affinity peptides and TFF, with many seeking to eliminate lyophilization for liquid API.
3. **Process optimization** emphasizes automation through solid-phase platforms and microfluidic synthesis, while maintaining consistent batch quality and exploring scale-out strategies.
4. **Emerging technologies** generating interest include circular oligonucleotides, antibody-oligo conjugates, nanoparticle formulations, and novel mRNA manufacturing approaches—all representing potential paradigm shifts in the field.

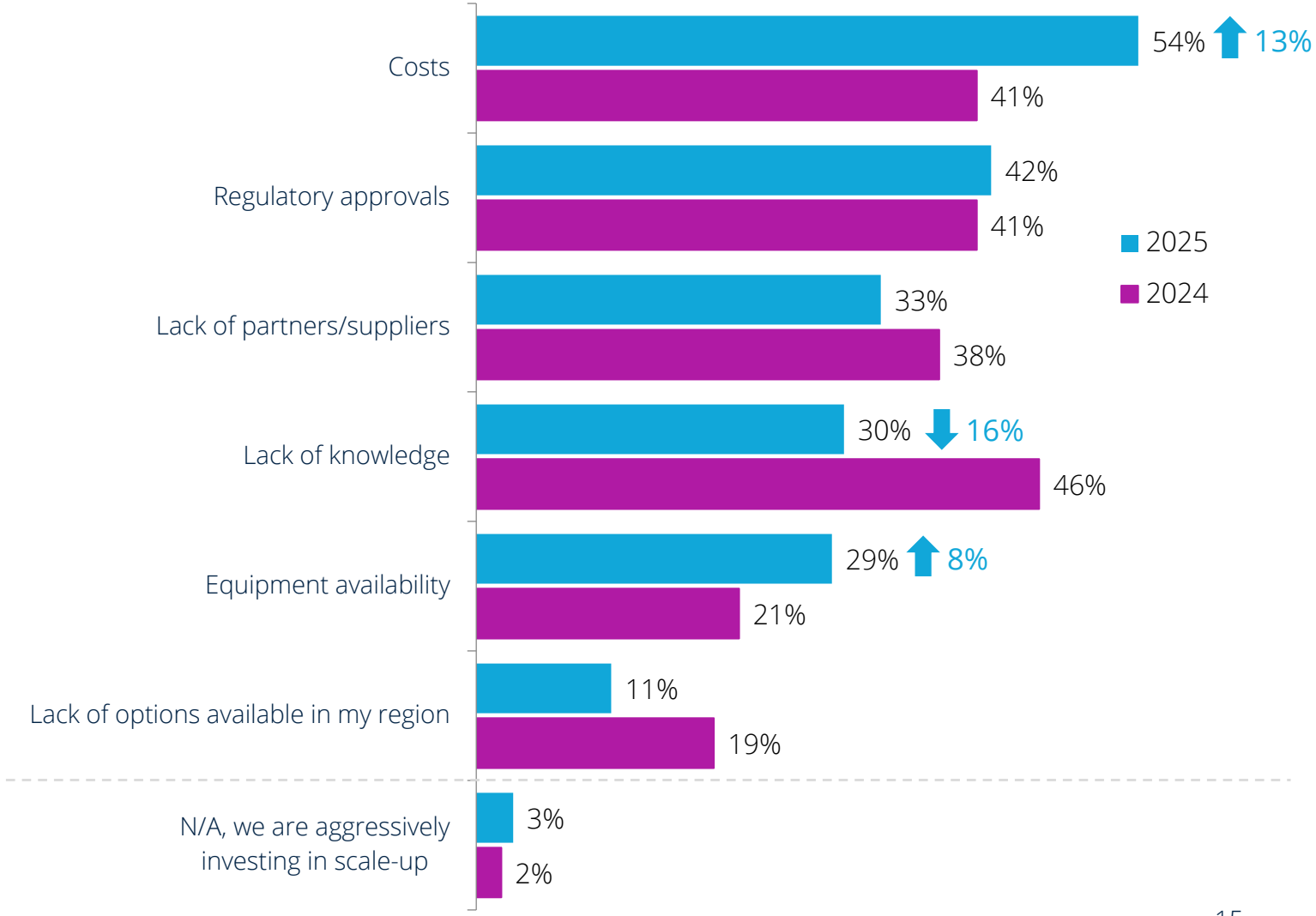
Question: What other oligonucleotide manufacturing scale-up solutions could be considered (both near- and long-term)?
Base: 2025 respondents providing a response (2025 n=37)

Barriers to More Aggressively Investing in Scale-Up Solutions

The key barriers to more aggressively investing in solutions that will facilitate manufacturing scale-up varied over time, with a bit more variation between barriers in 2025.

In 2025 the key barriers were costs (54%) and regulatory approvals (42%).

In 2024, lack of knowledge emerged as the primary barrier (46%), followed by costs (41%), regulatory approvals (41%) and lack of partners/suppliers (38%).



Question: What are the key barriers to more aggressively investing in solutions that will facilitate manufacturing scale-up? (Select all that apply.)
Base: All respondents; multiple answers permitted (2025 n=102; 2024 n=102).

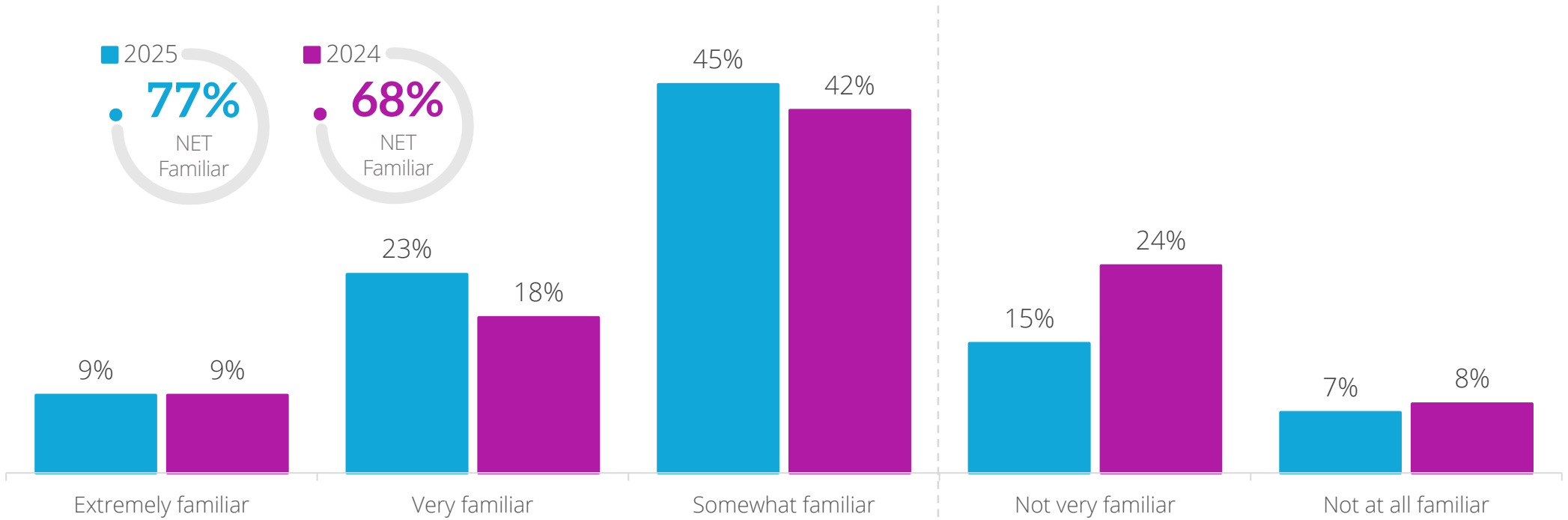
Section 4.

Liquid/Enzymatic Development for Oligonucleotide Synthesis

informa

Familiarity with the Advancements in Liquid/Enzymatic Development for Oligonucleotide Synthesis

Familiarity with the advancements in liquid/enzymatic development for oligonucleotide synthesis increased notably in 2025 (up 9% over 2024).

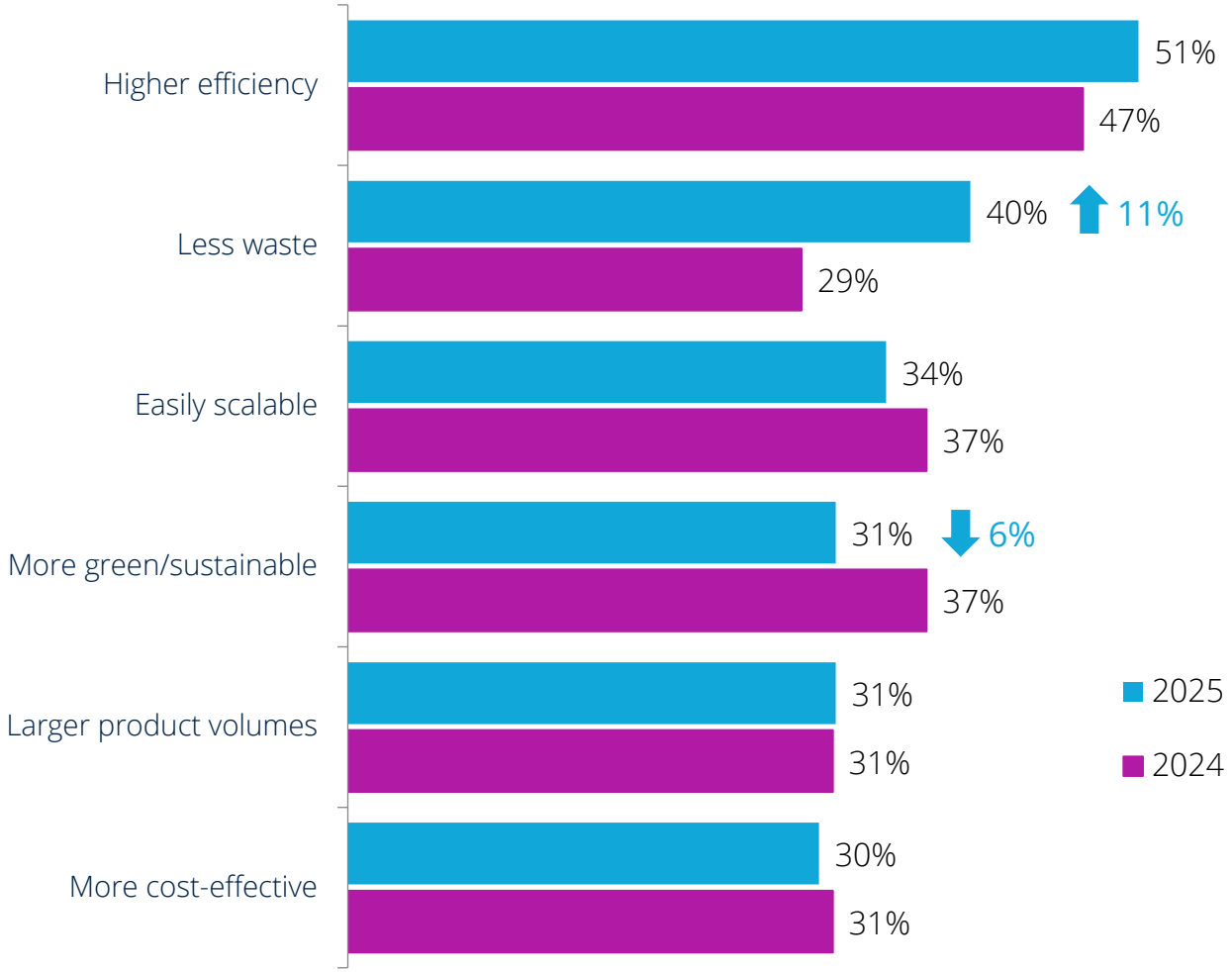


Question: Are you familiar with the advancements in liquid/enzymatic development for oligonucleotide synthesis?
Base: All respondents (2025 n=102; 2024 n=102).

Main Advantages of Liquid/Enzymatic Development Over Solid-Phase Synthesis for Oligonucleotides

The key main advantages of liquid/enzymatic development over solid-phase synthesis for oligonucleotides remained largely stable over time, with two exceptions:

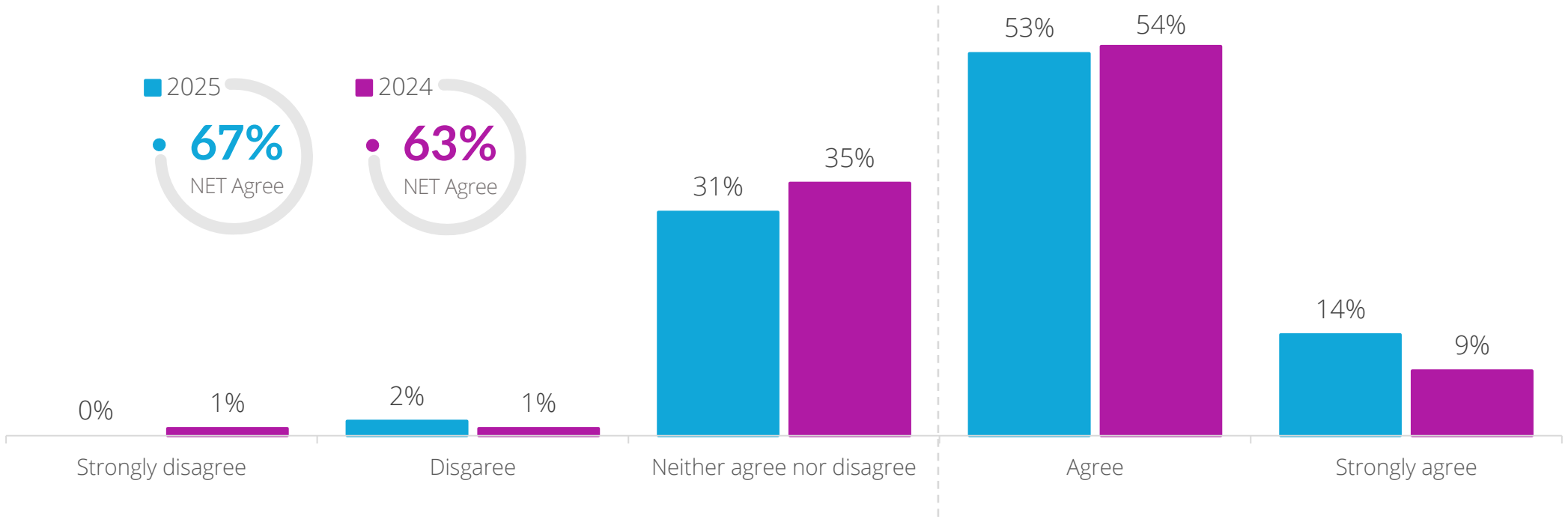
- Less waste increased 11%
- More green/sustainable decreased 6%



Question: In your opinion, what are the main advantages of liquid/enzymatic development over solid-phase synthesis for oligonucleotides? (Select all that apply.)
Base: All respondents; multiple answers permitted (2025 n=102; 2024 n=102).

Can Liquid/Enzymatic Development Realistically be Implemented to Manufacture Large Amounts of Oligonucleotides More Efficiently?

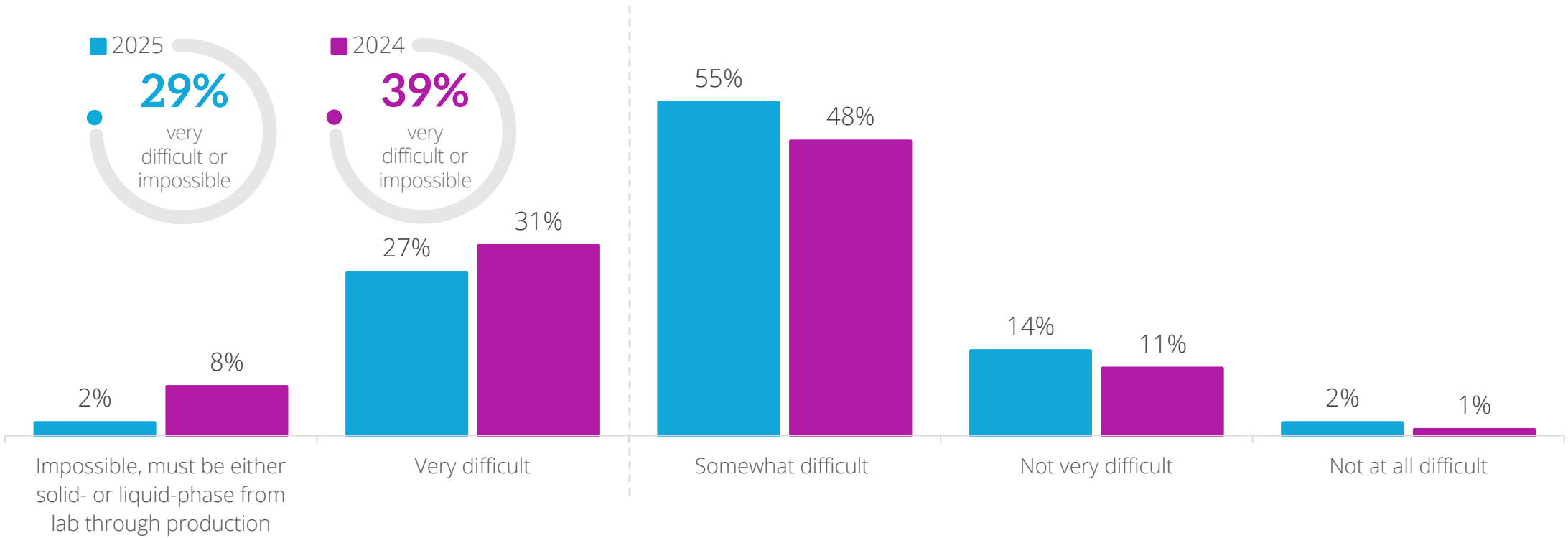
Most respondents continue to agree that liquid/enzymatic development can realistically be implemented to manufacture large amounts of oligonucleotides more efficiently.



Question: How strongly do you agree or disagree that liquid/enzymatic development can realistically be implemented to manufacture large amounts of oligonucleotides more efficiently?
Base: All respondents (2025 n=102; 2024 n=102).

Difficulty of Switching to Enzymatic Process for Large-Scale Production of an Oligonucleotide Drug Developed via Solid-Phase Synthesis

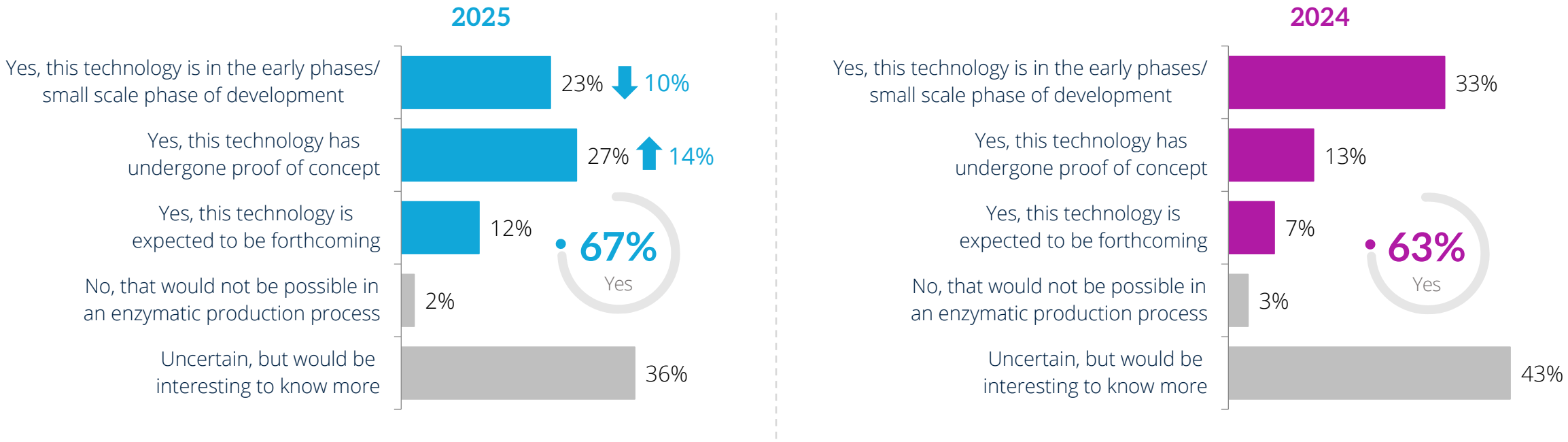
In the 2025 sample, significantly fewer respondents (down 10%) believe it would be "very difficult" or "impossible" to switch to an enzymatic process for large-scale production of an oligonucleotide drug developed via solid-phase synthesis. However, most still believe doing so would be at least "somewhat" difficult.



Question: How strongly do you agree or disagree that liquid/enzymatic development can realistically be implemented to manufacture large amounts of oligonucleotides more efficiently?
Base: All respondents (2025 n=102; 2024 n=102).

Can an Oligonucleotide Sequence be Prepared for Post-Synthetic Conjugation During the Enzymatic Production Process

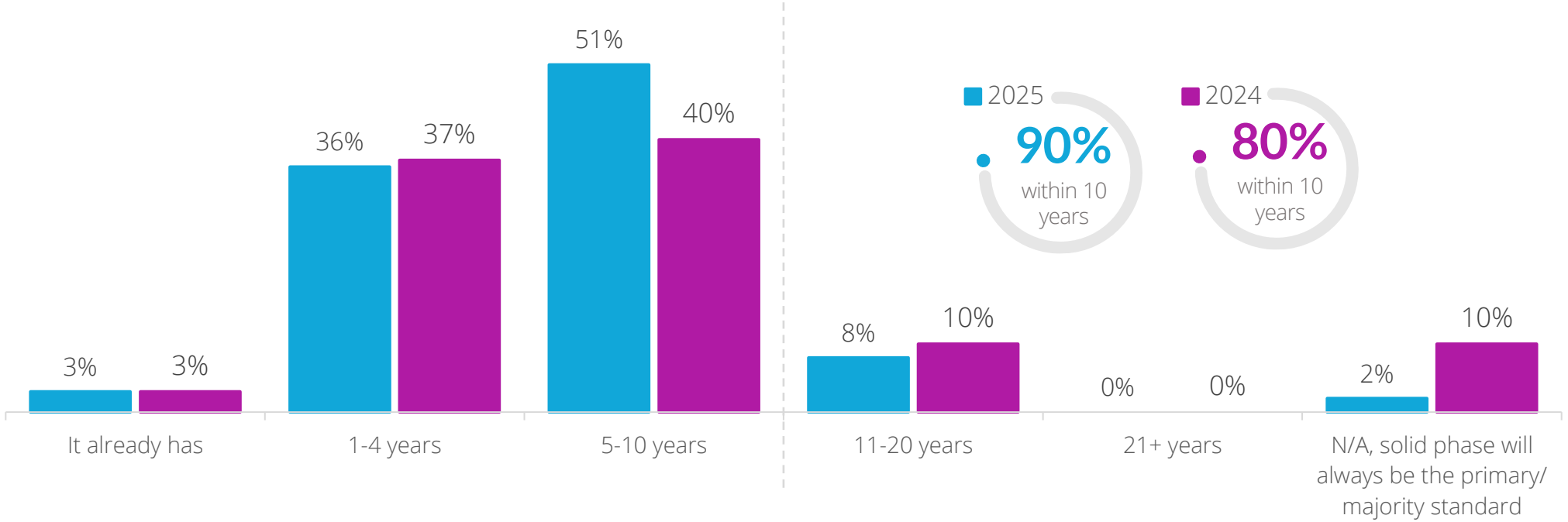
In 2025, slightly more respondents (increased 4%) believe an enzymatically produced oligonucleotide to improve drug delivery/uptake, half or respondents. However, 2025 saw fewer respondents reporting this technology is in the early phases/small scale phase of development (decreased 10%) and more reporting the technology has undergone proof of concept (increased 14%).



Question: Considering potential modification to an enzymatically produced oligonucleotide to improve drug delivery/uptake, can an oligonucleotide sequence be prepared for post-synthetic conjugation during the enzymatic production process (addition of a linker)?
Base: All respondents (2025 n=102; 2024 n=102).

Timeframe for Liquid/Enzymatic Production Overtaking Solid Phase Synthesis as the Primary Development Mode

In the 2025 sample, 90% of respondents believe liquid/enzymatic production of oligonucleotides will overtake solid phase synthesis as the primary mode of development within the next ten years. This is a 10% increase over the 2024 sample.



Question: In what timeframe do you believe liquid/enzymatic production of oligonucleotides may overtake solid phase synthesis as the primary mode of development?
Base: All respondents (2025 n=102; 2024 n=102).

informa

Thank you

TIDES | Oligonucleotide & Peptide Therapeutics