BACHEM

OLIGONUCLEOTIDE THERAPEUTICS

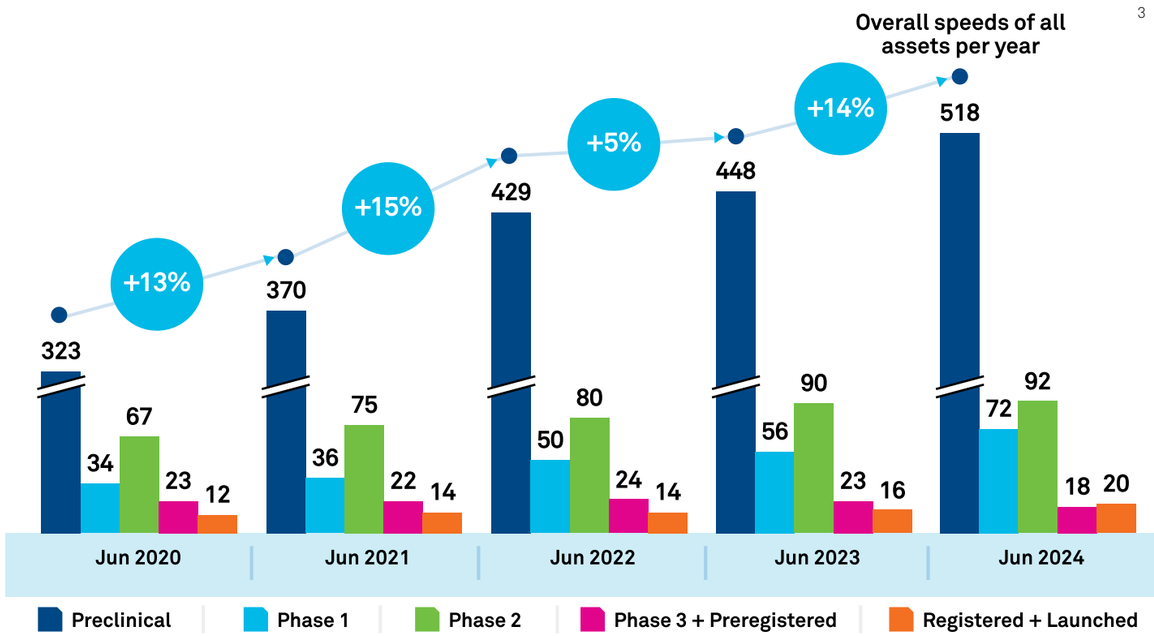
Pioneering a New Era of Precision and Efficacy

OLIGONUCLEOTIDES: THE FUTURE OF TARGETED THERAPIES

Oligonucleotide therapeutics are a groundbreaking class of drugs with the potential to transform how we treat many diseases. These short, single-stranded DNA or RNA molecules bind to specific targets within cells, modulating gene expression and cellular pathways through several mechanisms (for example, by targeting pre-mRNA, mRNA, non-coding RNA, modulating splicing events, interfering with protein translation).[1] As such, oligonucleotides (oligos) not only offer highly targeted therapies for previously unmet medical needs, their applications continue to expand beyond rare diseases into broader patient populations, such as cardiovascular diseases and central nervous system disorders.[2]

The Global Oligo Pipeline Keeps Growing

The oligonucleotide market is rapidly expanding, with increasing regulatory approvals and a growing pipeline of promising candidates.



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Further growth expected, in particular for stages Preclinical to Phase 2 as well as Launched

Relative stagnation of the numbers in Phase 3 as also observed for the overall global pharma pipeline, according to data presented at Pharma R&D Annual Review 2024

FDA approval of at least one more drug, expected by end of 2024

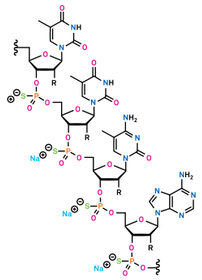
BACHEM: YOUR TRUSTED PARTNER FOR OLIGONUCLEOTIDE PRODUCTS

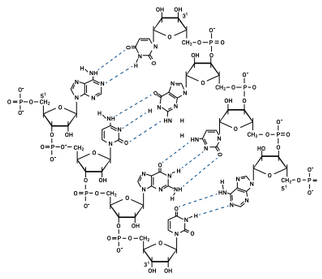
Oligonucleotides offer a distinct advantage over traditional small molecule drugs by expanding the druggable genome. While small molecules primarily target proteins, oligonucleotides can target non-coding RNA and other previously inaccessible therapeutic targets, allowing drug developers to impact many cellular processes.[4]

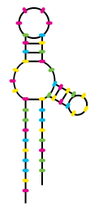
Oligo Platforms

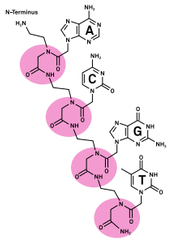
To help achieve your therapeutic goals, Bachem offers oligonucleotide platforms that include:

- siRNA (small interfering RNA)
- ASO (antisense oligonucleotides)
- Aptamers
- Anti-miR (anti-microRNA)


ASO (Single Stranded)


siRNA (double stranded)


Aptamers (folded)



Peptide Nucleic Acid (PNA)

Oligonucleotide Conjugates

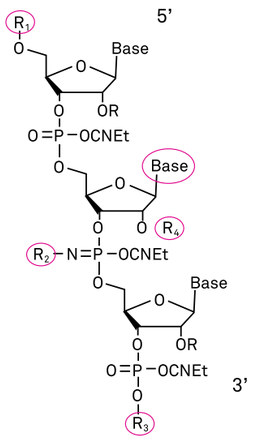
Bachem has extensive experience in conjugation chemistries, linkers and modifications:

- Conjugates: Fatty acids, phosphates, linker-conjugates
- Conjugation Chemistries: Thiol-maleimide, click chemistry and disulfide formation
- Linkers: SMCC, BCN-NHS, DBCO, DPDS-NHS
- Modifications: Cysteine or azide (peptide/protein); amines (oligonucleotide)

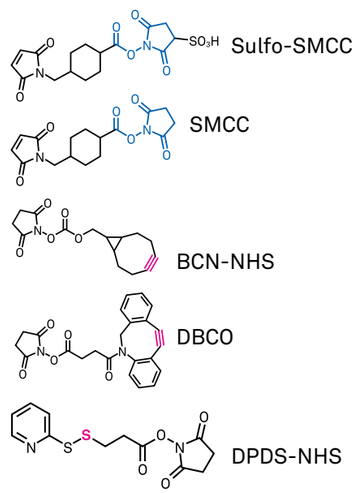
Conjugation Chemistry

Bachem's Experience

- Bachem has applied different conjugation reactions, most common ones are thiol-maleimide, click chemistry or disulfide formation
- Different commercially available linkers established for several conjugation reactions
- Different modifications of the peptide/protein and oligonucleotide applicable; most common ones are Cysteine or an azide at the peptide/protein and amines for the oligonucleotide
- Different ligation sites feasible; most common one at 5' end



Potential ligation sites oligonucleotide



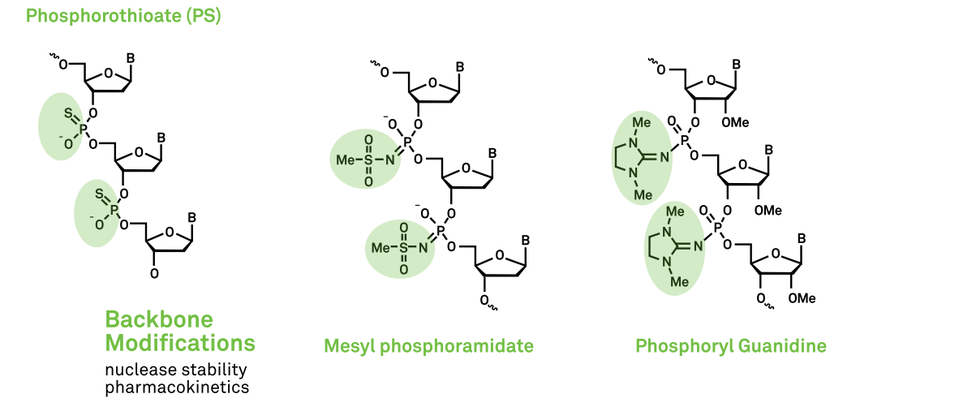
Common linkers for peptide/protein conjugation

Chemical Modifications

Bachem offers a suite of chemical modifications to optimize your oligonucleotide therapeutics, enhancing stability, improving delivery and reducing immunogenicity:

- 2'-F, 2'-OMe, 2'-MOE, bridged nucleic acids (e.g., LNA, etc.)
- PS (phosphorothioate), PN (phosphoramidate), vinyl phosphonates and methyl phosphonates backbone modifications

Process development and manufacturing of these oligonucleotide modalities is well established at Bachem, with four commercial products and over a hundred commercial API batches produced.

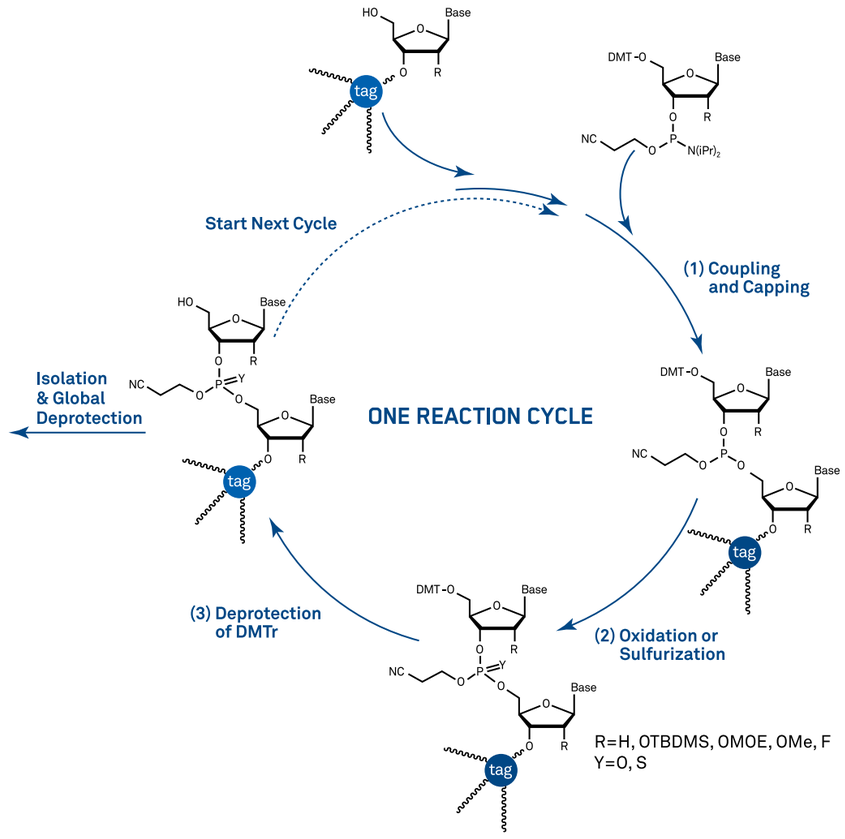


Also: Fatty acids, Phosphates, Linker- Conjugates

INNOVATIVE TECHNOLOGIES FOR A SUSTAINABLE AND EFFICIENT FUTURE

Current oligonucleotide manufacturing technologies are resource and waste intensive, posing constraints on large-scale production and sustainability.[5] We are driving innovation in oligonucleotide manufacturing by developing and implementing cutting-edge technologies that enhance sustainability, cost-efficiency and scalability:

- **SBT SPOS (stirred bed technology for solid phase oligonucleotide synthesis):** Enables efficient oligonucleotide synthesis with reduced waste generation and improved environmental impact
- **MCSGP (multicolumn countercurrent solvent gradient purification):** Continuous chromatography process that reduces solvent consumption and increases purification efficiency
- **LPOS/Jitsubo (liquid phase oligonucleotide synthesis):** A favorable technology for large-scale production, offering a promising alternative to traditional solid-phase synthesis and the potential for further reductions in environmental impact



LPOS is based on a soluble support (tag) enabling product isolation by precipitation/ filtration or extraction.

Speed to Market

Our streamlined processes and efficient project management enable us to deliver GMP material **in as little as 8 months**. With our ongoing capacity expansion, new projects can be started immediately.

YOUR PROJECT, OUR PRIORITY

Our comprehensive suite of services and capabilities empowers you to achieve your oligonucleotide development and manufacturing goals.

Success Starts With the Right Team for the Job

SIX SITES ON THREE CONTINENTS

Reliable partner with chemical expertise
We accompany you from preclinical development to commercialization, producing your high-quality, complex API

An unmatched technology toolbox
From state-of-the-art synthesis to cutting-edge and sustainable manufacturing of the future, we've got your needs covered

GMP from lab to commercial scale
Scale your manufacturing process with predictable yield and quality; from gram to kilogram

Fast drug substance supply
We can deliver high quality material even under very aggressive CMC timelines

Your project can start today
We are currently doubling our capacity and maximum output; there is no waiting time to start your project

We manufacture safe, reliable and high-quality oligonucleotide API to make your mission a reality

STRONG SYNTHESIS CAPABILITIES FOR ALL SCALES OF OLIGONUCLEOTIDE PROCESS R&D, SCALE-UP AND PRODUCTION

RESEARCH AND DEVELOPMENT
0.5 – 4 mmol

- Cytiva OP100
- ÄKTA Oligosynt

SMALL-MID SCALE GMP PRODUCTION
15 - 200 mmol

- Cytiva OP400
- AKBA OligoSynth200

LARGE-SCALE GMP PRODUCTION
0.2 – 2 mol

- AKBA OligoSynth2000
- Cytiva OligoProcess

ESTABLISHED FULL RANGE OF CMC SERVICES FOR TIDES CUSTOMERS AND PARTNERS

R&D Scale Process Transfer / Establishment / Development → R&D Scale Confirmation Batch Production → Scale-up Preparation → Non-GMP Production → GMP Preparation Work → GMP Production, Release & Dispositioning

ANALYTICAL TRANSFER / DEVELOPMENT / VALIDATION WORK

MICROBIOLOGY / ENDOTOXIN METHOD DEVELOPMENT & VALIDATION

From Clinical to Commercial API

Bachem offers a full range of CMC services, from early-stage process development to commercial API production. Services include:

- Process R&D, scale-up and GMP production
- Supporting documentation and life cycle management
- Analytical development, stability and degradation studies
- Microbiology and endotoxin method validation
- Failure mode analysis, batch comparison and reference standards

Bachem accelerates your advancement from clinical to commercial API.

Success Starts Now

Our streamlined processes, rapid drug substance supply and expanding capacity ensure that your project stays on track and reaches the market rapidly.

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Drug innovators rely on Bachem's expertise, speed and efficient, sustainable manufacturing practices to get therapies to patients faster. Partner with Bachem to start your project today.

THE FUTURE OF OLIGONUCLEOTIDE APIS STARTS HERE

References

[1] Moumné, L., et al. Oligonucleotide Therapeutics: From Discovery and Development to Patentability. *Pharmaceutics*. Published 2022 February.

[2] Kirkpatrick, P. Widening the horizons of oligonucleotide drug platforms. *Nature Biopharma Dealmakers*. Published 2023 November.

[3] Pharmaprojects. Data as of June 12, 2024. mRNA programs omitted. Webinar "Pharma R&D Annual Review 2024," Chaline, May 25, 2024.

[4] Wang, J., et al. Noncoding RNAs Emerging as Drugs or Drug Targets: Their Chemical Modification, Bio-Conjugation and Intracellular Regulation. *Molecules*. Published 2022 October.

[5] Andrews, B.I., et al. Sustainability Challenges and Opportunities in Oligonucleotide Manufacturing. *The Journal of Organic Chemistry*. Published 2020 November.

BACHEM

GLOBAL BUSINESS

Bachem facilities are located in Switzerland, the U.K. and in the U.S. All cGMP manufacturing sites are inspected by the U.S. FDA and national authorities.

About Bachem

Bachem is a leading, innovation-driven company specializing in the development and manufacture of peptides and oligonucleotides. The company, which has over 50 years of experience and expertise, provides products for research, clinical development and commercial application to pharmaceutical and biotechnology companies worldwide and offers a comprehensive range of services. Bachem operates internationally with headquarters in Switzerland and locations in Europe, the U.S. and Asia. The company is listed on the SIX Swiss Exchange. For further information, see www.bachem.com.

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2044207 Published by Global Marketing, Bachem AG, Dezember 2024