

PlasmidFactory®

Solutions for AAV vector production

Powering your AAV therapies with DNA made by experts

PlasmidFactory 25 YEARS

Your trusted CDMO Partner

Why choose PlasmidFactory



- 25+ years of DNA manufacturing expertise
- Independent, flexible & trusted European CDMO
- Scalable production: Research → High Quality → GMP Grades
- Proprietary technologies: Minicircle, ITRPROTECT®, ITRRESCUE®, POLYARESCUE®
- 3,500+ plasmid & Minicircle projects delivered, incl.136 GMP-like projects & 5 production runs in the GMP facility
- 99.9% success rate

Company info

Minicircle info

GMP Manufacturing You Can Trust

Designed for highest plasmid & Minicircle DNA quality requirements



Status: Commissioning completed
First GMP batches successfully produced

State-of-the-art GMP facility

- Dedicated building for GMP Grade plasmid & Minicircle DNA
- 450 m^2 cleanrooms suites (grades C & D)
- Facility designed to prevent cross-contamination

Flexible manufacturing with highest safety standards

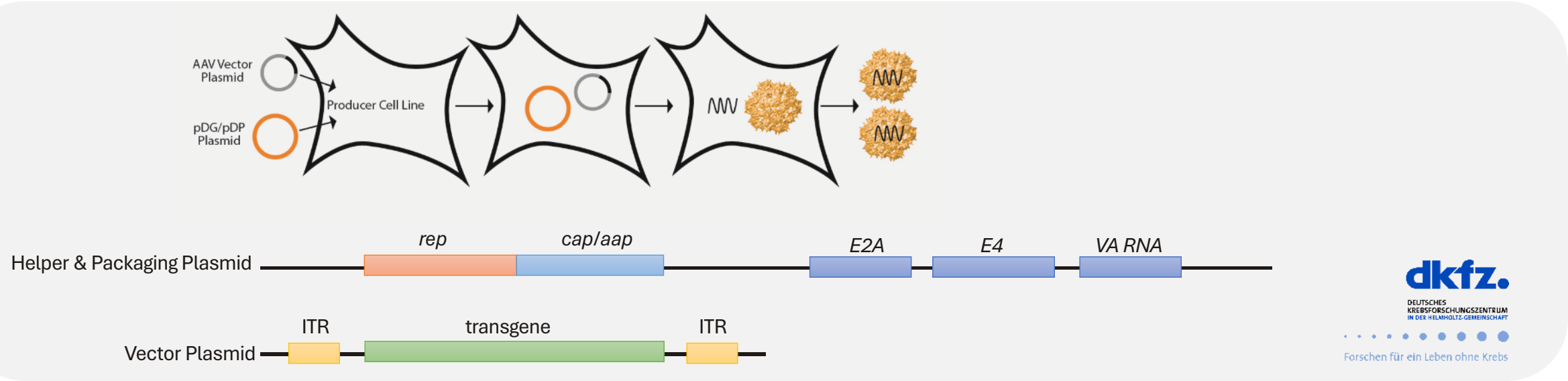
- End-to-end single-use USP- and DSP- process
- Ph. Eur. / USP grade WFI supply
- EU GMP-Part 2 and 4, Annex 1 & 2, AMWHV
- Various fill & finish options
- QP batch release

Full GMP compliance

- Data integrity measures and systems in place
- Appendix 11/21 CFR Part 11

GMP info

Exclusive 2-Plasmid System

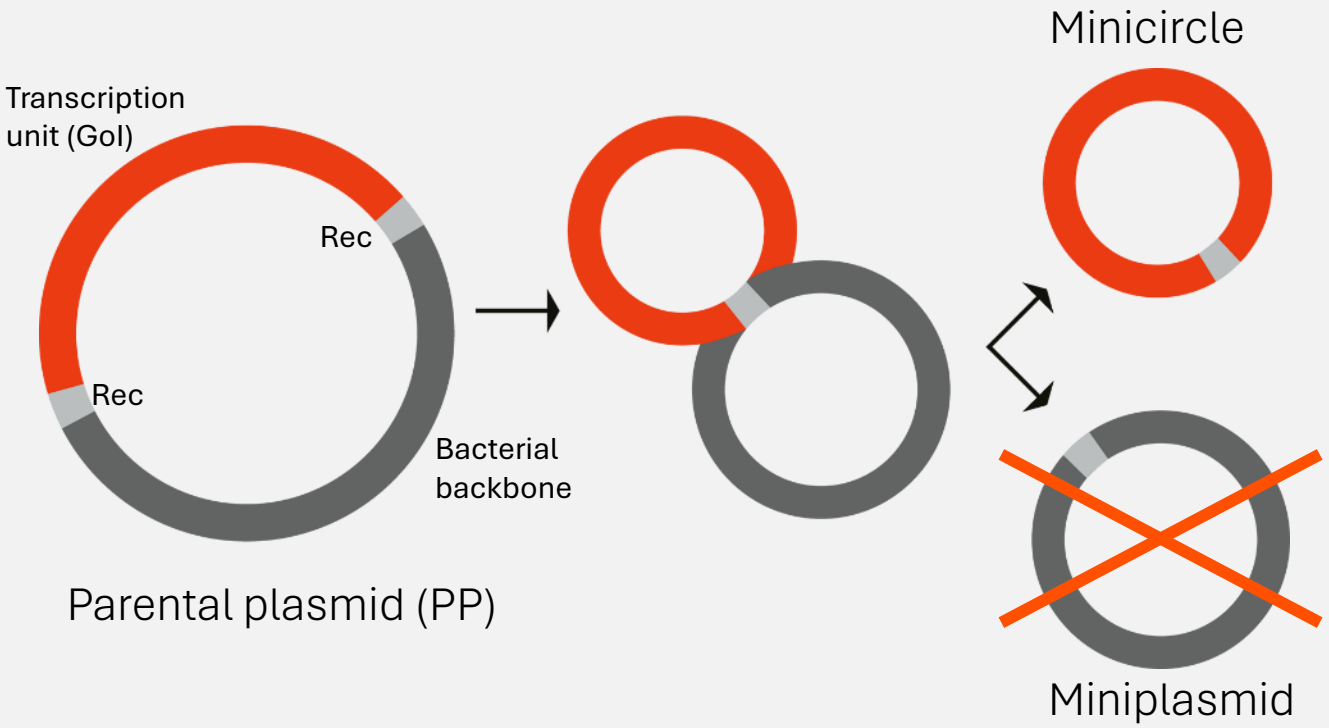


- **Simplified AAV workflow:** Helper + Packaging on one plasmid; fewer components, less complexity
- **Higher efficiency & consistency:** Consistent transfection performance with lower DNA input
- **Cost-effective & GMP-ready:** Reduced DNA production and QC burden, easily scalable to GMP production
- **Future-proof design:** Available as Minicircle and compatible with ITRPROTECT® / ITRRESCUE® technologies
- **Full flexibility**: Either use "full“ Minicircle system, or replace just the vector plasmid and keep individual packaging/helper plasmids

Minicircle: Proprietary Production Method

Minimalistic DNA vector reduced to the gene of interest (GoI) and available in GMP

Minicircle production

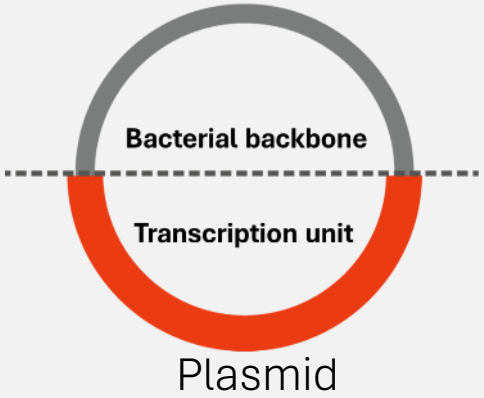


Minicircle vs. plasmid features



- No bacterial backbone
- Small, supercoiled

- Bacterial sequences
- Larger size



Minicircle: Small, monomeric, supercoiled

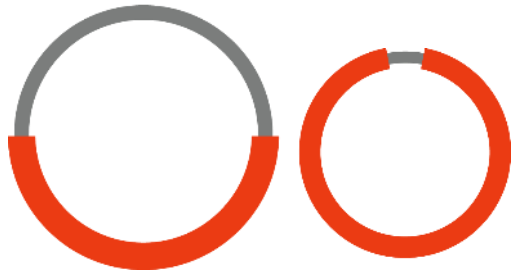
Minicircle info

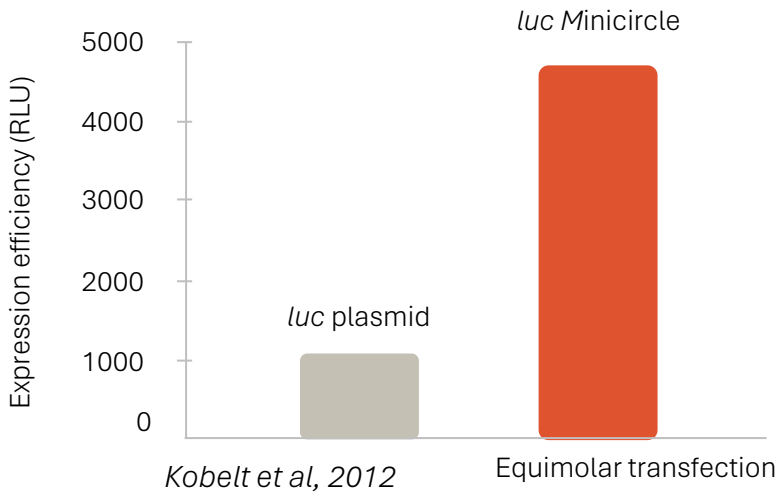
Minicircle: Advantages at a Glance

The ideal DNA format for AAV manufacturing

Bacterial backbone-free Minicircles

- No antibiotic resistance or other bacterial markers
- Less immunogenicity
- Lower DNA toxicity
- Higher transfection efficiency
- Reduced transgene silencing
- Stronger, more stable gene expression
- Compatible with **ITRPROTECT®/ITRRESCUE®** for functional ITRs
- **Better yield & transduction efficiency, reduced costs**
- **No "back-packing“ & improved safety in AAV production**



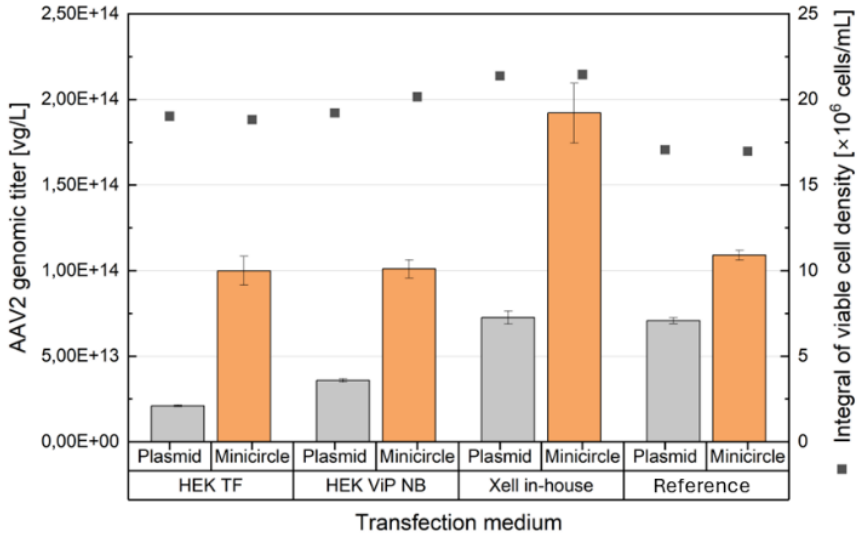


Minicircle: Small, monomeric, supercoiled

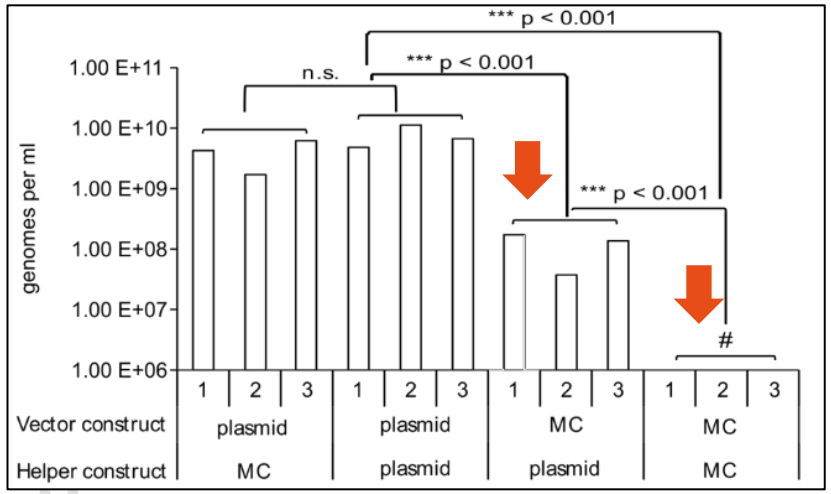
AAV products

Minicircles in AAV Production for higher Vector Purity and increased Titers

A)



B)



Kraemer et al., ESGCT Annual Congress 2021
Schnödt et al., Mol. Ther.-Nucl. Acids 2016

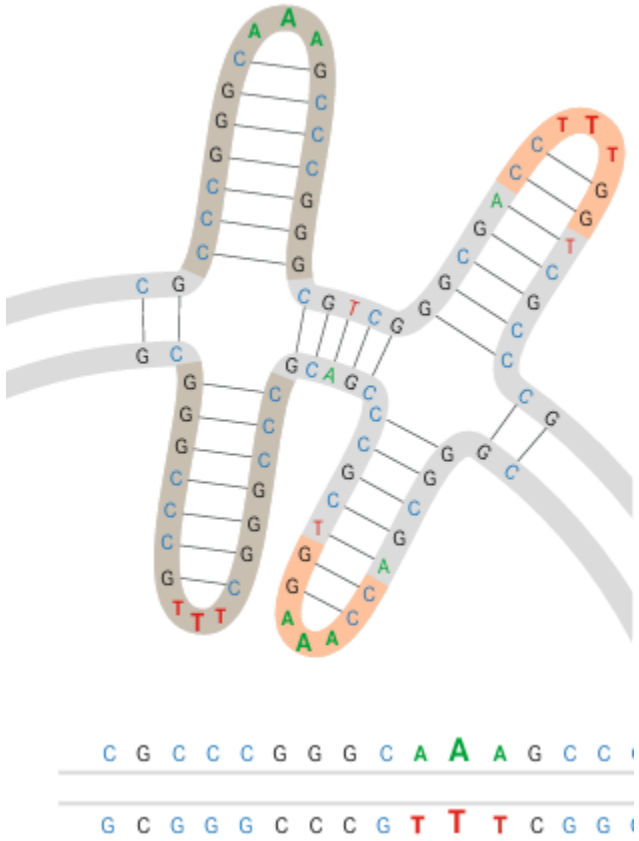
- **Marked increase in viral titers**: 3 to 4-fold (A)
- **No back-packaging**: higher vector purity and product consistency (B)
- **Improved transduction efficiency**: up to 30× higher (scAAV; data not shown)
- **Cleaner & safer** – lower immunogenicity, less silencing, up to GMP Grade (data not shown)

Article title: DNA Minicircle Technology Improves Purity of Adeno-associated Viral Vector Preparations

AAV webinar

Keeping ITRs Intact: ITRPROTECT® & ITRRESCUE®

Preserved ITRs for better yield, purity and packaging efficiency



- **ITR instability is a known challenge:** In AAV transfer plasmids, inverted terminal repeats (ITRs) are prone to truncation during plasmid amplification, reducing vector yield, purity, and packaging efficiency (Radukic et al., Mol. Ther.-Nucl. Acids 2025).
- **ITRPROTECT® safeguards your sequences:** Our proprietary technology ensures stable amplification while preserving ITRs exactly as provided by the customer
- **ITRRESCUE® restores functionality:** We can analyze ITR integrity and, if necessary, replace truncated regions with full-length wild-type ITRs to recover fully functional AAV plasmids.
- **Reduce variability:** Full-length ITRs, either restored when needed and preserved during amplification, ensure stable vector performance and predictable AAV packaging.

Minicircle: Might improve AAV Safety

Minicircle DNA represents the new responsible standard for safer AAV manufacturing


nature medicine

Brief Communication

Contaminating plasmid sequences and disrupted vector genomes in the liver following adeno-associated virus gene therapy

DNA Minicircle Technology Improves Purity of Adeno-associated Viral Vector Preparations

Contaminating plasmid sequences and disrupted vector genomes in the liver following adeno-associated virus gene therapy Zolgensma *(Buddle et. al; Nature Med. 2026)*

- Plasmid-based AAVs can carry unintended DNA sequences ("back-packing“)
- Manufacturing plasmid DNA is detectable in patient hepatocytes
- This carryover may correlate with liver toxicity in high-dose AAV therapy

DNA Minicircle Technology Improves Purity of Adeno-associated Viral Vector Preparations *(Schnödt et al., Mol. Ther.-Nucl. Acids 2016)*

- Plasmid-based AAV production leads to bacterial backbone DNA packaging
- Minicircle DNA reduces backbone sequences below detectable levels
- Resulting AAV vectors are free of plasmid-derived DNA impurities
- Vector yields and transduction efficiency are signaficantly increased

AAV safety

AAV Production: Flexibility at its Best

PlasmidFactory®

Option 1 **PlasmidFactory's own 2-plasmid system**	Option 2 **Hybrid system**	Option 3 **Amplification of existing system**
Rationale: No customer AAV production system existing yet	**Rationale:** Keeps existing system, but upgrade with MC benefits	**Rationale:** DNA amplification only at scale needed
• Proprietary 2-plasmid AAV system (transfer plasmid + helper/packaging plasmid) • Chose classical plasmids or Minicircle systems (or hybrid) • Compatible with ITRRESCUE®/ITRPROTECT® ○ **Best for:** New programs & platform development ○ **Key benefit:** Modern & efficient 2-plasmid system	• Replace just transfer plasmid of existing 2- or 3-plasmid system with Minicircle • Customer's helper/ packaging plasmids remain unchanged • Compatible with ITRRESCUE®/ITRPROTECT® ○ **Best for:** Established platforms ○ **Key benefit:** Quality upgrade without revalidation (e.g. reduced backpacking, increased productivity)	• Amplification of any existing AAV system, fully or partially • Scalable up to GMP Grade • ITRRESCUE®/ITRPROTECT® as service option • **Best for:** Already established late-stage & commercial programs • **Key benefit:** Reliable & scalable supply by experts

Your system of choice, our manufacturing expertise: Adopt ours. Upgrade yours. Scale your own!

Testimonials

Selected Publications

1. Schnödt *et al.*, Mol. Ther.-Nucl. Acids 2016
2. Grimm D *et al.*, Mol Ther, 2003



References

Reithera SRL, Italy
Successfully tested PlasmidFactory's 2-plasmid & Minicircle system. Data available.

Sartorius Xell GmbH, Germany
Successfully tested PlasmidFactory's 2-plasmid & Minicircle system. Data available.

DINAMIQS, Switzerland
Successfully tested PlasmidFactory's 2-plasmid & Minicircle system. Testimonial available.

Additional 30+ customers
Application of PlasmidFactory's 2-plasmid & Minicircle system in AAV manufacturing. No disclosure due to NDA.

Minicircle DNA: Clinical Footprint

Snapshot of registered and planned clinical trials using Minicircle for cell engineering

Registered clinical trials

2020 — **CARAMBA-1 - SLAMF7 CAR-T (Multiple Myeloma)** — Recruitment ended

- Phase I/IIa (FiH) • EUCT 2024-512643-23-00 • NCT04499339
- Virus-free Sleeping Beauty gene transfer using Minicircle DNA + transposase mRNA
- Opened Jun 2020 • 33 participants • DE site (multi-country approvals reported in EU project updates)

2024 — **TranspoCART19 - CD19 CAR-T (r/r B-cell Lymphoma)** — Recruiting

- Phase I/IIa • EUCT 2024-514544-90-00 • NCT06378190
- Non-viral Sleeping Beauty transposon delivered as a Minicircle + SB100X mRNA
- Start Mar 2024 • 27 participants • 9 sites (Spain)

2025 — **LION-1 - ROR1 CAR-T (ROR1$^+$ tumors)** — Recruiting

- Phase I (FiH) • EUCT 2024-512019-36-00 • NCT pending (CTIS)
- Start Apr 2025 • 46 participants • 1 site (Germany)
- Includes hematologic + solid tumors (e.g., MCL, CLL, TNBC, OC, ACC)

2026 — **TCX-001 - Siglec-6 CAR-T (r/r AML & CLL)** — Recruiting

- Phase I (FiH) • SNCTP000006901 • BASEC2026-00192
- Non-viral Sleeping Beauty CAR-T program using Minicircle DNA
- Recruiting • 1 site (Zurich)

Studies in preparation

Oncology (engineered cells)

- ROR2 CAR-T (Uniklinikum Würzburg; Phase I (FiH) start planned in 2026)
- FLT3 CAR-T (Uniklinikum Würzburg)

Autoimmune / gene therapy

- Nimvec™ AM510 (Amarna; Type 1 Diabetes)

Undisclosed / confidential

- At least 4 additional clinical studies in preparation

Minicircles in AAV Production: The Time is Now!

Key considerations when evaluating Minicircle DNA for AAV production

- **Is backbone-free DNA really needed?**
  Yes — recent clinical findings (Buddle et al.) highlight backbone DNA carryover as a potential safety concern.
- **Does it cost more?**
  No — pricing is typically equimolar to standard plasmids, with added quality and safety benefits.
- **Is it future-proof?**
  Yes — aligned with increasing regulatory expectations and supported by GMP manufacturing capabilities.
- **Is it truly unique?**
  Yes — unlike “mini/nano-plasmids,” PlasmidFactory’s Minicircles completely lack bacterial backbone sequences.
- **Is the company established?**
  Yes — strong European presence for 25 years and expanding capabilities toward the U.S. market.



- **Higher yields:** 3–4× increased titers and up to 30× higher transduction rates
- **More functional AAV particles:** Fewer empty capsids, no back-packaging
- **Cleaner & safer:** Lower immunogenicity, reduced gene silencing, improved vector quality
- **Secure**: Compatible with **ITRPROTECT®** and **ITRRESCUE®** to ensure functional ITRs
- **Future-ready:** Scalable GMP production and better long-term regulatory fit



Get in touch:

contact@PlasmidFactory.com

www.plasmidfactory.com/contact/

PlasmidFactory 25 YEARS

PlasmidFactory GmbH

Meisenstraße 96 | 33607 Bielefeld | Germany

PlasmidFactory.com