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# Abbreviations

AC, anthracycline-cyclophosphamide;

CHMP, Committee for Medicinal Products for Human Use;

CTD, common technical document;

EGFR, epidermal growth factor receptor;

EMA, European Medicines Agency;

FDA, Food and drug administration;

FIH, first in human;

FMECA, failure modes effects and criticality analysis;

GCP Good clinical practice;

GLP Good laboratory practice;

GMP, Good manufacturing practice;

HER, human epidermal growth factor receptor;

IV, Intravenous;

IR, inspection readiness;

MABEL, minimal anticipated biological-effective level;

MAPK, mitogen-activated protein kinase;

MED, minimum effective dose;

MEK, MAPK/extracellular signal–related kinase kinase;

MFD maximal feasible dose;

MSRD, maximum recommended starting dose;

MTD, maximum tolerated dose;

NDA, new drug application;

NOAEL, no-observed-adverse-effect level;

PAD, pharmacologically active dose;

PI3K, phosphoinositide 3-kinase;

PRA, process risk assessment;

PSA, parallel scientific advice;

QbD, quality by design;

REC, response evaluation committee;

RPN, risk priority number;

SAWP, Scientific Advice Working Part;

SmPC, summary of product characteristics;

SOS, son of sevenless;

TTF, time to treatment failure;

VEGF, vascular endothelial growth factor.

# Guidelines used

[ICH M3](https://www.ema.europa.eu/en/ich-m3-r2-non-clinical-safety-studies-conduct-human-clinical-trials-pharmaceuticals) Non-clinical safety studies for the conduct of human clinical trials for pharmaceuticals (R2) [1]

[ICH E6](https://www.ema.europa.eu/en/ich-e6-r2-good-clinical-practice): Guideline for good clinical practice (R2) [32],

[ICH Q8](https://www.ema.europa.eu/en/ich-q8-r2-pharmaceutical-development) Pharmaceutical development [2, p. 8].

[ICH Q9](https://www.ema.europa.eu/en/ich-q9-quality-risk-management) Quality risk management[3, p. 9].

[ICH Q6B](https://www.ema.europa.eu/en/ich-q6b-specifications-test-procedures-acceptance-criteria-biotechnologicalbiological-products) Specifications: test procedures and acceptance criteria for biotechnological/biological products[4],

[ICH Q10](https://www.ema.europa.eu/en/ich-q10-pharmaceutical-quality-system) Pharmaceutical quality system[5, p. 10], the

[ICH M4](https://www.ema.europa.eu/en/ich-m4-common-technical-document-ctd-registration-pharmaceuticals-human-use-organisation-ctd) Common technical document (CTD) for the registration of pharmaceuticals for human use - organisation of CTD (R4) [6, p. 4]

[EudraLex Volume 10 clinical trials guidelines](https://ec.europa.eu/health/documents/eudralex/vol-10_en) [7].

Good manufacturing practice: [(EMA GMP)](https://www.ema.europa.eu/en/human-regulatory/research-development/compliance/good-manufacturing-practice)

Good laboratory practice compliance ([EMA GLP](https://www.ema.europa.eu/en/human-regulatory/research-development/compliance/good-laboratory-practice-compliance))

Good clinical practice ([EMA GCP](https://www.ema.europa.eu/en/human-regulatory/research-development/compliance/good-clinical-practice))

# Product Overview

Product Profile: Name, Treatment, Delivery, mechanism/target, discussion.

Dylan: Product details - Chemical Name, Composition, Availability, Structure, MoA.

Dylan: Preclinical and clinical trials overview – from successes in nonclinical to planned phase 1-3 trials.

# Part A: Preclinical Plan

Dylan: Acute toxicity

Dylan: Dosage

Table 1Overall Summary of Nonclinical Acute Toxicity Studies with Hertumig

Table

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# Part B: Clinical Plan

Dylan: Trial design

Dylan: Dosage

Table 2 Overall Summary of Planned Clinical Studies with Hertumig

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# Part C: Chemistry, Manufacturing and Controls, CMC

Description of Manufacturing Process and Process Controls

Quality attributes and methods

Design spaces

Process Risk Assessment Specifications

Process Risk Assessment Control strategy

Regulatory Filing and Process Monitoring

# Part D: Scientific Advice

Dylan: EMA Scientific Advice overview

Dylan: Parallel scientific advice

Dylan: Application timetable

Dylan: Qs on Dose response studies

Dylan: Qs on Non-clinical aspects

Table 4 2023 Submission deadlines - Scientific advice, protocol assistance, qualification of biomarkers

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# Part E: Inspection Readiness

Dylan: Reasons

Dylan Readiness key points.

# Overall strategy

Dylan: List of key points

# Advice to Management

Dylan: List of key achievements and list of next steps and outcome reasoning.

# Conclusion

Dylan: Summary

# Supplemental

Dylan: introduction on therapeutic mAb.

# References

[1] I. C. H. Guideline, “ICH: M3 (R2) Guidance on nonclinical safety studies for the conduct of human clinical trials and marketing authorization for pharmaceuticals. Version step 4 2009.,” 2009. [Online]. Available: https://database.ich.org/sites/default/files/M3\_R2\_\_Guideline.pdf

[2] I. C. H. Guideline, “ICH: Q8 Pharmaceutical development (R2),” 2009. [Online]. Available: https://database.ich.org/

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