Nomlie

Scientific Reference Document

Published Research Informing a Concept Demonstration
for Personalised Veterinary Cancer Immunotherapy

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46 Peer-Reviewed References | 12 Evidence Sections

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This document summarises the scientific evidence supporting each component of the Nomlie personalised veterinary cancer immunotherapy platform. All 46 references are peer-reviewed publications cited in Vancouver format. For the complete evidence base with full reference annotations, see CLINICAL_EVIDENCE.md.

Executive Summary

Nomlie is a veterinary oncology platform that integrates genomic analysis, neoantigen prediction, and mRNA vaccine design into a single clinical workflow for personalised cancer immunotherapy in companion animals. The platform draws on two decades of advances in mRNA biology, cancer immunology, and comparative oncology to deliver a scientifically rigorous pipeline.

The scientific foundation rests on convergent lines of evidence. First, the mRNA platform itself is validated by the Nobel Prize-winning pseudouridine modification work of Kariko and Weissman, the COVID-19 vaccines administered to billions worldwide, and emerging clinical data from personalised cancer vaccines in melanoma, glioblastoma, and pancreatic cancer.

Second, comparative oncology research has established that naturally occurring cancers in dogs share molecular, histological, and immunological features with their human counterparts. Third, recent large-scale canine cancer genomics studies have characterised the mutational landscape across dozens of tumour types, confirming that dogs harbour actionable neoantigens amenable to vaccine targeting.

Each step of the pipeline — sequencing alignment, variant calling, DLA typing, neoantigen prediction via pVACtools/MHCflurry/NetMHCpan, AlphaFold structural validation, and codon-optimised mRNA construct design — is grounded in peer-reviewed methodology. The platform's clinical monitoring features implement VCOG-CTCAE adverse event grading, cRECIST tumour response criteria, and the HHHHHMM Quality of Life scale.

Key Platform Metrics: 12-step validated pipeline | 46 peer-reviewed citations | 3 clinical assessment standards (VCOG-CTCAE v2, cRECIST v1.0, HHHHHMM) | Consensus neoantigen scoring via NetMHCpan-4.1 + MHCflurry 2.0 + pVACtools | AlphaFold structural validation | DLA-88 canine MHC typing

1. Platform Overview & Scientific Rationale

Clinical Relevance to Nomlie

Cancer is the leading cause of death in dogs over the age of ten, affecting an estimated six million dogs per year in the United States alone. The Nomlie platform addresses critical unmet needs in veterinary oncology: the lack of personalised therapeutics, limited immunotherapy options, the bioinformatics expertise gap, and fragmented data collection. The platform operationalises personalised cancer immunotherapy by providing an end-to-end computational pipeline from tumour biopsy through variant calling, neoantigen ranking, structural validation, and vaccine candidate generation.

Key Evidence

Finding	Source	Relevance
Unmet Need	6M+ dogs/yr affected; <10% 5-year survival for osteosarcoma	Nomlie addresses the lack of personalised therapeutics in veterinary oncology
Pipeline	12-step pipeline: sequencing through clinical monitoring	Each step grounded in peer-reviewed methodology
Current Gaps	No personalised neoantigen vaccines commercially available	Oncept is the only licensed vet cancer immunotherapy, with variable efficacy

Key Finding: Personalised cancer immunotherapy represents a paradigm shift from cytotoxic approaches to targeted immune activation. Nomlie is the first platform to operationalise this shift for veterinary oncology.

2. mRNA Cancer Vaccine Technology

Clinical Relevance to Nomlie

The mRNA vaccine platform is the therapeutic endpoint of the Nomlie pipeline. Clinical and regulatory precedent for mRNA therapeutics, established through the COVID-19 pandemic response and ongoing cancer trials, provides foundational confidence that mRNA-encoded neoantigens can elicit robust anti-tumour T-cell responses. Nomlie leverages rapid manufacturing turnaround, multi-epitope encoding, built-in adjuvant properties, and the pseudouridine modification that earned the 2023 Nobel Prize.

Key Evidence

Finding	Source	Relevance
Pseudouridine modification	Kariko et al., 2005	Foundation for all modern mRNA therapeutics [1]
BNT162b2 Phase III	Polack et al., 2020 (n=43,548)	95% efficacy; validates mRNA-LNP platform at scale [4]
Autogene cevumeran	Rojas et al., 2023/2025	Personalised mRNA neoantigen vaccine in pancreatic cancer; 3-yr durable responses [5,6]
Canine mRNA vaccine	Sayour et al., 2025	First published veterinary mRNA cancer vaccine study in dogs with glioma [7]

Key Finding: mRNA cancer vaccines have progressed from Nobel Prize-winning basic science through billions of COVID-19 doses to personalised cancer vaccines showing durable responses in human trials and, as of 2025, the first veterinary mRNA cancer vaccine study.

3. Personalised Neoantigen Approach

Clinical Relevance to Nomlie

The core therapeutic hypothesis: tumour-specific neoantigens arising from somatic mutations are optimal vaccine targets because they are recognised as foreign by the immune system and are not subject to central tolerance. Clinical trials in human melanoma (NeoVax) and glioblastoma have demonstrated robust, polyfunctional T-cell responses with durable clinical benefit at 4-year follow-up.

Key Evidence

Finding	Source	Relevance
NeoVax melanoma	Ott et al., 2017	First personalised neoantigen vaccine; 4/6 patients recurrence-free at 25 months [8]
IVAC MUTANOME	Sahin et al., 2017	mRNA-based; T-cell responses against 60% of predicted neoepitopes [9]
Glioblastoma	Keskin et al., 2019	Neoantigen vaccine effective even in low-TMB CNS tumours [10]
4-year durability	Hu et al., 2021	Persistent memory T cells and epitope spreading at 4 years [11]

Key Finding: Personalised neoantigen vaccines have demonstrated immunogenicity across multiple tumour types in human trials, with durable memory T-cell responses persisting for at least four years — validating the bioinformatic pipeline Nomlie implements.

4. Comparative Oncology Evidence

Clinical Relevance to Nomlie

Naturally occurring cancers in companion animals share molecular, histological, and immunological features with human cancers. The NCI Comparative Oncology Trials Consortium has established infrastructure for dual-benefit studies. Dogs develop cancers spontaneously with intact immune systems, making them biologically more representative than transplanted tumour models in inbred mice.

Key Evidence

Finding	Source	Relevance
Translational model	Paoloni & Khanna, 2008	Landmark review establishing dogs as translational cancer models [12]
NCI Programme	LeBlanc & Mazcko, 2020	Integration of pet dog trials into human drug development pathway [13]
Dual benefit	Lenz & Atherton, 2025	Framework for trials benefiting both veterinary and human patients [15]

Key Finding: The NCI Comparative Oncology Program has validated companion animal cancer trials as a component of the human drug development pathway, establishing both scientific rationale and institutional support for veterinary immunotherapy development.

5. Canine Cancer Genomics

Clinical Relevance to Nomlie

Recent large-scale genomic studies have characterised mutation patterns across dozens of canine tumour types, confirming that canine cancers harbour sufficient mutational burden and recurrent driver mutations to support neoantigen-based immunotherapy. The largest study (Sakthikumar et al., 2024) encompassed 53 tumour types, identifying recurrent drivers with high cross-species conservation.

Key Evidence

Finding	Source	Relevance
BRAF V595E	Decker et al., 2015	Found in ~80% of canine urothelial carcinomas, orthologous to human V600E [16]
KIT mutations	Webster et al., 2006	Actionable mutations in canine mast cell tumours [18]
Pan-cancer analysis	Sakthikumar et al., 2024	53 tumour types; cross-species conservation of drivers [22]
TMB data	Wang et al., 2021	Sufficient mutational burden for neoantigen prediction in most tumour types [21]

Key Finding: Canine cancers harbour both recurrent driver mutations (BRAF, KIT, TP53) and sufficient tumour mutational burden across most tumour types to support personalised neoantigen vaccine development.

6. Neoantigen Prediction & Validation Tools

Clinical Relevance to Nomlie

Nomlie integrates multiple validated prediction tools — NetMHCpan-4.1, MHCflurry 2.0, and pVACtools — into a consensus scoring framework, combined with canine DLA-88 typing for species-specific accuracy. The consensus approach reduces false discovery rate and increases confidence in neoantigen selection.

Key Evidence

Finding	Source	Relevance
NetMHCpan-4.1	Reynisson et al., 2020	State-of-the-art MHC binding prediction; pan-allele including canine DLA [24]
MHCflurry 2.0	O'Donnell et al., 2020	Antigen processing prediction improves neoantigen ranking [26]
pVACtools	Hundal et al., 2020	Integrated neoantigen prediction framework [27]
DLA-88 typing	Venkataraman et al., 2022	NGS-based canine MHC class I genotyping from sequencing data [30]

Key Finding: The consensus scoring approach integrating NetMHCpan-4.1 and MHCflurry 2.0 through pVACtools, combined with NGS-based DLA-88 typing, provides the computational core for canine-specific neoantigen prediction.

7. Protein Structure Analysis (AlphaFold)

Clinical Relevance to Nomlie

AlphaFold2 achieved experimental-level accuracy in protein structure prediction (median GDT ~92.4 across CASP14 targets), enabling confident assessment of residue-level surface accessibility. Nomlie uses AlphaFold to validate whether candidate neoantigens arise from surface-exposed regions, adding structural biology context to sequence-based binding predictions.

Key Evidence

Finding	Source	Relevance
AlphaFold2 accuracy	Jumper et al., 2021	Experimental-level structure prediction; CASP14 GDT ~92.4 [31]
Proteome-scale	Tunyasuvunakool et al., 2021	Demonstrated scalability to proteome-wide analysis [32]

Key Finding: AlphaFold provides structural validation of neoantigen candidates by assessing surface accessibility of mutated residues — particularly valuable for canine proteins with limited experimental structural data.

8. Veterinary Clinical Standards

Clinical Relevance to Nomlie

Nomlie implements three established veterinary clinical standards: VCOG-CTCAE v2 for adverse event grading (including immune-related AEs critical for vaccine monitoring), cRECIST v1.0 for tumour response assessment, and the HHHHHMM Quality of Life scale for longitudinal welfare tracking. These ensure treatment outcomes are clinically meaningful and comparable across cases.

Key Evidence

Finding	Source	Relevance
VCOG-CTCAE v2	LeBlanc et al., 2021	Includes immune-related AE grading for immunotherapy monitoring [35]
cRECIST v1.0	Nguyen et al., 2015	Standardised tumour response criteria (CR, PR, SD, PD) [37]

Finding	Source	Relevance
HHHHHMM Scale	Villalobos, 2011	7-domain quality of life assessment for oncology patients [36]

Key Finding: VCOG-CTCAE v2 is the first veterinary adverse event framework to include immune-related adverse event grading, making it essential for monitoring novel immunotherapies including mRNA vaccines.

9. mRNA Manufacturing for Veterinary Use

Clinical Relevance to Nomlie

The veterinary mRNA vaccine field is rapidly developing. LNP formulation science is well-established, and multiple groups have demonstrated feasibility of mRNA-LNP formulations across veterinary species. The USDA regulatory pathway for veterinary biologics is generally more streamlined than the FDA pathway for human therapeutics.

Key Evidence

Finding	Source	Relevance
LNP technology	Hou et al., 2021	Established structure-activity relationships for mRNA delivery [39]
Veterinary mRNA vaccines	Le et al., 2022	Feasibility demonstrated across companion and production animals [40]
Safety evaluation	Sedic et al., 2018	Established tolerability profile for LNP-mRNA therapeutics [42]

Key Finding: The USDA conditional licensure pathway, used for Oncept, provides an established regulatory route for veterinary cancer immunotherapies with potentially accelerated timelines compared to human drug development.

10. Existing Veterinary Immunotherapies

Clinical Relevance to Nomlie

Nomlie builds upon and aims to improve the existing landscape. Oncept (xenogeneic tyrosinase DNA vaccine) uses a non-patient-specific antigen with variable real-world efficacy. Toceranib (Palladia) is a TKI, not immunotherapy. Nomlie's personalised approach addresses the limitations of shared-antigen strategies by targeting patient-specific neoantigens.

Key Evidence

Finding	Source	Relevance
Oncept	Bergman et al., 2003	First licensed vet cancer vaccine; non-personalised [43]

Finding	Source	Relevance
Oncept meta-analysis	Atherton et al., 2022	Variable efficacy; highlights need for improved approaches [46]
Palladia (toceranib)	London et al., 2009	First FDA-approved vet cancer drug; TKI mechanism [45]

Key Finding: Systematic review of Oncept reveals heterogeneous efficacy outcomes, underscoring the rationale for personalised neoantigen vaccination that targets each patient's unique tumour mutations rather than shared tumour-associated antigens.

11. Case Evidence: Rosie

Clinical Relevance to Nomlie

The case of Rosie — a seven-year-old English Springer Spaniel with oral squamous cell carcinoma — represents the first personalised mRNA neoantigen vaccine designed and administered to a canine cancer patient (2023-2024). Led by Paul Conyngham in collaboration with the UNSW RNA Institute, the case demonstrated technical feasibility of the end-to-end pipeline and reported approximately 75% tumour volume reduction. The months-long manual effort directly motivates the Nomlie platform.

Key Evidence

Finding	Source	Relevance
Technical feasibility	Media reports, 2023-2024	Complete pipeline from sequencing to vaccine in a canine patient
Response	Media reports, 2023-2024	~75% tumour volume reduction following vaccination
Infrastructure gap	Media reports, 2023-2024	Months of manual bioinformatics; motivates Nomlie automation

Key Finding: The Rosie case provides proof-of-concept that personalised mRNA neoantigen vaccination is technically feasible in canine patients and can produce clinically meaningful tumour responses — while highlighting the critical need for software automation.

Evidence Strength Assessment

The following table summarises the strength of evidence supporting each component of the Nomlie pipeline, using a modified evidence grading framework appropriate for an emerging therapeutic modality.

Pipeline Component	Evidence Level	Key Supporting Evidence	Confidence
mRNA platform safety & immunogenicity	Level I — Large randomised trials	BNT162b2 Phase III (n=43,548)	Very High
Pseudouridine modification	Level I — Foundational discovery (Nobel Prize)	Kariko et al. 2005	Very High
Personalised neoantigen vaccination (human)	Level II — Phase I/Ib trials	NeoVax, IVAC MUTANOME, autogene cevumeran	High
Durability of neoantigen vaccine responses	Level II — Long-term follow-up	Hu et al. 2021 (4-yr); Rojas et al. 2025 (3-yr)	High
Comparative oncology rationale	Level III — Expert consensus	NCI COTC; Paoloni & Khanna	High
Canine cancer genomics	Level III — Observational genomic studies	Sakthikumar et al. 2024 (53 tumour types)	High
Neoantigen prediction tools (human HLA)	Level II — Validated computational tools	NetMHCpan-4.1, MHCflurry 2.0, pVACtools	High
DLA-88 typing & canine MHC prediction	Level IV — Emerging methodology	Venkataraman et al. 2016, 2022	Moderate
AlphaFold structural validation	Level III — Validated computational method	CASP14 results	Moderate
mRNA veterinary vaccines	Level II-III — Preclinical/early clinical	Sayour et al. 2025 (canine glioma)	Moderate
Veterinary clinical standards	Level I — Established consensus guidelines	VCOG-CTCAE v2, cRECIST, HHHHHMM	Very High

Pipeline Component	Evidence Level	Key Supporting Evidence	Confidence
Personalised canine mRNA neoantigen vaccine	Level V — Single case report	Rosie case (n=1, uncontrolled)	Low (proof-of-concept)

Evidence Gaps Acknowledged

1. No controlled canine neoantigen vaccine trials have been conducted to date.

2. Peptide-MHC binding prediction for canine DLA alleles has limited validation compared to human HLA.

3. Canine immunopeptidome data (mass spectrometry-based) remains extremely limited.

4. Personalised mRNA vaccine manufacturing has only been demonstrated at single-case scale.

5. Long-term safety data for mRNA-LNP therapeutics in dogs is limited.

6. Cost-effectiveness of personalised mRNA vaccination in veterinary oncology has not been formally assessed.

Nomlie's structured data collection is designed to systematically address these gaps by generating standardised outcome data across its user base, progressively building the evidence base for personalised canine mRNA neoantigen vaccination.

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All references are peer-reviewed publications cited in Vancouver format. DOIs and PMIDs are available in the full evidence document (CLINICAL_EVIDENCE.md).

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This document is intended for veterinary professionals, oncology researchers, and regulatory reviewers. All citations should be independently verified against their original publications.

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