Supplementary Table 1. SiRNA Clinical Trials (2020-2025)

Clinical Trial ID	Description	Reference
NCT06154278 Sponsor: University of Maryland, Baltimore Recruitment Status: Recruiting Phase: II Start/Completion Date: July 25th 2024 to July 1st 2027	This trial evaluates intrahepatic and peripheral responses to siRNA, Imdusiran (AB-729), in patients with chronic Hepatitis B.	[1]
NCT06424301 Sponsor: Eye & ENT Hospital of Fudan University Recruitment Status: Recruiting Phase: I Start/Completion Date: December 20th 2024 to September 30th 2025	This trial evaluates the short-term safety and preparatory potency of NUDT21 siRNA in patients with resistant retinoblastoma, and to confirm future large-scale clinical trials.	[2]
NCT05844293 Sponsor: Sirnaomics Recruitment Status: Recruiting Phase: I Start/Completion Date: May 16th 2023 to June 2024	This study assesses the pharmacokinetics, pharmacodynamics, safety, and tolerability of single ascending dose (SAD) of FXI-GalNAc-siRNA when administered subcutaneously to healthy people.	[3]
NCT05438069 Sponsor: Jena University Hospital Recruitment Status: Recruiting Phase: N/A (Not Applicable) Start/Completion Date: December 11th 2020 to December 11th 2025	This study evaluates the hypercholesterinemia following to the administration of siRNA Inclisiran in German patients.	[4]
NCT06138964 Sponsor: National Skin Centre Recruitment Status: Recruiting Phase: II Start/Completion Date: November 14th 2023 to November 14th 2024	This study compares the effect of siRNA against the secreted protein acidic and cysteine rich SPARC coding gene (siSPARC) microneedle patch versus siRNA against SPARC and interleukin-4 receptor alpha (IL4-RA) (siSPARC + siLR4A) microneedle patch on post-surgical scars formation.	[5]
NCT06586684 Sponsor: First Affiliated Hospital of Xinjiang Medical University Recruitment Status: Not yet recruiting Phase: IV Start/Completion Date: September 20th 2024 to September 30th 2026	This study assesses the effect of siRNA Inclisiran on carotid plaques in patients with atherosclerosis using carotid ultrasound.	[6]
NCT03608631 Sponsor: M.D. Anderson Cancer Center Recruitment Status: Recruiting Phase: I/II Start/Completion Date: January 27th 2021 to April 30th 2027	This study evaluates the effect of dose-escalation of mesenchymal stromal cells-derived exosomes with KRASG12D siRNA for patients with metastatic pancreas cancer enclosing KRASG12D mutation.	[7]
NCT06960213 Sponsor: ADARx Pharmaceuticals, Inc. Recruitment Status: Recruiting Phase: III Start/Completion Date: August 28th 2025 to December 31st 2026	The STOP-HAE study evaluates the efficacy of siRNA (ADX-324) targeting the coagulating factor (Prekallikrein) in Hereditary Angioedema participants. The study also assesses PK, PD, safety, and patient-reported outcome measures.	[8]

Clinical Trial ID	Description	Reference
NCT05519475 Sponsor: Regeneron Pharmaceuticals Recruitment Status: Recruiting Phase: II Start/Completion Date: February 9th 2023 to September 8th 2027	This study evaluates siRNA for the treatment of metabolic dysfunction-associated steatohepatitis (MASH) in patients with genetic predisposition factors.	[9]
NCT06923280 Sponsor: Huashan Hospital Recruitment Status: Not yet recruiting Phase: N/A Start/Completion Date: May 1st 2025 to May 31st 2028	This study compares successive pegylated interferon (PEG-IFNα) therapy protocols in chronic hepatitis B (CHB) patients formerly treated with antisense oligonucleotide (ASO) or siRNA.	[10]
NCT05902520 Sponsor: AgonOx, Inc. Recruitment Status: Recruiting Phase: I Start/Completion Date: June 19th 2023 May 19th 2026	This study evaluates the adoptive transfer of immune markers (CD39, CD103, CD8) along with cancer-isolated T cells (AGX148) alone or in combination with siRNA modulation of a novel cancer immunotherapy approach PD-1 (AGX148/PH-762) combining a tumor-specific Tumor-Infiltrating Lymphocyte (TIL) product (AGX148) and siRNA targeting the PD-1 immune checkpoint on those T-cells (PH-762) in patients with advanced solid cancers.	[11]
NCT05648214 Sponsor: Regeneron Pharmaceuticals Recruitment Status: Active, not recruiting Phase: I Start/Completion Date: December 27th 2022 to October 18th 2025	This study evaluates the PK, safety, and tolerability of ALN-PNP, a siRNA targeting patatin-like phospholipase domain-containing protein-3 (PNPLA3), in healthy subjects with non-alcoholic fatty liver disease (NAFLD).	[12]
NCT07187401 Sponsor: Regeneron Pharmaceuticals Recruitment Status: Recruiting Phase: I/II Start/Completion Date: November 28th 2025 to January 4th 2030	This study evaluates the PK, safety, tolerability, and efficacy of a siRNA treatment against complement factor B (ALN-CFB) in patients with paroxysmal nocturnal hemoglobinuria and persistent anemia with C5-inhibitor therapy	[13]
NCT06024408 Sponsor: Regeneron Pharmaceuticals Recruitment Status: Completed Phase: I Start/Completion Date: May 21st 2024 to July 7th 2025	This study evaluates the PK, PD, safety, and tolerability of ALN-PNP siRNA in subjects NAFLD and a PNPLA3 genetic risk factor	[14]
NCT04601844 Sponsor: Regeneron Pharmaceuticals Recruitment Status: Completed Phase: I Start/Completion Date: November 16th 2020 to July 23rd 2021	This study evaluates the PK, PD, safety, and tolerability of single doses of subcutaneously administered human monoclonal antibody (Pozelimab) combined with single doses of subcutaneously administered siRNA (Cemdisiran) in healthy subjects	[15]
NCT05876312 Sponsor: ADARx Pharmaceuticals, Inc. Recruitment Status: Recruiting Phase: I/II Start/Completion Date: August 7th 2023 to September 30th 2026	This study evaluates the PK, PD, safety, and tolerability of siRNA (ADX-038) in both healthy participants and in in patients with paroxysmal nocturnal hemoglobinuria (PNH).	[16]

Clinical Trial ID	Description	Reference
NCT05637255 Sponsor: Sylentis, S.A. Recruitment Status: Recruiting Phase: II Start/Completion Date: November 22nd 2022 to July 22nd 2023	This study evaluates the safety and efficacy of siRNA (SYL1801) eye drops doses in patients with neovascular age-related macular degeneration (AMD).	[17]
NCT07271186 Sponsor: Regeneron Pharmaceuticals Recruitment Status: Not yet recruiting Phase: II Start/Completion Date: 2025-12-09 2027-12-08 December 9th 2025 to December 8th 2027	This study evaluates the safety, efficacy, PK, and PD effects of ANGPTL3 inhibition with siRNA alone or in combination with an ANGPTL3 antibody in patients with diabetic kidney disease.	[18]
NCT06845202 Sponsor: Alnylam Pharmaceuticals Recruitment Status: Recruiting Phase: I/II Start/Completion Date: March 3rd 2025 to August 31st 2027	This study evaluates the efficacy, safety, tolerability, PK, and PD of a single dose of siRNA (ALN-4324) in overweight and obese healthy subjects and it evaluates the multiple doses of ALN-4324 in overweight and obese patients with type 2 diabetes mellitus (T2DM)	[19]
NCT05661916 Sponsor: Alnylam Pharmaceuticals Recruitment Status: Completed Phase: I Start/Completion Date: January 16th 2023 to September 30th 2025	This study evaluates the safety, tolerability, PK, and PD of a single dose of subcutaneously administration of siRNA (ALN-TTRSC04) in healthy participants.	[20]
NCT05783206 Sponsor: National Research Center - Institute of Immunology Federal Medical-Biological Agency of Russia Recruitment Status: Completed Phase: II/III Start/Completion Date: February 10th 2022 to July 28th 2023	This study evaluates the safety and efficacy of aerosolized siRNA (MIR 19®) inhalation in mild COVID-19 patients.	[21]
NCT05256810 Sponsor: Alnylam Pharmaceuticals Recruitment Status: Terminated Phase: I/II Start/Completion Date: February 25th 2022 to January 25th 2023	This study evaluates the efficacy, safety, tolerability, PK, and PD of a single escalating dose and multiple doses of siRNA (ALN-XDH) in healthy participants and gout patients.	[22]
NCT05208996 Sponsor: National Research Center - Institute of Immunology Federal Medical-Biological Agency of Russia Recruitment Status: Completed Phase: I Start/Completion Date: January 22nd 2021 to March 26th 2021	This study evaluates the safety of administration of siRNA of SARS-CoV-2 (siCoV) uploaded on cationic peptide dendrimer (KK-46) to determine the highest daily dose as a single therapy in healthy subjects.	[23]

Clinical Trial ID	Description	Reference
NCT05184127 Sponsor: National Research Center - Institute of Immunology Federal Medical-Biological Agency of Russia Recruitment Status: Completed Phase: II Start/Completion Date: April 27th 2021 to September 7th 2021	This study evaluates the safety and efficacy of aerosolized siRNA (MIR 19®) inhalation in moderate COVID-19 patients who didn't require admission to the intensive care unit.	[24]
NCT04765657 Sponsor: Novartis Pharmaceuticals Recruitment Status: Active, not recruiting Phase: III Start/Completion Date: March 1st 2021 December 28th 2026	This study evaluates the efficacy and safety of siRNA (Inclisiran) in Asian patients with atherosclerotic cardiovascular disease (ASCVD) or in ASCVD high risk and elevated low-density lipoprotein cholesterol patients as complementary to diet accompanied with maximum dose of statins with or without adjunct lipid-lowering agent (ORION-18).	[25]
NCT05974345 Sponsor: Novartis Pharmaceuticals Recruitment Status: Completed Phase: Observational Start/Completion Date: November 3rd 2023 to December 15th 2023	This virtual study predicts the efficacy of siRNA (Inclisiran) on serious adverse CV effects and CV death in virtual patients with ASCVD and elevated LDL-C.	[26]
NCT05888103 Sponsor: Novartis Pharmaceuticals Recruitment Status: Completed Phase: III Start/Completion Date: July 11th 2023 to October 24th 2024	This study evaluates the safety and efficacy of siRNA (inclisiran) as a single treatment in Chinese patients with low or moderate ASCVD risk and elevated LDL-C and lacking any lipid lowering treatment.	[27]
NCT05310422 Sponsor: Sylentis, S.A. Recruitment Status: Completed Phase: III Start/Completion Date: March 24th 2022 to October 11th 2023	This study evaluates the safety of siRNA (tivanisiran sodium) eye drops administered once daily for 24 months in dry eye disease (DED) participants.	[28]
NCT04877756 Sponsor: Olix Pharmaceuticals, Inc. Recruitment Status: Completed Phase: II Start/Completion Date: August 19th 2021 July 7th 2023	This study evaluates the efficacy of siRNA (OLX10010) as an additional treatment to prevent the recurrence of hypertrophic scars following revision surgery	[29]
NCT04819269 Sponsor: Sylentis, S.A. Recruitment Status: Completed Phase: III Start/Completion Date: May 25th 2021 to December 11th 2023	This study evaluates the efficacy and safety of siRNA (tivanisiran sodium) eye drops after 2-week administered once daily for 3 months in DED subjects due to Sjögren's Syndrome.	[30]

Clinical Trial ID	Description	Reference
NCT05761301 Sponsor: Alnylam Pharmaceuticals Recruitment Status: Terminated Phase: I/II Start/Completion Date: March 10th 2023 to April 3rd 2025	This study evaluates the efficacy, safety, tolerability, PK, and PD of a single dose of siRNA (ALN- KHK) in overweight and obese healthy subjects and it evaluates the multiple doses of ALN- KHK in overweight and obese patients with type 2 diabetes mellitus (T2DM)	[31]
NCT04666298 Sponsor: Novartis Pharmaceuticals Recruitment Status: Completed Phase: II Start/Completion Date: January 29th 2021 to October 19th 2022	This study evaluates the effect of different doses of siRNA (Inclisiran) administered subcutaneously in Japanese subjects with high cardiovascular (CV) risk and elevated Low-density lipoprotein cholesterol (LDL-C)	[32]
NCT06423352 Sponsor: Alnylam Pharmaceuticals Recruitment Status: Completed Phase: I/II Start/Completion Date: June 5th 2024 to July 17th 2025	This study evaluates the efficacy, safety, tolerability, PK, and PD of siRNA (Zilebesiran) in Japanese patients with mild to moderate hypertension	[33]
NCT05484206 Sponsor: Vir Biotechnology, Inc. Recruitment Status: Recruiting Phase: I Start/Completion Date: September 21st 2022 to April 30th 2027	This study evaluates the safety and PK of siRNA (VIR-2218) and (VIR-3434) as a single therapy and adjunct Therapy in hepatic dysfunction patients	[34]
NCT05103332 Sponsor: Alnylam Pharmaceuticals Recruitment Status: Completed Phase: II Start/Completion Date: November 5th 2021 to September 13th 2024	This study evaluates the efficacy and safety of siRNA (Zilebesiran) as an adjunct treatment in hypertension patients who aren't properly treated by antihypertensive medication	[35]
NCT04936035 Sponsor: Alnylam Pharmaceuticals Recruitment Status: Completed Phase: II Start/Completion Date: July 7th 2021 to December 5th 2024	This study evaluates the efficacy and safety of siRNA (ALN-AGT01) in patients with mild to moderate hypertension	[36]
NCT06115967 Sponsor: AstraZeneca Recruitment Status: Completed Phase: I Start/Completion Date: November 15th 2023 to October 16th 2025	This study evaluates the safety, tolerability, PK, and PD of an escalating dose of subcutaneous siRNA (AZD6912) in healthy subjects.	[37]

Clinical Trial ID	Description	Reference
NCT04152200 Sponsor: Alnylam Pharmaceuticals Recruitment Status: Completed Phase: III Start/Completion Date: January 21st 2020 to June 23rd 2025	This study evaluates the efficacy, safety, PK, and PD of siRNA (Lumasiran) in advanced primary hyperoxaluria type I (PH1) patients.	[38]
NCT04659863 Sponsor: Novartis Pharmaceuticals Recruitment Status: Completed Phase: III Start/Completion Date: February 16th 2021 to November 18th 2024	This study evaluates the efficacy, safety, and tolerability of siRNA (Inclisiran) in homozygous familial hypercholesterolemia (HoFH) and elevated low density lipoprotein cholesterol (LDL-C) adolescents.	[39]
NCT04652726 Sponsor: Novartis Pharmaceuticals Recruitment Status: Completed Phase: III Start/Completion Date: January 27th 2021 to November 27th 2024	This study evaluates the efficacy, safety, and tolerability of siRNA (Inclisiran) in heterozygous familial hypercholesterolemia (HeFH) and elevated low density lipoprotein cholesterol (LDL-C) adolescents.	[40]
NCT06597019 Sponsor: Novartis Pharmaceuticals Recruitment Status: Recruiting Phase: III Start/Completion Date: December 9th 2024 to April 15th 2029	This study evaluates the efficacy, tolerability, and safety of siRNA (Inclisiran) in children (aged 6 -12 years) with HeFH and elevated LDL-C.	[41]
NCT06597006 Sponsor: Novartis Pharmaceuticals Recruitment Status: Recruiting Phase: III Start/Completion Date: 2025-02-28 2029-04-15 February 28th 2025 to April 15th 2029	This study evaluates the efficacy, tolerability, and safety of siRNA (Inclisiran) in children (aged 6 -12 years) with HoFH and elevated LDL-C.	[42]
NCT06452771 Sponsor: Regeneron Pharmaceuticals Recruitment Status: Recruiting Phase: I Start/Completion Date: June 27th 2024 to December 3rd 2026	This study evaluates the Pk, safety, and tolerability of siRNA (ALN-ANG3) in healthy subjects.	[43]
NCT07181109 Sponsor: Alnylam Pharmaceuticals Recruitment Status: Recruiting Phase: III Start/Completion Date: September 22nd 2025 to October 29th 2030	This study evaluates the safety and efficacy of siRNA (Zilebesiran) in decreasing serious adverse CV events in adult subjects with uncontrolled hypertension accompanied with diagnosed cardiovascular disease (CVD) or risky CVD.	[44]

Clinical Trial ID	Description	Reference
NCT05030428 Sponsor: Novartis Pharmaceuticals Recruitment Status: Active, not recruiting Phase: III Start/Completion Date: November 23rd 2021 to October 13th 2027	This study evaluates the effect of siRNA (Inclisiran) on serious CV events in diagnosed (CVD) patients.	[45]
NCT04782271 Sponsor: Sylentis, S.A. Recruitment Status: Completed Phase: I Start/Completion Date: March 17th 2021 to December 21st 2021	This study evaluates the tolerability, safety, and PK of doses of siRNA (SYL1801) eye drops in healthy subjects.	[46]
NCT06272487 Sponsor: Alnylam Pharmaceuticals Recruitment Status: Active, not recruiting Phase: II Start/Completion Date: February 29th 2024 to December 19th 2025	This study evaluates the effect of siRNA (Zilebesiran) as an additional therapy in patients with CV risk and hypertension not properly regulated by antihypertensive medications.	[47]
NCT05643118 Sponsor: Olix Pharmaceuticals, Inc. Recruitment Status: Completed Phase: I Start/Completion Date: January 4th 2023 to November 10th 2025	This study evaluates the tolerability and safety of siRNA (OLX10212) in AMD patients.	[48]
NCT06585449 Sponsor: Alnylam Pharmaceuticals Recruitment Status: Recruiting Phase: I Start/Completion Date: October 14th 2024 to July 5th 2028	This study evaluates the tolerability, safety, PD, and PK of a single dose of siRNA (ALN-HTT02) in Huntington's disease patients.	[49]
NCT06172894 Sponsor: invIOs GmbH Recruitment Status: Completed Phase: I Start/Completion Date: August 22nd 2023 October 1st 2024	This study evaluates the dose of siRNA (APN401) in advanced solid cancer patients.	[50]
NCT04270760 Sponsor: Amgen Recruitment Status: Completed Phase: II Start/Completion Date: July 28th 2020 to November 8th 2022	This study evaluates the efficacy, tolerability, and safety of siRNA (Olpasiran) (AMG 890) in high Lipoprotein patients.	[51]

Clinical Trial ID	Description	Reference
NCT04555486 Sponsor: Dicerna Pharmaceuticals, Inc., a Novo Nordisk company Recruitment Status: Completed Phase: I Start/Completion Date: September 14th 2020 to September 7th 2021	This study evaluates the tolerability, safety, PK, and PD of a single dose of siRNA (DCR-PHXC) in primary hyperoxaluria type 3 patients.	[52]

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