Supplementary Materials

A1 The Drug Development Process

Since the passing of the Food, Drug, and Cosmetic Act in 1938, pharmaceuticals developed by companies have to be reviewed by the Food and Drug Administration (FDA) for safety and efficacy before they can be marketed in the U.S. The application for marketing approval differs slightly by the type of therapy: New Drug Applications (NDAs) are for small molecules, and Biologics License Applications (BLAs) are for biologics. Gene therapy is considered a biologic product, hence the BLA designation applies.

Clinical investigations in human subjects typically take place in three phases—phases 1, 2 and 3—before marketing approvals are sought. Phase 1 trials are designed to investigate the dosage and safety of the treatment, while phase 2 trials attempt to detect early signs of efficacy and possible side effects in a relatively small sample of patients. Phase 3 trials are intended to demonstrate a statistically significant treatment effect when compared to the best standard of care in a broader population of patients. Some clinical trials combine multiple phases into a single design, with the phase numbers separated by a slash. For example, a phase 2/3 trial combines elements of phase 2 and phase 3 investigations into a single trial design in order to reduce the overall development time and cost, and maximize the participation of subjects with orphan disease willing to participate in trials. The clinical development of therapeutics is a tedious and costly process that may span decades and cost billions of dollars, with the bulk of the cost and time spent conducting phase 3 clinical trials [60, 82]. The process is also very risky, with only 13.8% of therapeutic development programs entering phase 1 reaching approval [166].

A2 Pseudo-Code and Implementation Details

Pseudo-code

We perform a Monte Carlo simulation to determine the total number of patients undergoing gene therapy and the cost of these gene therapies at specific points in time. The sequence of computations for each iteration of the simulation is detailed in Algorithm 1.

Input : $\mathbb{D}$: A list of diseases
Output: Arrays of $[1 \times T]$, where T is the number of time steps.
$\mathbb{P}$: Number of patients over time
$\mathbb{C}$: Total cost over time
$\mathbb{P} \leftarrow$ `1 × T array of zeros`
$\mathbb{C} \leftarrow$ `1 × T array of zeros`
for *d* in $\mathbb{D}$ **do**
  p ← getPoS(d) `// Get probability of success`
  if `random.uniform`(0,1) $\leq p$ **then**
    `// If the disease gets an approval...`
    `existing` ← `getExistingPatients(d)` ; `// Get existing patients (1 × T)`
    `new` ← `getNewPatients(d) // Get new patients (1 × T)`
    ρ ← `getRampFunction(d) // Get penetration ramp (1 × T)`
    `price` ← `getPrice(d) // Get price of GT (scalar)`
    $\mathbb{P}+ =$ (`existing` + `new`)$\otimes\rho$ `// Store number of patients`
    $\mathbb{C}+ = \mathbb{P}\times$ `price // Store cost of treatment`
  end
end
return $\mathbb{P}$, $\mathbb{C}$

Algorithm 1: Pseudocode for one iteration of the simulation.

Implementation

All the equations are discretized for computation from their continuous forms. When solving the integrals using the trapezoidal rule to obtain ΔQALY, we use strip widths of 1 year across a range from 0 to 110 years old, the resolution offered by the life tables. When simulating the number of patients and the cost over time, we use steps of 1 month.

Our codes are implemented on Python 3.6 backed by Numpy. Our vectorized implementation averages 6.120ms per iteration over 1,000,000 runs on a single thread of an Intel Xeon Gold 5120, clocked at 2.20GHz with 20GB of RAM. We attempted to use PyTorch to speed up the computations using a GPU, but it ran more slowly than a single-threaded CPU. We determined this took place for two reasons. First, generating random numbers must be sequential, since PyTorch delegates it solely to the CPU, which limits the amount of parallelization that can be achieved, as dictated by Amdahl's law. Second, because our computations require a large amount of data from different sources, they must be batched

due to the GPU's limited RAM. The constant movement of data through the PCIe bridge, however, turns out to be a massive bottleneck to the overall speed.

A3 Simulation Convergence Criteria

Let X_k be the results of the k-th simulation. X_k has a true mean of μ and variance σ^2. Let the mean of the Monte Carlo simulations over n runs be $\hat{\mu}_n = \frac{1}{n}\sum_k^n X_k$. Then, by Lindeberg–Lévy's Central Limit Theorem, $\hat{\mu}_n$ converges in distribution to a normal distribution with mean μ and variance of $n\sigma^2$. The 95 percent confidence interval for μ is given by:

$$\hat{\mu}_n \pm \frac{1.96 s_n}{\sqrt{n}} \tag{27}$$

where s_n is the sample variance of $\{X_1, \cdots, X_n\}$.

Since we are using 1-by-T vectors, we investigated the error in our simulation by dividing the half-range of the confidence interval in each time-step by $\hat{\mu}_n$ before taking the maximum across the time series. As can be seen from Figure A1, we should expect the simulated mean to be within 1.89% of the true mean 95% of the time with 1,000,000 iterations.

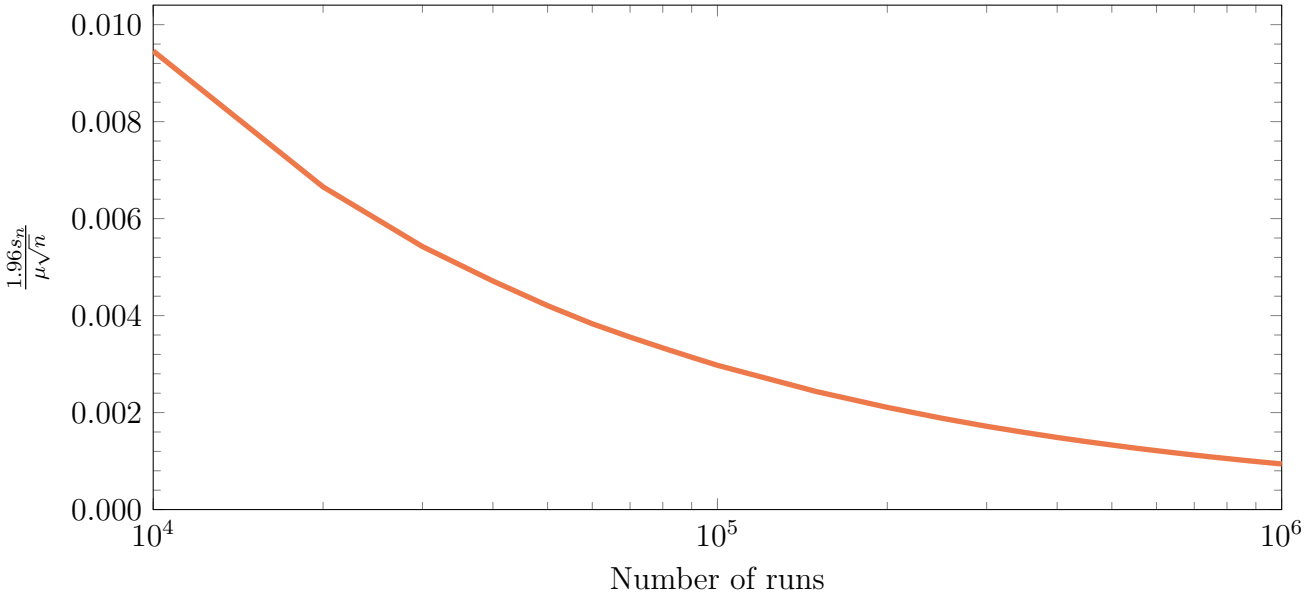

Figure A1: Plot of $\frac{1.96 s_n}{\mu\sqrt{n}}$ against the number of iterations of simulations of the cost.

A4 Current Gene Therapy Clinical Trials

As mentioned in the main paper, we list the clinical trials that are used in this study in the following table.

Table A1: List of clinical trials used in this study. 'TT' and 'CT' indicates 'TrialTrove' and '*clinicaltrials.gov*' respectively.

Trial Title	Disease	Sponsors	Source
Randomized, double-blind, placebo-controlled study of AMG0(HGF plasmid) for patients with arteriosclerosis obliterans	Arteriosclerosis Obliterans	AnGes	TT
Tisagenlecleucel Versus Standard of Care in Adult Patients With Relapsed or Refractory Aggressive B-cell Non-Hodgkin Lymphoma: A Randomized, Open Label, Phase III Trial (BELINDA)	B-Cell Non-Hodgkin's Lymphoma	Novartis	TT
A Global Randomized Multicenter Phase III Trial of JCAR017 Compared to Standard of Care in Adult Subjects With High-risk, Second-line, Transplant-eligible Relapsed or Refractory Aggressive B-cell Non-Hodgkin Lymphomas (TRANSFORM).	B-Cell Non-Hodgkin's Lymphoma	Celgene	TT
A Phase III, Open Label Study to Evaluate the Safety and Efficacy of INSTILADRIN (rAd-IFN)/Syn3) Administered Intravesically to Patients With High Grade, BCG Unresponsive Non-Muscle Invasive Bladder Cancer (NMIBC)	BCG Unresponsive NMIBC	FKD Therapeutics	TT
A Phase III Study of BC-819 in Patients with Bladder Cancer who Failed Initial Treatment of BCG	BCG Unresponsive NMIBC	Anchiano Therapeutics	TT

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Table A1 – continued from previous page

Trial Title	Disease	Sponsors	Source
A Phase 3 Single Arm Study Evaluating the Efficacy and Safety of Gene Therapy in Subjects With Transfusion-dependent beta-Thalassemia, Who do Not Have a beta0/beta0 Genotype, by Transplantation of Autologous CD34+ Stem Cells Transduced Ex Vivo With a Lentiviral betaA-T87Q-Globin Vector in Subjects < or = 50 Years of Age	Beta-Thalassemia	bluebird bio	TT
A Phase 3 Single Arm Study Evaluating the Efficacy and Safety of Gene Therapy in Subjects With Transfusion-dependent beta-Thalassemia, Who Have a beta0/beta0 Genotype, by Transplantation of Autologous CD34+ Stem Cells Transduced Ex Vivo With a Lentiviral betaA-T87Q-Globin Vector in Subjects < or = 50 Years of Age	Beta-Thalassemia	bluebird bio	TT
An Integrated Phase II/III, Open Label, Randomized and Controlled Study of the Safety and Efficacy of CG0070 Adenovirus Vector Expressing GM-CSF in Patients With Non-Muscle Invasive Bladder Cancer With Carcinoma In Situ Disease Who Have Failed BCG Bladder Oncolytic virus for Non-muscle invasive bladder cancer Disease (BOND)	Bladder Cancer, in situ concurrent with Papillary Tumors	Cold Genesys	TT
A Phase 2/3 Study of the Efficacy and Safety of Hematopoietic Stem Cells Transduced With Lenti-D Lentiviral Vector for the Treatment of Cerebral Adrenoleukodystrophy (CALD)	Cerebral Adrenoleukodystrophy (CALD)	bluebird bio	CT
Efficacy and Safety of AAV2-REP1 for the Treatment of Choroideremia	Choroideremia	Nightstar Therapeutics	CT

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Table A1 – continued from previous page

Trial Title	Disease	Sponsors	Source
A Phase 3 Double-Blind, Randomized, Placebo-Controlled Study to Evaluate the Safety and Efficacy of AMG0 in Subjects With Critical Limb Ischemia Efficacy and Safety of AMG0 in Subjects With Critical Limb Ischemia (AGILITY)	Critical Limb Ischemia	AnGes	TT
Safety and Efficacy of Recombinant Adeno-Associated Virus Containing the CFTR Gene in the Treatment of Cystic Fibrosis	Cystic Fibrosis	Targeted Genetics Corporation/ Cystic Fibrosis Foundation Therapeutics	CT
A Placebo Controlled, Double-blind, Randomized, Parallel-group, Multi-center Phase III study to determine the Efficacy and Safety of TisssueGene-C in Patients with Degenerative Arthritis	Degenerative Arthritis	Kolon Life Science	TT
Safety and Efficacy Study of Pl-VEGF165 to Treat Diabetic Foot Syndrome	Diabetic Foot Syndrome	Human Stem Cells Institute	TT
A Phase III, Double-blind, Randomized, Placebo-controlled, Multicenter Study to Asses the Safety and Efficacy of VM202 to Treat Chronic Nonhealing Foot Ulcers in Diabetic Patients With Concomitant Peripheral Arterial Disease (PAD)	Diabetic Foot Ulcers	Helixmith	TT
A Phase III, Double-Blind, Randomized, Placebo-Controlled, Multicenter Study to Assess the Safety and Efficacy of VM202 in Subjects With Painful Diabetic Peripheral Neuropathy	Diabetic Peripheral Neuropathy	Helixmith	TT
A Phase III, Randomized, Open-Label Study Evaluating Efficacy of Axicabtagene Ciloleucel Versus Standard of Care Therapy in Subjects With Relapsed/Refractory Diffuse Large B Cell Lymphoma	Diffuse Large B Cell Lymphoma (DLBCL)	Gilead Sciences/Kite Pharma	TT

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Table A1 – continued from previous page

Trial Title	Disease	Sponsors	Source
A Multi-center Phase III, Randomized, Open-Label Trial of Vigil (Bi-shRNAfurin and GMCSF Augmented Autologous Tumor Cell Immunotherapy) in Combination With Irinotecan and Temozolomide as a Second-Line Regimen for Ewing's Sarcoma	Ewing's Sarcoma	Gradalis	TT
A Phase III Study of INGN 241 in Combination with Radiation Therapy in Patients with Advanced Solid Tumors and Head and neck cancer.	Head and Neck Cancer	Introgen Therapeutics	TT
An Open-Label, Randomized, Multi-Center Phase III Clinical Trial Comparing E10A Plus Chemotherapy And Chemotherapy Alone For Treatment Of Head And Neck Cancer	Head and Neck Cancer	Marsala Biotech	TT
A Randomized, Open-label, Multi-center Phase III Study Designed to Evaluate the Safety and Efficacy of E10A in Patients With Recurrent/Unresectable Squamous Cell Carcinoma of the Head and Neck Region	Head and Neck Cancer	Guangzhou Double Bioproducts Co.	TT
A Phase III, Pivotal, Randomized, Placebo-controlled, Double-Blind, Multicenter Study to Evaluate RT-100 AC6 Gene Transfer in Patients with Heart Failure and Reduced Left Ventricular Ejection Fraction;Heart Failure with Reduced Left Ventricular Ejection Fraction: One-time Gene Transfer Using RT-100 Intracoronary Administration of Adenovirus 5 encoding Human AC6 (FLOURISH)	Heart Failure	Renova Therapeutics	TT

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Table A1 – continued from previous page

Trial Title	Disease	Sponsors	Source
A Phase 3 Open-Label, Single-Arm Study To Evaluate The Efficacy and Safety of BMN 270, an Adeno-Associated Virus Vector-Mediated Gene Transfer of Human Factor VIII in Hemophilia A Patients With Residual FVIII Levels = 1 IU/dL Receiving Prophylactic FVIII Infusions	Hemophilia A	BioMarin	TT
Phase 3 Study To Evaluate Efficacy/Safety of Valoctocogene Roxaparvovec an AAV Vector-Mediated Gene Transfer of hFVIII at a Dose of 4E13vg/kg in Hemophilia A Patients With Residual FVIII Levels < or = 1IU/dL Receiving Prophylactic FVIII Infusions	Hemophilia A	BioMarin	TT
A Phase III Run In trial to Evaluate SPK-8011 in Patients with Hemophilia A	Hemophilia A	Roche/Spark Therapeutics	TT
An open-label, single-dose, multi-center, multi-national, Phase III pivotal trial to investigate efficacy and safety of AMT-061 in severe or moderately severe hemophilia B; HOPE-B: Trial of AMT-061 in Severe or Moderately Severe Hemophilia B Patients; Phase III, Open-label, Single-dose, Multi-center, Multinational Trial Investigating a Serotype 5 Adeno-associated Viral Vector Containing the Padua Variant of a Codon-optimized Human Factor IX Gene (AAV5-hFIXco-Padua, AMT-061) Administered to Adult Subjects With Severe or Moderately Severe Hemophilia B	Hemophilia B	uniQure	TT

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Table A1 – continued from previous page

Trial Title	Disease	Sponsors	Source
A Pivotal Phase III Study of PF-06838435 in Patients with Hemophilia B; Phase 3, Open Label, Single Arm Study To Evaluate Efficacy And Safety Of Fix Gene Transfer With Pf-06838435 (Raav-Spark100-Hfix-Padua) In Adult Male Participants With Moderately Severe To Severe Hemophilia B (Fix:C < or =2%)	Hemophilia B	Pfizer	TT
A Pivotal Phase III Study to Evalaute AMT-060 in Patients with Hemophilia B	Hemophilia B	uniQure	TT
Multicenter Randomized Controlled Trial of Adenovirus-mediated Adjuvant Gene Therapy Improving Outcome of Liver Transplantation in Patients With Advanced Hepatocellular Carcinoma	Hepatocellular Carcinoma	Wuhan Tiandakang Bio-Tech Engineering Co./ Shenzhen Tiandakang Gene Engineering Co.	TT
A Phase III Randomized, Open-Label Study Comparing Pexa Vec (Vaccinia GM CSF / Thymidine Kinase-Deactivated Virus) Followed by Sorafenib Versus Sorafenib in Patients With Advanced Hepatocellular Carcinoma (HCC) Without Prior Systemic Therapy	Hepatocellular Carcinoma	Transgene/ Sillajen Biotherapeutics /Jennerex/ Lees Pharmaceutical	TT
Phase III Prospective, Open-Label, Parallel-Group, Randomized, Multicenter Trial Comparing the Efficacy of Surgery, Radiation, and Injection of Murine Cells Producing Herpes Simplex Thymidine Kinase Vector Followed by Intravenous Ganciclovir Against the Efficacy of Surgery and Radiation in the Treatment of Newly Diagnosed, Previously Untreated Glioblastoma Multiforme	High-Grade Glioma	Novartis/Sandoz	TT

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Table A1 – continued from previous page

Trial Title	Disease	Sponsors	Source
A Controlled, Randomised, Parallel Group Study Of The Efficacy And Safety Of Herpes Simplex Virus Thymidine Kinase Gene Therapy (Cerepro) with Subsequent Ganciclovir For The Treatment Of Patients With Operable High-Grade Glioma.	High-Grade Glioma	Trizell	TT
A Randomized, Double-Blind, Placebo-Controlled, Multi-Center, Phase 3 Study to Determine the Efficacy of TG-C in Subjects With Kellgren and Lawrence Grade (KLG) 2 or 3 Osteoarthritis of the Knee	Knee Osteoarthritis with Kellgren & Lawrence Grade 2 or 3	Kolon TissueGene	TT
A Multicenter, Randomized, Placebo Controlled, Double-blind, Parallel, Phase III Clinical Trial to Evaluate the Efficacy and Safety of Invossa K Injection in Patients Diagnosed as Knee Osteoarthritis With Kellgren & Lawrence Grade 2	Knee Osteoarthritis with Kellgren & Lawrence Grade 2 or 3	Kolon Life Science	TT
Safety and Efficacy Study in Subjects With Leber Congenital Amaurosis	Leber Congenital Amaurosis due to RPE65 Mutations	Spark Therapeutics	CT
Efficacy Study of GS010 for Treatment of Vision Loss From 7 Months to 1 Year From Onset in LHON Due to the ND4 Mutation	Leber Hereditary Optic Neuropathy	GenSight Biologics	CT
Efficacy Study of GS010 for the Treatment of Vision Loss up to 6 Months From Onset in LHON Due to the ND4 Mutation	Leber Hereditary Optic Neuropathy	GenSight Biologics	CT
Efficacy and Safety Study of Bilateral Intravitreal Injection of GS010 for the Treatment of Vision Loss up to 1 Year From Onset in LHON Due to the ND4 Mutation	Leber Hereditary Optic Neuropathy	GenSight Biologics	CT

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Table A1 – continued from previous page

Trial Title	Disease	Sponsors	Source
Tisagenlecleucel Versus Blinatumomab or Inotuzumab for Adult Patients With Relapsed/Refractory B-cell Precursor Acute Lymphoblastic Leukemia: A Randomized Open Label, Multicenter, Phase III Trial	Leukemia (Acute Lymphoblastic)	Novartis	TT
Phase IIIb Study for Relapsed/Refractory Pediatric/Young Adult Acute Lymphoblastic Leukemia Patients to be Treated With CTL019	Leukemia (Acute Lymphoblastic)	Novartis	TT
A Phase II/III Prospective, Open Label Study to Evaluate Safety and Efficacy of Intravenous Autologous CD19 CAR-T Cells for Relapsed/ Refractory B-Acute Lymphoblastic Leukemia	Leukemia (Acute Lymphoblastic)	Gaia Science	TT
A Randomized Phase II/III Study of $\alpha\beta$ T Cell-Depleted, Related, Haploidentical Hematopoietic Stem Cell Transplant (Haplo-HSCT) Plus Rivogenlecleucel vs. Haplo-HSCT Plus Post-Transplant Cyclophosphamide (PTCy) in Patients With AML or MDS	Leukemia (Acute Myelogenous)	Bellicum Pharmaceuticals	TT
Randomized, Registrational, Controlled Study of BPX-501 with Allogeneic Hematopoietic Stem Cells (Allo-HSCT) in Patients with Acute Myelogenous Leukemia	Leukemia (Acute Myelogenous)	Bellicum Pharmaceuticals	TT
TK008: Randomized Phase III Trial of Haploidentical HCT With or Without an Add Back Strategy of HSV-Tk Donor Lymphocytes in Patients With High Risk Acute Leukemia	Leukemia (Acute Myelogenous)	Molmed	TT
A Phase IIb/III Study of AST-VAC1 in Patients with Acute Myelogenous Leukemia (AML)	Leukemia (Acute Myelogenous)	Asterias/Lineage Cell Therapeutics	TT
A Study of Glybera for the Treatment of Lipoprotein Lipase (LPL) Deficiency	Lipoprotein Lipase Deficiency (LPLD)	uniQure	TT

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Table A1 – continued from previous page

Trial Title	Disease	Sponsors	Source
A Study to Determine the Safety and Efficacy in Lipoprotein Lipase-Deficient Subjects After Intramuscular Administration of AMT-011, an Adeno-Associated Viral Vector Expressing Human Lipoprotein LipaseS447X.	Lipoprotein Lipase Deficiency (LPLD)	uniQure	TT
An Open-label Study to Assess the Efficacy and Safety of Alipogene Tiparvovec (AMT-011), Human LPL [S447X], Expressed by an Adeno-Associated Viral Vector After Intramuscular Administration in LPL-deficient Adult Subjects	Lipoprotein Lipase Deficiency (LPLD)	uniQure	TT
A Study of AMT-011 in Patients With LPL Deficiency	Lipoprotein Lipase Deficiency (LPLD)	uniQure	TT
A Phase III Trial of Glybera for Dyslipidemia	Lipoprotein Lipase Deficiency (LPLD)	uniQure	TT
Phase II/III study of Ad-IFNg in Cutaneous T-cell lymphoma	Lymphoma	Transgene	TT
A Safety and Efficacy Study of Cryopreserved GSK2696274 for Treatment of Metachromatic Leukodystrophy (MLD)	Metachromatic Leukodystrophy	GlaxoSmithKline	CT
PV-10 Intralesional Injection vs Systemic Chemotherapy or Oncolytic Viral Therapy for Treatment of Locally Advanced Cutaneous Melanoma	Melanoma (Locally Advanced Cutaneous)	Provectus Biopharmaceuticals	TT
A Phase Ib/III, Multicenter, Trial of Talimogene Laherparepvec in Combination With Pembrolizumab (MK-3475) for Treatment of Unresectable Stage IIIB to IVM1c Melanoma (MASTERKEY-265/KEYNOTE-034)	Melanoma (Metastatic)	Amgen/ Merck & Co./Merck Sharp & Dohme (MSD)	TT

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Table A1 – continued from previous page

Trial Title	Disease	Sponsors	Source
A Phase III Clinical Trial to Evaluate the Safety and Efficacy of Treatment With 2 mg Intralesional Allovectin-7 Compared to Dacarbazine (DTIC) or Temozolomide (TMZ) in Subjects With Recurrent Metastatic Melanoma;Allovectin-7 Immunotherapeutic for Metastatic Melanoma (AIMM).	Melanoma (Metastatic)	Brickell Biotech, AnGes	TT
A Randomized Phase III Clinical Trial to Evaluate the Efficacy and Safety of Treatment With OncoVEXGM-CSF Compared to Subcutaneously Administered GM-CSF in Melanoma Patients With Unresectable Stage IIIb, IIIc and IV Disease	Melanoma (Metastatic)	Amgen	TT
An Extension Protocol to Evaluate the Efficacy and Safety of Extended Use Treatment With OncoVEXGM-CSF for Eligible Melanoma Patients Participating in Study 005/05	Melanoma (Metastatic)	Amgen	TT
A Controlled, Randomized Phase III Trial Comparing the Response to Dacarbazine With and Without Allovectin-7 in Patients With Metastatic Melanoma.	Melanoma (Metastatic)	Brickell Biotech	TT
Open-label, Single-arm, Multi-center Study of Intracerebral Administration of Adeno-associated Viral (AAV) Serotype rh.10 Carrying Human N-sulfoglucosamine Sulfohydrolase (SGSH) cDNA for Treatment of Mucopolysaccharidosis Type IIIA	Mucopolysaccharidosis Type IIIa	LYSOGENE	TT

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Table A1 – continued from previous page

Trial Title	Disease	Sponsors	Source
A Phase III, Single Arm, Multi-Center Study to Assess the Efficacy and Safety of Clarithromycin(Biaxin)-Lenalidomide-Low-Dose-Dexamethasone (BiRd) Combined With B-cell Muturation Antigen (BCMA)-Directed Chimeric Antigen Receptor (CAR) T-cell Therapy in Patients With Newly Diagnosed Multiple Myeloma	Multiple Myeloma (Newly Diagnosed)	Shanghai Unicar-Therapy Bio-medicine	TT
Clinical Trial of Recombinant Adenovirus-p53 (Gendicine) Combined with Radiotherapy in Nasopharyngeal Carcinoma Patients.;	Nasopharyngeal Carcinoma	Shenzhen SiBiono GeneTech Co.	TT
A Phase II/III, Multi-Center, Open-Label, Randomized Study to Compare the Effectiveness and Safety of Intralesional Administration of RPR/INGN 201 in Combination with Taxotere and Carboplatin and Radiotherapy Versus Taxotere and Carboplatin and Radiotherapy Alone in Patients with Locally Advanced Unresectable Non-Small Cell Lung Cancer (NSCLC)	NSCLC	Introgen Therapeutics	TT
A Phase IIB/III Randomized, Double-blind, Placebo Controlled Study Comparing First Line Therapy With or Without TG4010 Immunotherapy Product in Patients With Stage IV Non-Small Cell Lung Cancer (NSCLC)	NSCLC	Transgene	TT
Phase III multi-center, open, randomized clinical trial of percutaneous intratumoral injection of genetically engineered adenovirus (injection of H101), IL-2, TB hyperthermia and systemic chemotherapy in the treatment of advanced non-small cell lung cancer	NSCLC	Shanghai Sunway Biotech	TT

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Table A1 – continued from previous page

Trial Title	Disease	Sponsors	Source
Phase III Study of Lucanix (Belagenpumatucel-L) in Advanced Non-small Cell Lung Cancer: An International Multicenter, Randomized, Double-blinded, Placebo-controlled Study of Lucanix Maintenance Therapy for Stages III/IV NSCLC Subjects Who Have Responded to or Have Stable Disease Following One Regimen of Front-line, Platinum-based Combination Chemotherapy; Survival, Tumor-free, Overall and Progression-free (STOP)	NSCLC Stage 3	Activate Immunotherapy	TT
rAd-p53 Combined Chemotherapy Via Selective Arterial Cannula in The Treatment of Advanced Oral Cancer, A Randomized Controlled Trial	Oral Cancer (Advanced)	Shenzhen SiBiono GeneTech Co.	TT
A Randomized, Controlled, Double-Arm, Open-Label, Multi-Center Study of Ofranergene Obadenovec (VB-111) Combined With Paclitaxel vs. Paclitaxel Monotherapy for the Treatment of Recurrent Platinum-Resistant Ovarian Cancer	Ovarian Cancer (Platinum-Resistant)	Gynecologic Oncology Group (GOG)/ VBL Therapeutics	TT
A Phase II/III Trial of Chemotherapy Alone Versus Chemotherapy Plus SCH 58500 in Newly Diagnosed Stage III Ovarian and Primary Peritoneal Cancer Patients With Greater Than or Equal to 0.5 cm and Less Than or Equal to 2 cm Residual Disease Following Surgery	Ovarian Cancer, Primary Peritoneal Cavity Cancer	Merck & Co./Merck Sharp & Dohme (MSD)	TT
A Randomized, Phase II/III, Study of TNFerade Biologic With 5-FU and Radiation Therapy for First-Line Treatment of Unresectable Locally Advanced Pancreatic Cancer	Pancreatic Cancer (Locally Advanced)	Precigen	TT

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Table A1 – continued from previous page

Trial Title	Disease	Sponsors	Source
Phase II/III Study of ProSavin for the Treatment of Parkinson's Disease	Parkinson's Disease	Oxford BioMedica	TT
Phase III Trial of CERE-120 for Parkinson's Disease	Parkinson's Disease	Sanofi/Sanofi Genzyme, Sangamo Therapeutics	TT
A Randomized, Placebo-controlled Phase IIIa Pivotal Confirmatory Study to Evaluate Safety and Efficacy of VY-AADC in Patients with Parkinson's Disease	Parkinson's Disease	Neurocrine Biosciences	TT
A Randomized Double-Blind Placebo-Controlled Parallel Group Study of the Efficacy and Safety of XRP0038/NV1FGF on Amputation or Any Death in Critical Limb Ischemia Patients With Skin Lesions	Peripheral Artery Disease	Sanofi	TT
Efficiency, Safety and Portability of Neovasculgen	Peripheral Artery Disease	Human Stem Cell Institute, Russia	CT
Gene Therapy using Intramuscular Administration of AMG0001 in Patients with Peripheral Arterial Disease;	Peripheral Artery Disease	AnGes	TT
Hepatocyte Growth Factor to Improve Functioning in Peripheral Artery Disease: The HI-PAD Study;	Peripheral Artery Disease	Helixmith	TT
A phase III study of HGF Plasmid in Peripheral Arterial Disease (PAD) in the US	Peripheral Artery Disease	AnGes	TT
Phase 3 Study of Efficiency, Safety and Portability of Gene Therapy Drug Neovasculgen (DNA Encoding the 165-amino-acid Isoform of Human Vascular Endothelial Growth Factor (pCMV - VEGF165) for Peripheral Arterial Disease Complex Treatment	Peripheral Artery Disease	Human Stem Cells Institute	TT
Provenge (Sipuleucel-T) Active Cellular Immunotherapy Treatment of Metastatic Prostate Cancer After Failing Hormone Therapy	Prostate Cancer	Dendreon	CT

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Table A1 – continued from previous page

Trial Title	Disease	Sponsors	Source
A Randomized, Controlled Trial of Replication-Competent Adenovirus-Mediated Suicide Gene Therapy in Combination With IMRT Versus IMRT Alone for the Treatment of Newly-Diagnosed Prostate Cancer With an Intermediate Risk Profile	Prostate Cancer (Localized)	Henry Ford Health System	TT
A Randomized Controlled Trial of ProstAtak as Adjuvant to Up-front Radiation Therapy For Localized Prostate Cancer	Prostate Cancer (Localized)	Candel Therapeutics	TT
A Phase III Randomized, Open-Label Study of CG1940 and CG8711 Versus Docetaxel and Estramustine in Patients with Metastatic Hormone-Refractory Prostate Cancer Who are Chemotherapy-Naive.	Prostate Cancer (Metastatic Hormone-Refractory)	ANI Pharmaceuticals, Takeda	TT
A Phase III Randomized, Open-Label Study of CG1940 and CG8711 Versus Docetaxel and Prednisone in Patients With Metastatic Hormone-Refractory Prostate Cancer Who Are Chemotherapy-Naive.	Prostate Cancer (Metastatic Hormone-Refractory)	ANI Pharmaceuticals, Takeda	TT
A Phase III Randomized, Open-Label Study of Docetaxel in Combination With CG1940 and CG8711 Versus Docetaxel and Prednisone in Taxane-Nave Patients With Metastatic Hormone-Refractory Prostate Cancer With Pain.	Prostate Cancer (Metastatic Hormone-Refractory)	ANI Pharmaceuticals, Takeda	TT
A Randomized Controlled Trial Of AdV-tk + Valacyclovir Administered During Active Surveillance For Newly Diagnosed Prostate Cancer	Prostate Cancer (Newly Diagnosed)	Candel Therapeutics	TT
An Open label,Randomized, Multi-Centered, Intra-Patient Controlled Phase III Study of FCX-007 in Patients with Recessive Dystrophic Epidermolysis Bullosa (RDEB)	Recessive Dystrophic Epidermolysis Bullosa	Fibrocell Science	TT

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Trial Title	Disease	Sponsors	Source
VITAL: A Pivotal Phase 3 Study of EB-101 for the Treatment of Recessive Dystrophic Epidermolysis Bullosa (RDEB) (GENE TRANSFER)	Recessive Dystrophic Epidermolysis Bullosa	Stanford University Medical Center/ Abeona Therapeutics	TT
A Phase III, Randomized, Controlled, Double-Arm, Open-Label, Multi-center Study of VB-111 Combined With Bevacizumab vs. Bevacizumab Monotherapy in Patients With Recurrent Glioblastoma	Recurrent Glioblastoma	VBL Therapeutics	TT
A Phase II/III Randomized, Open-Label Study of Toca 511, a Retroviral Replicating Vector, Combined With Toca FC Versus Standard of Care in Subjects Undergoing Planned Resection for Recurrent Glioblastoma or Anaplastic Astrocytoma	Recurrent Glioblastoma	Tocagen	TT
A Randomized, Double-Blind, Placebo-Controlled, Parallel Group, Multicenter, Phase 3 Study to Evaluate the Safety and Efficacy of Ad5FGF-4 in Patients With Refractory Angina Due to Myocardial Ischemia;Ad5FGF-4 In Patients With Refractory Angina Due to Myocardial Ischemia (AFFIRM)	Refractory Angina due to Myocardial Ischemia (AFFIRM)	Gene Biotherapeutics/Angionetics	TT
A Phase III, Multicenter, Randomized, Open-label Study to Compare the Efficacy and Safety of bb2121 Versus Standard Triplet Regimens in Subjects With Relapsed and Refractory Multiple Myeloma (RRMM) (KarMMa-3)	Relapsed and Refractory Multiple Myeloma (RRMM)	Celgene	TT
A Single Global Phase 3 trial of RST-001 in Patients With Retinitis Pigmentosa (RP)	Retinitis Pigmentosa	Abbvie/Allergan	TT
A Phase II/III Expansion Study to Evaluate Safety and Efficacy of NSR-RPGR in Patients with a Diagnosis of X - Linked Retinitis Pigmentosa due to RPGR mutations	Retinitis Pigmentosa	NightstaRx	TT

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Table A1 – continued from previous page

Trial Title	Disease	Sponsors	Source
Phase 3 HGB-210 study of LentiGlobin in patients with SCD	Sickle Cell Anemia	bluebird bio	TT
Open-label, historical controlled study of AVXS-101 for treatment of spinal muscular atrophy	Spinal Muscular Atrophy	Novartis/AveXis	TT
A Multi-National Study of a One-Time Intrathecal Dose of AVXS-101 in Patients with Spinal Muscular Atrophy Types 1, 2, 3	Spinal Muscular Atrophy	Novartis/AveXis	TT
A Global Study of a Single, One-Time Dose of AVXS-101 Delivered to Infants With Genetically Diagnosed and Pre-symptomatic Spinal Muscular Atrophy With Multiple Copies of SMN2	Spinal Muscular Atrophy Type 1	Novartis/AveXis	TT
European, Phase 3, Open-Label, Single-Arm, Single-Dose Gene Replacement Therapy Clinical Trial for Patients With Spinal Muscular Atrophy Type 1 With One or Two SMN2 Copies Delivering AVXS-101 by Intravenous Infusion	Spinal Muscular Atrophy Type 1	Novartis/AveXis	TT
Phase 3, Open-Label, Single-Arm, Single-Dose Gene Replacement Therapy Clinical Trial for Patients With Spinal Muscular Atrophy Type 1 With One or Two SMN2 Copies Delivering AVXS-101 by Intravenous Infusion	Spinal Muscular Atrophy Type 1	Novartis/AveXis	TT
A Phase Ib/III Multicenter, Randomized, Trial of Talimogene Laherparepvec in Combination With Pembrolizumab for the Treatment of Subjects With Recurrent or Metastatic Squamous Cell Carcinoma of the Head and Neck	Squamous Cell Cancer of Head and Neck or Esophagus	Amgen/ Merck & Co./Merck Sharp & Dohme (MSD)	TT

Continued on next page

Table A1 – continued from previous page

Trial Title	Disease	Sponsors	Source
Phase III randomized clinical trial of intratumoral injection of E1B gene-deleted adenovirus (H101) combined with cisplatin-based chemotherapy in treating squamous cell cancer of head and neck or esophagus.	Squamous Cell Cancer of Head and Neck or Esophagus	Shanghai Sunway Biotech	TT
Phase III Randomized Study of Ad5CMV-p53 Gene Therapy (INGN 201) Versus Methotrexate in Patients With Refractory Squamous Cell Carcinoma of the Head and Neck (T301).	Squamous Cell Cancer of Head and Neck or Esophagus	Sanofi, Introgen Therapeutics	TT
A Phase III, Multi-Center, Open-Label, Randomized Study to Compare the Effectiveness and Safety of Intratumoral Administration of INGN 201 in Combination with Chemotherapy Versus Chemotherapy Alone in Patients with Squamous Cell Carcinoma of the Head and Neck (SCCHN)	Squamous Cell Cancer of Head and Neck or Esophagus	Introgen Therapeutics	TT
A Randomized, Controlled, Parallel Group, Multicenter Phase 3 Study to Evaluate the Efficacy and Safety of Ad5FGF-4 Using SPECT Myocardial Perfusion Imaging in Patients With Stable Angina Pectoris	Stable Angina	Gene Biotherapeutics/ Angionetics/ Gene Biotherapeutics	TT
A Randomized, Double Blind, Placebo Controlled, Parallel Group, Multicenter Study to Evaluate the Efficacy and Safety of Ad5FGF-4 in Female Patients With Stable Angina Pectoris Who Are Not Candidates for Revascularization;Angiogenesis in Women with Angina pectoris who are not candidates for Revascularization [AWARE]	Stable Angina	Gene Biotherapeutics/ Angionetics/ Gene Biotherapeutics	TT

Continued on next page

Table A1 – continued from previous page

Trial Title	Disease	Sponsors	Source
A Multinational Multicenter, Randomized, Double Blind, Placebo Controlled Study to Evaluate the Efficacy and Safety of Ad5FGF-4 in Patients With Stable Angina;(The Angiogenic Gene Therapy Trial - 4 [AGENT 4]).	Stable Angina	Bayer AG/Bayer HealthCare, Gene Biotherapeutics	TT
A Multicenter, Randomized, Double-Blind, Placebo Controlled Study to Evaluate the Efficacy and Safety of Ad5FGF-4 in Patients With Stable Angina (The Angiogeneic Gene Therapy Trial - 3 [AGENT 3])	Stable Angina	Bayer AG/Bayer HealthCare, Gene Biotherapeutics	TT
Multicentre, Randomized,Double Blind, Placebo Controlled Trial of Myocardial Angiogenesis Using VEGF165, Intramyocardial Gene Delivery in Patients With Severe Angina Pectoris	Stable Angina	Johnson & Johnson	TT
A Pivotal Study of NY-ESO-1 in Patients with Synovial Sarcoma including Myxoid Round Cell Liposarcoma	Synovial Sarcoma	GlaxoSmithKline/ AdaptImmune	TT

A5 Disease-to-Therapeutic Area Mapping

As mentioned in the main paper, we show how the diseases are related to the therapeutic areas in the table below.

Table A2: Diseases with ongoing gene therapy trials and their associated therapeutic areas.

Disease	Therapeutic Area
– General Conditions –	
Arteriosclerosis Obliterans	Cardiovascular
Critical Limb Ischemia	Cardiovascular
Degenerative Arthritis	Autoimmune/Inflammation
Diabetic Foot Symptoms	Metabolic/Endocrinology
Diabetic Foot Ulcers	Metabolic/Endocrinology
Diabetic Peripheral Neuropathy	Metabolic/Endocrinology
Heart Failure	Cardiovascular
Knee Osteoarthritis with Kellgren & Lawrence Grade 3	Autoimmune/Inflammation
Parkinson's Disease	CNS
Peripheral Artery Disease	Cardiovascular
Refractory Angina due to Myocardial Ischemia (AFFIRM)	Cardiovascular
Stable Angina	Cardiovascular
– Rare Diseases –	
Beta-Thalassemia	Metabolic/Endocrinology
Cerebral Adrenoleukodystrophy (CALD)	CNS
Choroideremia	Ophthalmology
Cystic Fibrosis	Cardiovascular
Ewing's Sarcoma	Oncology
Hemophilia A	Metabolic/Endocrinology
Hemophilia B	Metabolic/Endocrinology
Leber Congenital Amaurosis due to RPE65 Mutations	Ophthalmology
Leber Hereditary Optic Neuropathy	Ophthalmology
Lipoprotein Lipase Deficiency (LPLD)	Metabolic/Endocrinology
Metachromatic Leukodystrophy	Metabolic/Endocrinology
Mucopolysaccharidosis Type IIIa	CNS
Recessive Dystrophic Epidermolysis Bullosa	Autoimmune/Inflammation
Retinitis Pigmentosa	Ophthalmology
Sickle Cell Anemia	Metabolic/Endocrinology
Spinal Muscular Atrophy	CNS
Spinal Muscular Atrophy Type 1	CNS
– Cancer –	
B-Cell Non-Hodgkin's Lymphoma	Oncology
BCG Unresponsive NMIBC	Oncology
Bladder Cancer, in situ concurrent with Papillary Tumors	Oncology

Continued on next page

Table A2 – continued from previous page

Disease	**Therapeutic Area**
Diffuse Large B Cell Lymphoma (DLBCL)	Oncology
Head and Neck Cancer	Oncology
Hepatocellular Carcinoma	Oncology
High-Grade Glioma	Oncology
Leukemia (Acute Lymphoblastic)	Oncology
Leukemia (Acute Myelogenous)	Oncology
Lymphoma	Oncology
Melanoma (Locally Advanced Cutaneous)	Oncology
Melanoma (Metastatic)	Oncology
Multiple Myeloma (Newly Diagnosed)	Oncology
Nasopharyngeal Carcinoma	Oncology
NSCLC	Oncology
NSCLC Stage 3	Oncology
Oral Cancer (Advanced)	Oncology
Ovarian Cancer (Platinum-Resistant)	Oncology
Ovarian Cancer, Primary Peritoneal Cavity Cancer	Oncology
Pancreatic Cancer (Locally Advanced)	Oncology
Prostate Cancer	Oncology
Prostate Cancer (Localized)	Oncology
Prostate Cancer (Metastatic Hormone-Refractory)	Oncology
Prostate Cancer (Newly Diagnosed)	Oncology
Recurrent Glioblastoma	Oncology
Relapsed and Refractory Multiple Myeloma (RRMM)	Oncology
Squamous Cell Cancer of Head and Neck or Esophagus	Oncology
Synovial Sarcoma	Oncology

A6 Patient Population Estimation

We source the patient prevalence and incidence of the diseases from different sources. When necessary, we compute the prevalence from the incidence using Equation 1, or vice versa, using Equation 2. Our results are shown in Table A3. These numbers do not reflect the adjustments we make to NSC lung cancer, prostrate cancer and spinal muscular atrophy in order to minimize overlapping patient groups.

Table A3: Number of current patients and annual new patients for each disease. An asterisk (∗) indicates that either the prevalence is computed from the incidence using Equation 1, or vice versa, using Equation 2.

Disease	Current patients	New patients per year
– General Conditions –		
Arteriosclerosis Obliterans	[91]8500000	*192100
Critical Limb Ischemia	[83]975000	[83]300000
Degenerative Arthritis	[161]27000000	*486000
Diabetic Foot Ulcers	[129]2250000	[128]112500
Diabetic Peripheral Neuropathy	[66,92,168]9441480	[66,92,168]467400
Heart Failure	[100]5800000	[100]812000
Knee Osteoarthritis with Kellgren & Lawrence Grade 2 or/and 3	*2929730	[161]542000
Parkinson's Disease	[18]500000	[18]50000
Peripheral Artery Disease	[91]8500000	*564400
Refractory Angina due to Myocardial Ischemia (AFFIRM)	[4]8200000	[4,69]565000
Stable Angina	[42]10000000	[42]500000
– Rare Diseases –		
Beta-Thalassemia	[10]1000	[136]3277
Cerebral Adrenoleukodystrophy (CALD)	[63]411	[63]37
Choroideremia	[126]6554	[126]77
Cystic Fibrosis	[62]30000	[62]1000
Ewing's Sarcoma	[12,13,58]15003	[12,13,58]200
Hemophilia A	[45]16000	[45]360
Hemophilia B	[45]4000	[45]90
Leber Congenital Amaurosis due to RPE65 Mutations	[76]187	[76]19
Leber Hereditary Optic Neuropathy	[25]6540	[25]654
Lipoprotein Lipase Deficiency (LPLD)	[70]328	*33
Metachromatic Leukodystrophy	[46,138]9333	[46,138]771
Mucopolysaccharidosis Type IIIa	[28]1638	[28]39
Recessive Dystrophic Epidermolysis Bullosa	[107]100	*10

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Table A3 – continued from previous page

Disease	Current patients	New patients per year
Retinitis Pigmentosa	[143]87387	[143]8739
Sickle Cell Anemia	[55]100000	[56]58745
Spinal Muscular Atrophy	[123]8526	[123]290
Spinal Muscular Atrophy Type 1	[40]17500	[111]500
– Cancer –		
B-Cell Non-Hodgkin's Lymphoma	[8,9]694704	[8,9]74200
BCG Unresponsive NMIBC	[11,101,117,119]371933	[11,101,117,119]42625
Bladder Cancer, in situ concurrent with Papillary Tumors	[11]356720	[11]41040
Diffuse Large B Cell Lymphoma (DLBCL)	[108]257	[108]18351
Head and Neck Cancer	[48,51,52,53]134337	[48,51,52,53]75275
Hepatocellular Carcinoma	[14,96,98]11287	[14,96,98]2032
High-Grade Glioma	[2,7,47,49,146]87540	[2,7,47,49,146]16334
Leukemia (Acute Lymphoblastic)	[5]95764	[5]5930
Leukemia (Acute Myelogenous)	[6]61048	[6]21450
Lymphoma	[15,32]905678	[15,32]82310
Melanoma (Locally Advanced Cutaneous)	[16]107605	[16]8683
Melanoma (Metastatic)	[16]47824	[16]3859
Multiple Myeloma (Newly Diagnosed)	0	[1]32270
Nasopharyngeal Carcinoma	[109]5390	[109]327
NSC Lung Cancer	[33,54]454469	[54] 191646
NSC Lung Cancer Stage 3	[33,54,140]151490	[54,140]63882
Oral Cancer (Advanced)	[3]250000	[3]53000
Ovarian Cancer (Platinum-Resistant)	[34,35,36]141150	[34,35,36]13956
Ovarian Cancer, Primary Peritoneal Cavity Cancer	[38]2290	[38]240
Pancreatic Cancer (Locally Advanced)	[37,147]22066	[37,147]17031
Prostate Cancer	[17]3110403	[17]174650
Prostate Cancer (Localized)	[17]2395010	[17]134481
Prostate Cancer (Metastatic Hormone-Refractory)	[17]186624	[17]10479
Prostate Cancer (Newly Diagnosed)	0	[17]174650
Recurrent Glioblastoma	[7,47,49,146]64127	[7,47,49,146]12120
Relapsed and Refractory Multiple Myeloma (RRMM)	[39,80]48840	[39,80]16280
Squamous Cell Cancer of Head and Neck or Esophagus	[48,51,52,53]120903	[48,51,52,53]67747
Synovial Sarcoma	[41,87]7282	[87]655

A7 Calibration of Survival Functions $D_{alt}(x-a)$

We source either the survival or mortality rate from literature and use them to compute λ, the time parameter in the exponential survival function. We show our result in the table below.

Table A4: List of survival rate or mortality rate and λ, for each disease. An asterisk ($*$) under λ denotes that the disease does not affect mortality directly.

Disease	k years survival rate		k years mortality rate			λ
	$k=5$	$k=10$	$k=1$	$k=5$	$k=10$	
Arteriosclerosis Obliterans				[159]11.3		0.024
Critical Limb Ischemia				[84]50		0.139
Degenerative Arthritis		[163]82				0.020
Diabetic Foot Ulcers				[145]49		0.135
Diabetic Peripheral Neuropathy					[59]5	0.005
Heart Failure				[50]42.3		0.110
Knee Osteoarthritis with Kellgren & Lawrence Grade 2	[154]7.5					0.518
Knee Osteoarthritis with Kellgren & Lawrence Grade 3	[154]7.5					0.518
Parkinson's Disease	[165]40					0.174
Peripheral Artery Disease				[71]33.2		0.081
Refractory Angina due to Myocardial Ischemia (AFFIRM)			[103]3.9			0.040
Stable Angina	[104]90					0.021
Beta-Thalassemia		[169]98.3				0.002
Cerebral Adrenoleukodystrophy (CALD)	[142]55					0.120
Choroideremia						*
Cystic Fibrosis					[120]28	0.033
Ewing's Sarcoma	[130]70					0.071
Hemophilia A					[139]9.7	0.010
Hemophilia B					[139]9.7	0.010
Leber Congenital Amaurosis due to RPE65 Mutations						*

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Table A4 – continued from previous page

Disease	k years survival rate $k=5$	$k=10$	k years mortality rate $k=1$	$k=5$	$k=10$	λ
Leber Hereditary Optic Neuropathy						*
Lipoprotein Lipase Deficiency (LPLD)						*
Metachromatic Leukodystrophy	[127]52					0.131
Mucopolysaccharidosis Type III		[124]60				0.051
Recessive Dystrophic Epidermolysis Bullosa						*
Retinitis Pigmentosa						*
Sickle Cell Anemia		[94]96				0.004
Spinal Muscular Atrophy	[81]40					0.183
Spinal Muscular Atrophy Type 1	[170]10.13					0.458
B-Cell Non-Hodgkin's Lymphoma	[29]72					0.066
BCG Unresponsive Non-Muscle Invasive Bladder Cancer	[119]78					0.050
Bladder Cancer, Transitional Cell Carcinoma	[19]95.8					0.009
Diffuse Large B-Cell Lymphoma (DLBCL)	[24]63.2					0.092
Head and Neck Cancer	[20]64					0.089
Hepatocellular Carcinoma	[98]10					0.461
High-Grade Glioma	[106]9.87					0.463
Leukemia (Acute Lymphoblastic)	[5]68.8					0.075
Leukemia (Acute Myelogenous)	[6]28.7					0.250
Lymphoma	[27]72					0.066
Melanoma (Locally Advanced Cutaneous)	[26]64					0.089
Melanoma (Metastatic)	[26]23					0.294
Multiple Myeloma (Newly Diagnosed)	[57]52					0.131
Nasopharyngeal Carcinoma	[30]72					0.066
NSCLC	[43]23					0.294
NSCLC (Stage 3)	[43]33					0.222
Oral Cancer (Advanced)	[20]39.1					0.188

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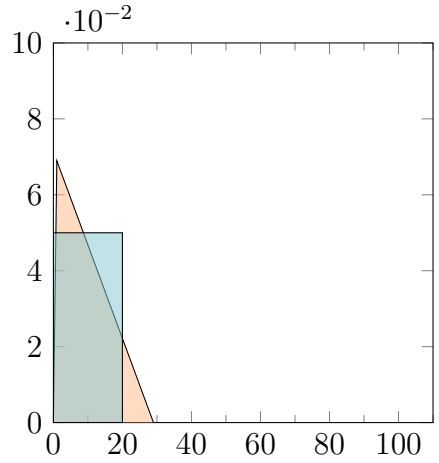
Table A4 – continued from previous page

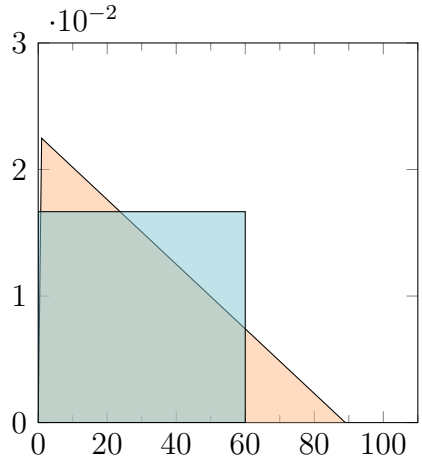
Disease	k years survival rate		k years mortality rate			λ
	$k = 5$	$k = 10$	$k = 1$	$k = 5$	$k = 10$	
Ovarian Cancer (Platinum-Resistant)	[162]1.9					0.793
Ovarian Cancer, Primary Peritoneal Cavity Cancer	[21]47.6					0.148
Pancreatic Cancer (Locally Advanced)	[22]12.4					0.417
Prostate Cancer	[23]98					0.004
Prostate Cancer (Localized)	[23]98					0.004
Prostate Cancer (Metastatic Hormone Refractory)	[23]30.5					0.237
Prostate Cancer (Newly Diagnosed)	[23]95.1					0.010
Recurrent Glioblastoma	[122]10					0.461
Relapsed and Refractory Multiple Myeloma (RRMM)	[44]9.92					0.462
Squamous Cell Cancer of Head and Neck or Esophagus	[20]64					0.089
Synovial Sarcoma	[31]55					0.120

A8 Calibration of Age Distribution $A(x)$

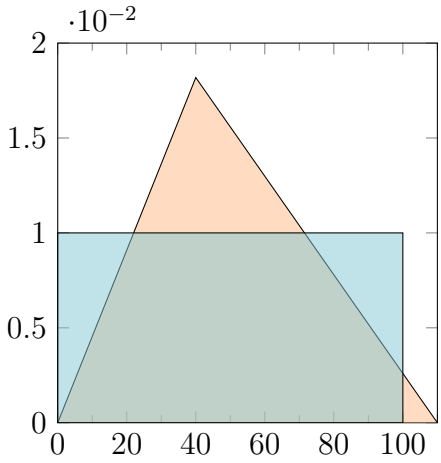
As mentioned in the main paper, our optimization program produces triangular age distributions that conforms to data, have wider support compared to fitting uniform distributions and, avoids sharp changes in the probability density. We illustrate some examples that compare triangle distributions with the uniform distributions with the same average age.



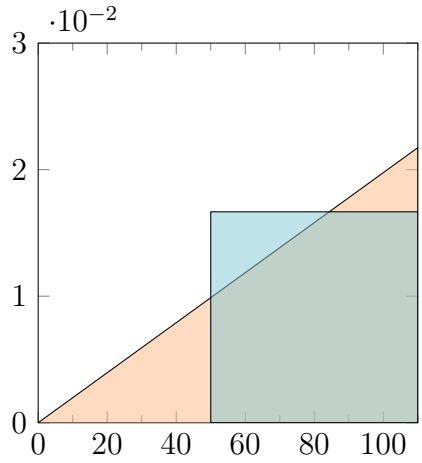
(a) Comparative probability distributions when $\mu_{age} = 10$



(b) Comparative probability distributions when $\mu_{age} = 30$



(c) Comparative probability distributions when $\mu_{age} = 50$



(d) Comparative probability distributions when $\mu_{age} = 80$

Figure A2: Age distributions given various mean ages, μ_{age}. The red triangles represent the solutions obtained by our optimization program, while the blue rectangles represent the solutions given by an uniform distribution. The distributions from the optimization program have a wider base of support and avoid sharp changes in density.

A9 Quality of Life Estimation

The results of our literature search and estimation for the change in QoL for each disease is shown in the table below.

Table A5: Table of disease scores (ζ), estimated quality of life values before treatment $\hat{f}_h(s_{alt})$, after treatment $\hat{f}_h(s_{gt})$, and the change in quality of life (ΔQoL). Asterisks ($*$) indicate that the values are interpolated. Cancers are not included, as we assume that the gains in survival dominate the gains in QoL.

Non-Cancer Disease	ζ	$\hat{\mathbf{f}}_\mathbf{h}(\mathbf{s_{alt}})$	**ΔQoL**	$\hat{\mathbf{f}}_\mathbf{h}(\mathbf{s_{gt}})$
Arteriosclerosis Obliterans	1	*0.775	*0.075	*0.850
Beta-Thalassemia	3	[150]0.870	*0.166	*1.000
Cerebral Adrenoleukodystrophy (CALD)	5	*0.654	*0.257	*0.911
Choroideremia	3	*0.715	*0.166	*0.881
Critical Limb Ischemia	4	*0.684	*0.212	*0.896
Cystic Fibrosis	3	[61]0.671	*0.166	*0.837
Degenerative Arthritis	3	*0.715	*0.166	*0.881
Diabetic Foot Ulcers	3	[153]0.703	[153]0.258	[153]0.961
Diabetic Peripheral Neuropathy	2	[152]0.630	[152]0.180	[152]0.810
Ewing's Sarcoma	2	[144]0.690	*0.121	*0.811
Heart Failure	4	*0.684	*0.212	*0.896
Hemophilia A	5	[72]0.750	*0.257	*1.000
Hemophilia B	5	[72]0.700	*0.257	*0.957
Knee Osteoarthritis, Kellgren & Lawrence Grade 2	2	[134]0.900	[134]0.042	*0.942
Knee Osteoarthritis, Kellgren & Lawrence Grade 3	2	[134]0.900	[134]0.048	*0.948
Leber Congenital Amaurosis (RPE65 Mutations)	3	*0.715	*0.166	*0.881
Leber Hereditary Optic Neuropathy	3	*0.715	*0.166	*0.881
Lipoprotein Lipase Deficiency	4	*0.684	*0.212	*0.896
Lysosomal Storage Disease	5	[93]0.640	*0.257	*0.897
Mucopolysaccharidosis Type IIIa	2	[102]0.582	[102]0.264	[102]0.846
Osteoarthritis	2	[157]0.900	[157]0.040	*0.940
Parkinson's Disease	4	[85,151]0.700	[85]0.150	[85]0.850
Peripheral Artery Disease	2	[105]0.660	[105]0.060	[105]0.720
Recessive Dystrophic Epidermolysis Bullosa	4	[116]0.590	*0.212	*0.802
Refractory Angina due to Myocardial Ischemia	2	[99]0.600	*0.121	*0.721
Retinitis Pigmentosa	3	[149]0.770	*0.166	*0.936
Sickle Cell Anemia	3	[90]0.732	[90]0.198	[90]0.930
Spinal Muscular Atrophy[5]	5	0.520	*0.257	*0.777
Spinal Muscular Atrophy Type 1	5	[171]0.520	*0.257	*0.777
Stable Angina	2	[121,167]0.750	[167]0.150	[167]0.900

[5]We are unable to find QoL values for SMA only and assume that they are the same as SMA Type 1.

Table A6: Estimated ΔQALY, assumed price per ΔQALY and estimated price of gene therapies per disease. Prices are given to 3 significant figures for display in this table.

Disease	ΔQALY	$\frac{\text{Cost}}{\Delta\text{QALY}}$ ($)	Price ($)
General Diseases:			
Arteriosclerosis Obliterans	2.96	41K	121K
Critical Limb Ischemia	7.32	41K	299K
Degenerative Arthritis	3.53	41K	144K
Diabetic Foot Ulcers	7.92	41K	323K
Diabetic Peripheral Neuropathy	3.95	41K	161K
Heart Failure	6.92	41K	282K
Knee Osteoarthritis with Kellgren & Lawrence Grade 3	10.62	41K	433K
Parkinson's Disease	8.26	41K	337K
Peripheral Artery Disease	4.52	41K	184K
Refractory Angina due to Myocardial Ischemia (AFFIRM)	3.80	41K	155K
Stable Angina	3.85	41K	157K
Rare Diseases:			
Beta-Thalassemia	4.58	102K	466K
Cerebral Adrenoleukodystrophy (CALD)	20.33	102K	2.07M
Choroideremia	4.24	102K	431K
Cystic Fibrosis	13.20	102K	1.34M
Ewing's Sarcoma	14.04	102K	1.43M
Hemophilia A	11.18	102K	1.14M
Hemophilia B	10.63	102K	1.08M
Leber Congenital Amaurosis due to RPE65 Mutations	4.63	102K	470K
Leber Hereditary Optic Neuropathy	3.97	102K	404K
Lipoprotein Lipase Deficiency (LPLD)	5.74	102K	584K
Metachromatic Leukodystrophy	21.06	102K	2.14M
Mucopolysaccharidosis Type IIIa	16.27	102K	1.65M
Recessive Dystrophic Epidermolysis Bullosa	5.89	102K	599K
Retinitis Pigmentosa	3.28	102K	333K
Sickle Cell Anemia	7.36	102K	748K
Spinal Muscular Atrophy	19.23	102K	1.96M
Spinal Muscular Atrophy Type 1	20.56	102K	2.09M
Cancer:			
B-Cell Non-Hodgkin's Lymphoma	4.90	41K	200K
BCG Unresponsive NMIBC	2.86	41K	117K
Bladder Cancer, in situ concurrent with Papillary Tumors	0.66	41K	26.9K

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Table A6 – continued from previous page

Disease	**ΔQALY**	$\frac{\textbf{Cost}}{\textbf{ΔQALY}}$ **($)**	**Price ($)**
Diffuse Large B Cell Lymphoma (DLBCL)	6.19	41K	253K
Head and Neck Cancer	6.13	41K	250K
Hepatocellular Carcinoma	9.30	41K	380K
High-Grade Glioma	12.56	41K	512K
Leukemia (Acute Lymphoblastic)	13.04	41K	532K
Leukemia (Acute Myelogenous)	8.55	41K	349K
Lymphoma	4.90	41K	200K
Melanoma (Locally Advanced Cutaneous)	6.23	41K	254K
Melanoma (Metastatic)	9.22	41K	376K
Multiple Myeloma (Newly Diagnosed)	5.90	41K	241K
Nasopharyngeal Carcinoma	5.20	41K	212K
NSC Lung Cancer	7.04	41K	287K
NSC Lung Cancer Stage 3	6.52	41K	266K
Oral Cancer (Advanced)	8.21	41K	335K
Ovarian Cancer (Platinum-Resistant)	10.83	41K	442K
Ovarian Cancer, Primary Peritoneal Cavity Cancer	7.93	41K	324K
Pancreatic Cancer (Locally Advanced)	7.64	41K	312K
Prostate Cancer	0.42	41K	17.1K
Prostate Cancer (Localized)	0.42	41K	17.1K
Prostate Cancer (Metastatic Hormone-Refractory)	7.75	41K	316K
Prostate Cancer (Newly Diagnosed)	0.99	41K	40.4K
Recurrent Glioblastoma	12.55	41K	512K
Relapsed and Refractory Multiple Myeloma (RRMM)	8.33	41K	340K
Squamous Cell Cancer of Head and Neck or Esophagus	5.51	41K	225K
Synovial Sarcoma	8.65	41K	353K

A10 Visualization of the Cost over Time

In this section, we visualize how the monthly cost of treating patients with gene therapy will be affected by changes to the variables. The results are summarized in the tornado chart presented in the main paper.

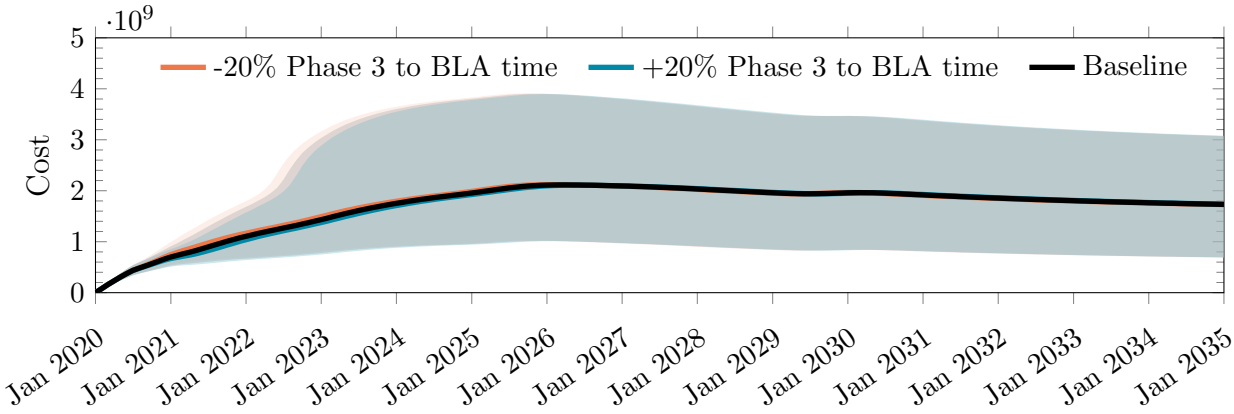

Figure A3: Impact on monthly cost of treating patients given a ±20% change in the time from phase 3 to BLA.

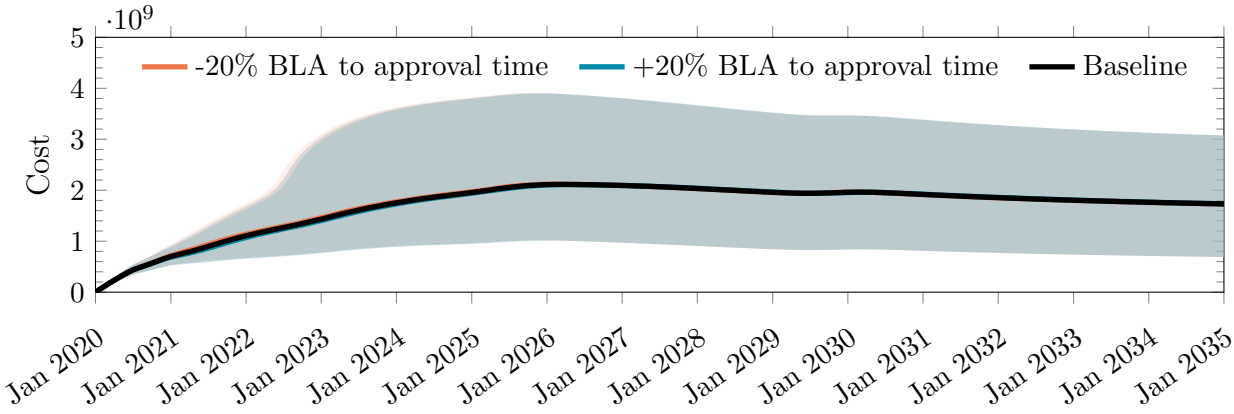

Figure A4: Impact on monthly cost of treating patients given a ±20% change in the time from BLA to approval.

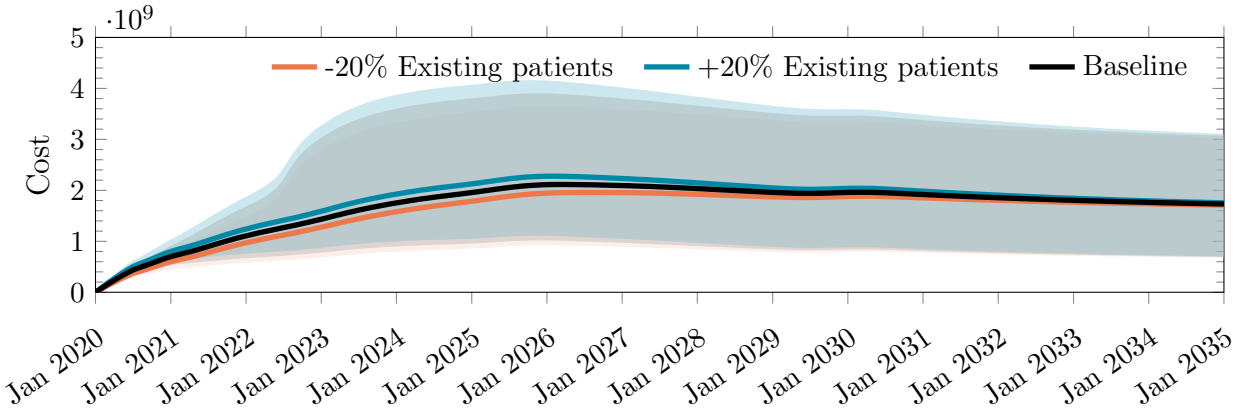

Figure A5: Impact on monthly cost of treating patients given a ±20% change in the number of existing patients.

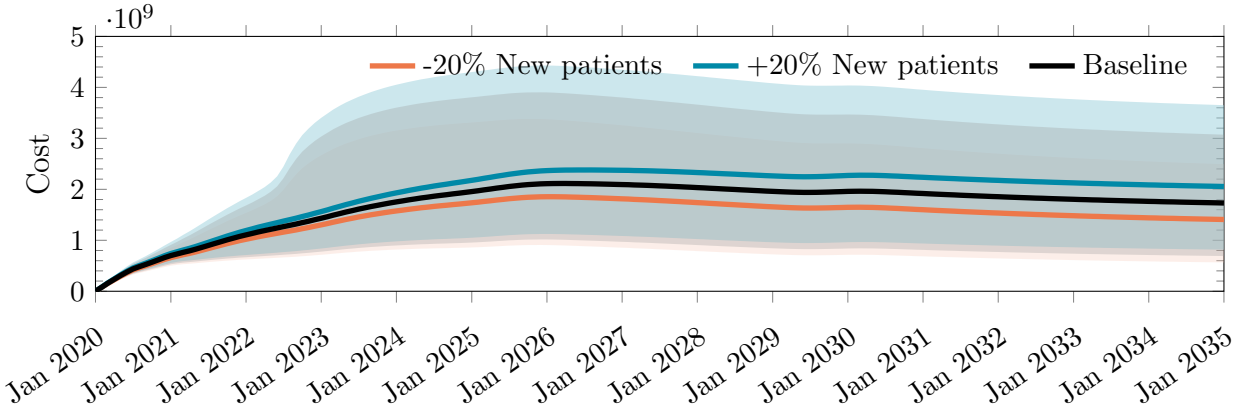

Figure A6: Impact on monthly cost of treating patients given a ±20% change in the number of new patients.

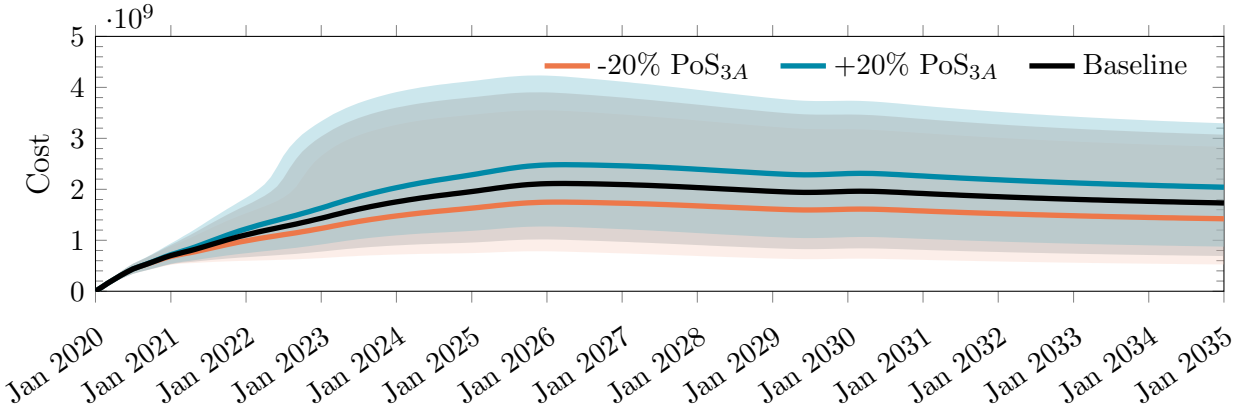

Figure A7: Impact on monthly cost of treating patients given a ±20% change in the PoS_{3A}.

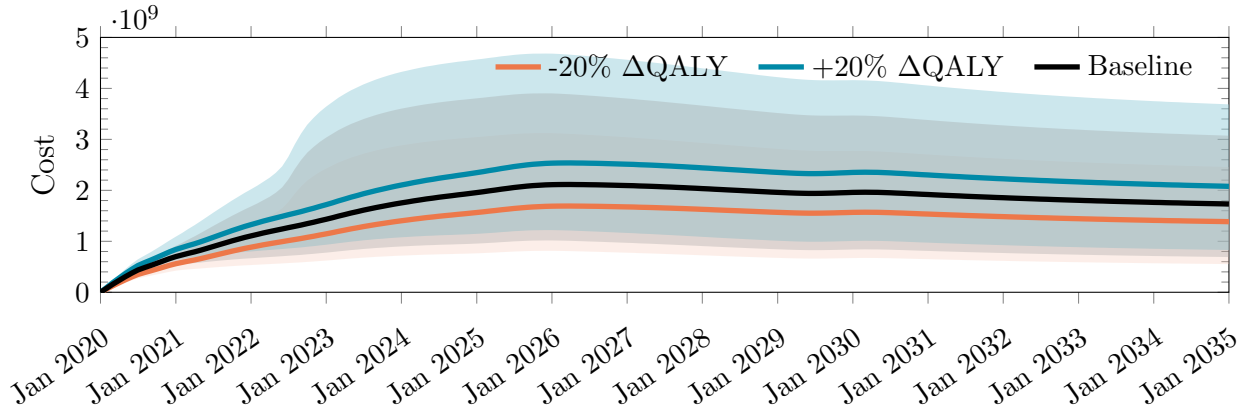

Figure A8: Impact on monthly cost of treating patients given a ±20% change in ΔQALY gained.

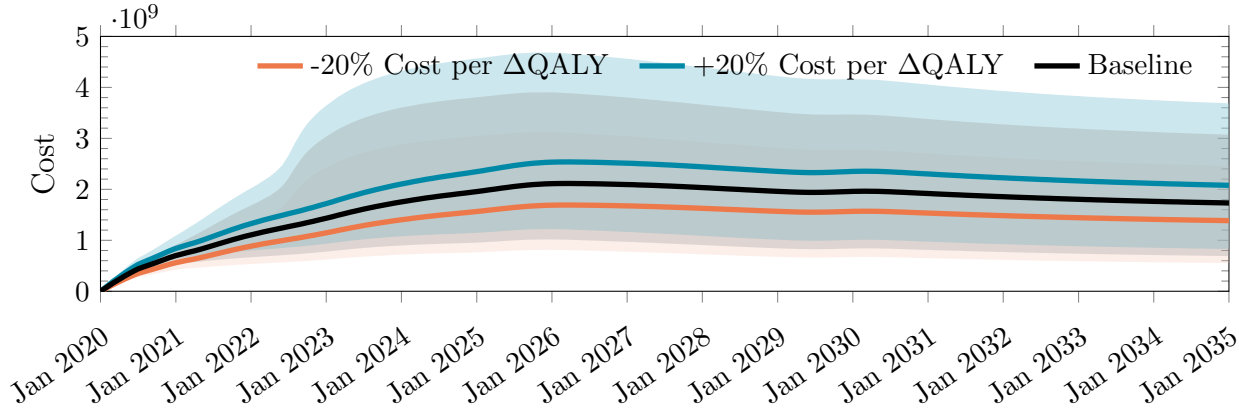

Figure A9: Impact on monthly cost of treating patients given a ±20% change in the cost per ΔQALY.

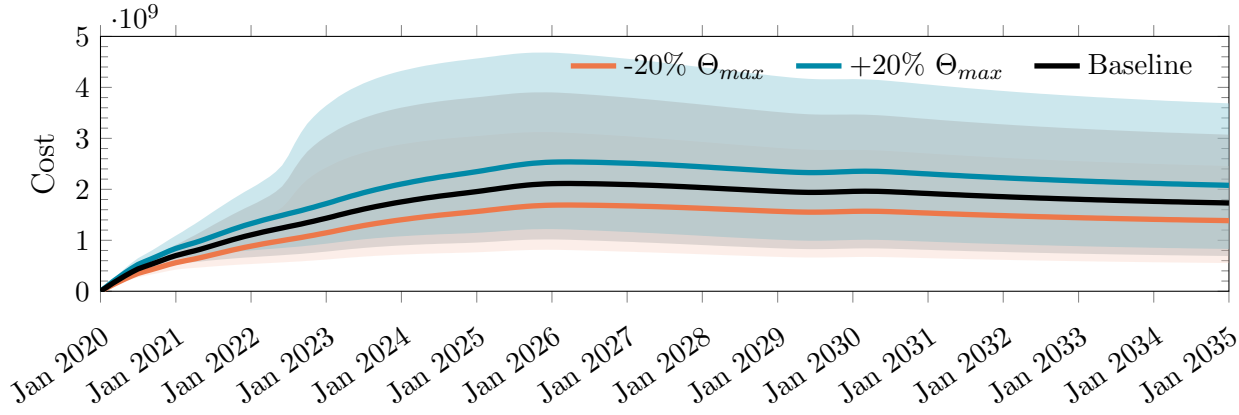

Figure A10: Impact on monthly cost of treating patients given a ±20% change in Θ_{max}.

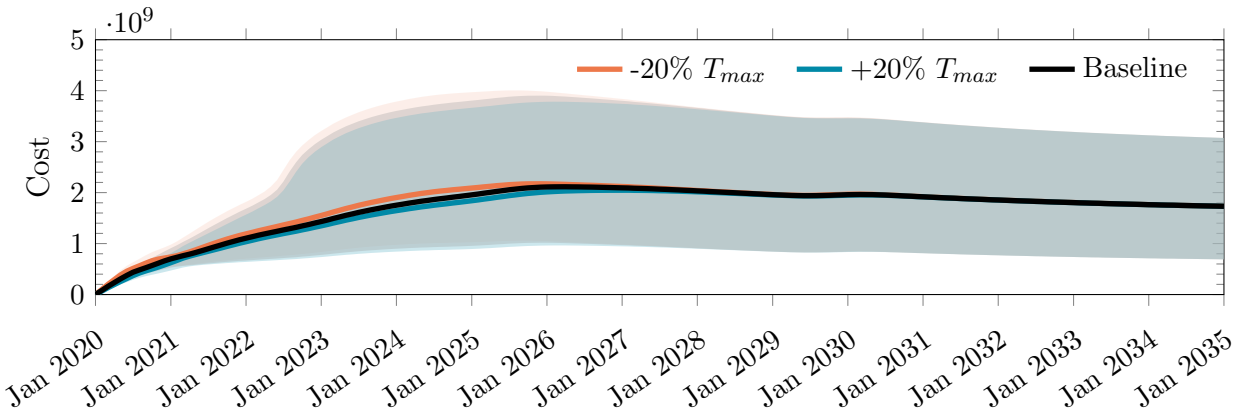

Figure A11: Impact on monthly cost of treating patients given a ±20% change in T_{max}.