Supporting Information

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SI Methods

Vector Construction. The original production of laboratory grade adenoviral (Ad5) vector encoding human aquaporin-1 (hAQP1) was previously reported (1). For this study, Good Manufacturing Practice (GMP) AdhAQP1 was produced at the Belfer Gene Therapy Vector Core Facility at the Weill College of Medicine of Cornell University in New York, NY, according to the GMP guidelines of the Food and Drug Administration (FDA). This vector was placed into sterile 1.5-mL polypropylene cryogenic vials (Corning) and kept frozen at −60 °C. Each cryovial contained 0.35 ± 0.05 mL of AdhAQP1 at one concentration [10^{11} vector particles (vp)/mL], which was diluted with GMP-grade vehicle (10 mM Tris, pH 7.8, 10 mM $MgCl_2$, 150 mM NaCl, 88 mM sucrose) as clinically needed, by the National Institutes of Health (NIH) Clinical Center Pharmaceutical Development Service.

Safety Parameters Measured. The clinical laboratory tests routinely included the following: complete blood count with differential, erythrocyte sedimentation rate, C-reactive protein, clotting parameters (prothrombin time, partial thromboplastin time, fibrinogen level), serum chemistries [sodium, potassium chloride, total CO_2, blood urea nitrogen, creatinine, alkaline phosphatase, alanine amino transferase, aspartate amino transferase, bilirubin (total and direct), total protein, albumin, calcium, magnesium, phosphate, uric acid, glucose, creatine phosphatase, lactate dehydrogenase, cholesterol, triglycerides, ferritin, amylase], thyroid stimulating hormone (TSH), with T4 performed only if TSH abnormal, urinalysis, C3 complement, C4 complement, IgA, IgG, and IgM.

Anti-Ad5 neutralizing antibodies in serum were measured before vector administration, as previously described (2). Titers are reported as the serum dilution resulting in 50% inhibition of 293-cell transduction with an Ad5 vector encoding luciferase.

Aliquots of serum were assayed for the presence of antibodies to hAQP1 using a recently reported, highly sensitive luciferase immunoprecipitation method (3). This assay used C-terminal antigen fusions to the *Renilla* luciferase gene, to generate a chimeric antibody target. Each assay contained negative and positive control samples, with the positive control generated by using a commercially available antibody against hAQP1 (Alpha Diagnostic). Control sera showed background levels of luciferase activity, typically <0.1% of the assay input. Aliquots of serum were assayed for the presence of antibodies to hAQP1 before AdhAQP1 administration and on days 2, 7, 14, and 28, per protocol.

Samples of serum and saliva were assayed for the presence of AdhAQP1 vector, before AdhAQP1 administration and on days 2 and 7, and thereafter if needed until two consecutive negative results were obtained postvector administration per protocol. This quantitative-PCR–based assay used primers specific for both hAQP1 and the CMV promoter/enhancer, as previously reported (4).

Serum and saliva also were assayed for the presence of replication-competent adenovirus using a quantitative-PCR assay designed to amplify part of the Ad5 E1 gene, as previously reported (4), before AdhAQP1 administration and on days 2, 7, 14, and 28, per protocol.

Clinical Outcome Measures. Parotid saliva flow rates, both at rest and following a physiological gustatory stimulus with 2% (wt/vol) citric acid, were determined with a Teflon Carlson-Crittenden/Lashley cup, placed over the orifice of the Stensen's duct, and held in place by slight negative pressure (5). On day 1, vector was administered at ∼0900 hours, and subjects were evaluated and saliva was collected at ∼1500 and ∼2100 hours. Thereafter, all saliva collections were at ∼0900 hours. Objective response was evaluated by comparing baseline parotid saliva flow rates to the peak parotid saliva flow rates in the targeted gland at times following vector administration until day 42. In a post hoc analysis, subjects were divided into responders if they had at least 50% increase in salivary flow, whereas those with less than 50% increase were considered nonresponders. Subjective responses were evaluated using validated visual analog scales (6). Subjects were asked to assess eight symptoms of salivary dysfunction (difficulty speaking, difficulty swallowing, amount of saliva perceived, dryness of their mouth, dryness of their throat, dryness of their lips, dryness of their tongue and thirst).

Imaging Studies. Magnetic resonance imaging of the salivary glands was performed at the first predose visit, and on days 2, 7, and 42, per protocol. In addition to assessment of anatomy and morphology of the major salivary glands, quantitative measurements of T1 relaxation, T2 relaxation, and apparent diffusion coefficient were made. These measurements were evaluated with particular attention to inflammatory and functional changes in the targeted glands. Two radionuclide-imaging studies also were performed: dynamic $^{99m}TcO_4$ salivary scans to assess functional salivary parenchyma present (at the first predose visit and on days 2, 7, and 28, per protocol), and planar ^{67}Ga citrate scans of the head and neck to assess salivary gland inflammation (at the first predose visit, and on days 2, 7, and 42; the latter two times only if the day 2 scan showed marked clinical changes compared with baseline, per protocol). In practice, gallium scans only were performed at baseline or at 24 h after AdhAQP1 delivery. Some subjects also underwent delayed imaging 3–6 d later, without additional ^{67}Ga citrate administration (Table 3). For the ^{67}Ga citrate scans, regions of interest were drawn around the parotid glands and target:nontarget control parotid uptake ratios were obtained. For the $^{99m}TcO_4$ scans, regions of interest were drawn around each parotid gland, the mouth, and the skull (background), and the number of counts per minute per pixel determined. The total signal present in each region was quantified at 1-min intervals typically for 60 min after the injection of the tracer. At each time point, a background signal calculated from the region of interest over the skull, corrected for region size, was subtracted. At time 40 min the subjects received a secretory stimulus of 6% (wt/vol) citric acid. In most cases (see below for exceptions) the $^{99m}TcO_4$ data from the targeted gland were analyzed as follows: Using the program SigmaPlot 10.0 (Systat Software) the background-corrected signals from 1 to 39 min were fit to an equation representing an exponential rise to a maximum value. This yielded a rate constant for $^{99m}TcO_4$ uptake and a predicted value for the $^{99m}TcO_4$ uptake signal at time 40 min. The data from 43 to 60 min were fit to a straight line, also using SigmaPlot 10.0, from which a predicted value for the $^{99m}TcO_4$ signal at time 43 min was calculated. Using the predicted signals at 40 and 43 min we calculated the percent $^{99m}TcO_4$ lost after the application of the secretory stimulus at 40 min. In a few instances (4 of a total of 44 scans) the $^{99m}TcO_4$ traces showed an apparent spontaneous $^{99m}TcO_4$ loss during the interval 1–40 min; in these cases the data obtained before and after the apparent spontaneous $^{99m}TcO_4$ loss were analyzed separately. In one subject (#73) two of the $^{99m}TcO_4$ signal datasets (at days 0 and 7) were so widely scattered that

the theoretical fit to an exponential rise to a maximum failed to converge; in these cases we fit the data from 1 to 40 min to a straight line.

Statistical Analyses. As this was a phase I study, sample size and assignment to a cohort of a standard three subjects per dose level was based on ≤30% (one-third or less) true rate of dose-limiting toxicity. The subjects were assigned to blocks of three as they were enrolled and deemed eligible to participate. There were only two subjects in dose tier 4 (5.8×10^9), as the AdhAQP1 expiration date was reached. Analyses of adverse events were descriptive in nature. Baseline and peak salivary flows were compared by a paired Wilcoxon test. Baseline characteristics between responders and nonresponders were compared for age, the amount of radiation received to the targeted parotid gland, the amount of viral particles received, as well as for their parotid salivary flow rate, with an unpaired *t* test. All statistical analyses were performed using GraphPad Prism Version 5.0d (GraphPad Software).

1. Delporte C, et al. (1997) Increased fluid secretion after adenoviral-mediated transfer of the aquaporin-1 cDNA to irradiated rat salivary glands. *Proc Natl Acad Sci USA* 94(7): 3268–3273.
2. Sprangers MC, et al. (2003) Quantifying adenovirus-neutralizing antibodies by luciferase transgene detection: Addressing preexisting immunity to vaccine and gene therapy vectors. *J Clin Microbiol* 41(11):5046–5052.
3. Burbelo PD, Ching KH, Bren KE, Iadarola MJ (2011) Searching for biomarkers: Humoral response profiling with luciferase immunoprecipitation systems. *Expert Rev Proteomics* 8(3):309–316.
4. Zheng C, et al. (2010) Transient detection of E1-containing adenovirus in saliva after the delivery of a first-generation adenoviral vector to human parotid gland. *J Gene Med* 12(1):3–10.
5. Fox PC, van der Ven PF, Sonies BC, Weiffenbach JM, Baum BJ (1985) Xerostomia: Evaluation of a symptom with increasing significance. *J Am Dent Assoc* 110(4): 519–525.
6. Pai S, Ghezzi EM, Ship JA (2001) Development of a Visual Analogue Scale questionnaire for subjective assessment of salivary dysfunction. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 91(3):311–316.

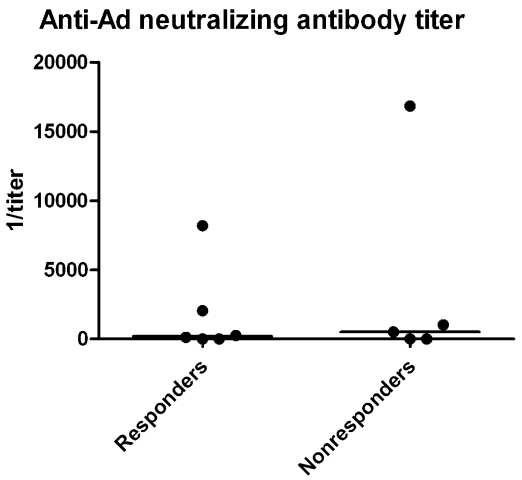

Fig. S1. Neutralizing antibodies at baseline in responders and nonresponders. The titers are expressed as the reciprocals of the highest serum dilution with neutralizing activity.

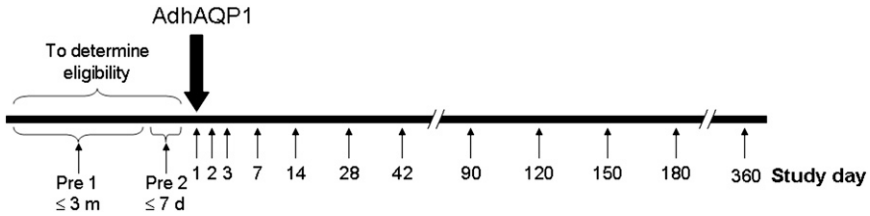

Fig. S2. Timeline of study visits. Pre 1 and Pre 2 indicate prevector administration screening visits to determine eligibility for enrollment. Pre 1 occurred within 3 mo of vector administration, and Pre 2 occurred within 1 wk of vector administration. The large downward arrow above the timeline indicates when AdhAQP1 was administered (i.e., on day 1). All other study visit days are indicated below the timeline by the small upward arrows and numbers. This figure is a modification of a figure that was published in the *Journal of Gene Medicine* in 2010 (1).

1. Zheng C, et al. (2010) Transient detection of E1-containing adenovirus in saliva after the delivery of a first-generation adenoviral vector to human parotid gland. *J Gene Med* 12(1):3–10.

Table S1. Summary of adverse events by treatment group, system organ class, and preferred term for all consented subjects

	Tier 1 *n* = 3		Tier 2 *n* = 3		Tier 3 *n* = 3		Tier 4 *n* = 2		Total *n* = 11	
System organ class preferred term*	# subject with AE	# of AE	# subject with AE	# of AE	# subject with AE	# of AE	# subject with AE	# of AE	# subject with AE	# of AE
All system organ classes	3 (100.0%)	20	3 (100.0%)	22	3 (100.0%)	20	2 (100.0%)	3	11 (100.0%)	65
Gastrointestinal disorders										
Any event	1 (33.3%)	1	3 (100.0%)	8	2 (66.7%)	3	0 (0.0%)	0	6 (54.5%)	12
Dry mouth	0 (0.0%)	0	1 (33.3%)	1	1 (33.3%)	1	0 (0.0%)	0	2 (18.2%)	2
Abdominal pain lower	0 (0.0%)	0	1 (33.3%)	1	0 (0.0%)	0	0 (0.0%)	0	1 (9.1%)	1
Dyspepsia	1 (33.3%)	1	0 (0.0%)	0	0 (0.0%)	0	0 (0.0%)	0	1 (9.1%)	1
Dysphagia	0 (0.0%)	0	1 (33.3%)	1	0 (0.0%)	0	0 (0.0%)	0	1 (9.1%)	1
Lip dry	0 (0.0%)	0	0 (0.0%)	0	1 (33.3%)	1	0 (0.0%)	0	1 (9.1%)	1
Mouth ulceration	0 (0.0%)	0	1 (33.3%)	1	0 (0.0%)	0	0 (0.0%)	0	1 (9.1%)	1
Odynophagia	0 (0.0%)	0	1 (33.3%)	1	0 (0.0%)	0	0 (0.0%)	0	1 (9.1%)	1
Paraesthesia oral	0 (0.0%)	0	1 (33.3%)	1	0 (0.0%)	0	0 (0.0%)	0	1 (9.1%)	1
Salivary gland pain	0 (0.0%)	0	1 (33.3%)	1	0 (0.0%)	0	0 (0.0%)	0	1 (9.1%)	1
Tongue coated	0 (0.0%)	0	1 (33.3%)	1	0 (0.0%)	0	0 (0.0%)	0	1 (9.1%)	1
Tongue hemorrhage	0 (0.0%)	0	0 (0.0%)	0	1 (33.3%)	1	0 (0.0%)	0	1 (9.1%)	1
Investigations										
Any event	2 (66.7%)	4	0 (0.0%)	0	3 (100.0%)	5	1 (50.0%)	1	6 (54.5%)	10
Blood creatine phosphokinase increased	1 (33.3%)	1	0 (0.0%)	0	1 (33.3%)	1	1 (50.0%)	1	3 (27.3%)	3
C-reactive protein increased	1 (33.3%)	1	0 (0.0%)	0	2 (66.7%)	2	0 (0.0%)	0	3 (27.3%)	3
Aspartate aminotransferase increased	1 (33.3%)	1	0 (0.0%)	0	0 (0.0%)	0	0 (0.0%)	0	1 (9.1%)	1
Blood amylase increased	0 (0.0%)	0	0 (0.0%)	0	1 (33.3%)	1	0 (0.0%)	0	1 (9.1%)	1
RBC sedimentation rate increased	0 (0.0%)	0	0 (0.0%)	0	1 (33.3%)	1	0 (0.0%)	0	1 (9.1%)	1
Saliva analysis abnormal	1 (33.3%)	1	0 (0.0%)	0	0 (0.0%)	0	0 (0.0%)	0	1 (9.1%)	1
Respiratory, thoracic and mediastinal disorders										
Any event	2 (66.7%)	3	0 (0.0%)	0	2 (66.7%)	2	1 (50.0%)	1	5 (45.5%)	6
Oropharyngeal pain	1 (33.3%)	1	0 (0.0%)	0	1 (33.3%)	1	0 (0.0%)	0	2 (18.2%)	2
Throat irritation	1 (33.3%)	1	0 (0.0%)	0	0 (0.0%)	0	1 (50.0%)	1	2 (18.2%)	2
Dry throat	0 (0.0%)	0	0 (0.0%)	0	1 (33.3%)	1	0 (0.0%)	0	1 (9.1%)	1
Nasal dryness/congestion	1 (33.3%)	1	0 (0.0%)	0	0 (0.0%)	0	0 (0.0%)	0	1 (9.1%)	1
Infections and infestations										
Any event	0 (0.0%)	0	3 (100.0%)	3	2 (66.7%)	3	0 (0.0%)	0	5 (45.5%)	6
Candidiasis	0 (0.0%)	0	1 (33.3%)	1	0 (0.0%)	0	0 (0.0%)	0	1 (9.1%)	1
Gastroenteritis viral	0 (0.0%)	0	1 (33.3%)	1	0 (0.0%)	0	0 (0.0%)	0	1 (9.1%)	1
Nasopharyngitis	0 (0.0%)	0	1 (33.3%)	1	0 (0.0%)	0	0 (0.0%)	0	1 (9.1%)	1
Parotitis	0 (0.0%)	0	0 (0.0%)	0	1 (33.3%)	1	0 (0.0%)	0	1 (9.1%)	1
Upper respiratory tract infection	0 (0.0%)	0	0 (0.0%)	0	1 (33.3%)	1	0 (0.0%)	0	1 (9.1%)	1
Viral upper respiratory tract infection	0 (0.0%)	0	0 (0.0%)	0	1 (33.3%)	1	0 (0.0%)	0	1 (9.1%)	1
Nervous system disorders										
Any event	1 (33.3%)	2	2 (66.7%)	4	0 (0.0%)	0	0 (0.0%)	0	3 (27.3%)	6
Dizziness	1 (33.3%)	1	1 (33.3%)	1	0 (0.0%)	0	0 (0.0%)	0	2 (18.2%)	2
Disturbance in attention	1 (33.3%)	1	0 (0.0%)	0	0 (0.0%)	0	0 (0.0%)	0	1 (9.1%)	1
Dysgeusia	0 (0.0%)	0	1 (33.3%)	1	0 (0.0%)	0	0 (0.0%)	0	1 (9.1%)	1
Headache	0 (0.0%)	0	1 (33.3%)	1	0 (0.0%)	0	0 (0.0%)	0	1 (9.1%)	1
Hypoaesthesia	0 (0.0%)	0	1 (33.3%)	1	0 (0.0%)	0	0 (0.0%)	0	1 (9.1%)	1
Vascular disorders										
Any event	2 (66.7%)	2	1 (33.3%)	2	1 (33.3%)	2	0 (0.0%)	0	4 (36.4%)	6
Haematoma	1 (33.3%)	1	1 (33.3%)	1	0 (0.0%)	0	0 (0.0%)	0	2 (18.2%)	2
Hypertension	1 (33.3%)	1	0 (0.0%)	0	1 (33.3%)	1	0 (0.0%)	0	2 (18.2%)	2
Hot flush	0 (0.0%)	0	0 (0.0%)	0	1 (33.3%)	1	0 (0.0%)	0	1 (9.1%)	1
Lymphoedema	0 (0.0%)	0	1 (33.3%)	1	0 (0.0%)	0	0 (0.0%)	0	1 (9.1%)	1
Cardiac disorders										
Any event	2 (66.7%)	2	1 (33.3%)	2	0 (0.0%)	0	0 (0.0%)	0	3 (27.3%)	4
Bradycardia	1 (33.3%)	1	1 (33.3%)	1	0 (0.0%)	0	0 (0.0%)	0	2 (18.2%)	2
Left ventricular hypertrophy	0 (0.0%)	0	1 (33.3%)	1	0 (0.0%)	0	0 (0.0%)	0	1 (9.1%)	1
Tachycardia	1 (33.3%)	1	0 (0.0%)	0	0 (0.0%)	0	0 (0.0%)	0	1 (9.1%)	1
Musculoskeletal and connective tissue disorders										
Any event	1 (33.3%)	1	1 (33.3%)	1	1 (33.3%)	1	1 (50.0%)	1	4 (36.4%)	4
Back pain	1 (33.3%)	1	1 (33.3%)	1	0 (0.0%)	0	0 (0.0%)	0	2 (18.2%)	2
Muscle mass	0 (0.0%)	0	0 (0.0%)	0	0 (0.0%)	0	1 (50.0%)	1	1 (9.1%)	1
Musculoskeletal stiffness	0 (0.0%)	0	0 (0.0%)	0	1 (33.3%)	1	0 (0.0%)	0	1 (9.1%)	1

Table S1. Cont.

System organ class preferred term*	Tier 1 $n = 3$		Tier 2 $n = 3$		Tier 3 $n = 3$		Tier 4 $n = 2$		Total $n = 11$	
	# subject with AE	# of AE	# subject with AE	# of AE	# subject with AE	# of AE	# subject with AE	# of AE	# subject with AE	# of AE
Blood and lymphatic system disorders										
Any event	1 (33.3%)	1	1 (33.3%)	1	0 (0.0%)	0	0 (0.0%)	0	2 (18.2%)	2
Anemia	0 (0.0%)	0	1 (33.3%)	1	0 (0.0%)	0	0 (0.0%)	0	1 (9.1%)	1
Lymph node pain	1 (33.3%)	1	0 (0.0%)	0	0 (0.0%)	0	0 (0.0%)	0	1 (9.1%)	1
General disorders and administration site conditions										
Any event	0 (0.0%)	0	0 (0.0%)	0	1 (33.3%)	2	0 (0.0%)	0	1 (9.1%)	2
Facial pain	0 (0.0%)	0	0 (0.0%)	0	1 (33.3%)	1	0 (0.0%)	0	1 (9.1%)	1
Fatigue	0 (0.0%)	0	0 (0.0%)	0	1 (33.3%)	1	0 (0.0%)	0	1 (9.1%)	1
Injury, poisoning and procedural complications										
Any event	0 (0.0%)	0	0 (0.0%)	0	2 (66.7%)	2	0 (0.0%)	0	2 (18.2%)	2
Mouth injury	0 (0.0%)	0	0 (0.0%)	0	1 (33.3%)	1	0 (0.0%)	0	1 (9.1%)	1
Tooth fracture	0 (0.0%)	0	0 (0.0%)	0	1 (33.3%)	1	0 (0.0%)	0	1 (9.1%)	1
Metabolism and nutrition disorders										
Any event	1 (33.3%)	2	0 (0.0%)	0	0 (0.0%)	0	0 (0.0%)	0	1 (9.1%)	2
Hyperglycemia	1 (33.3%)	2	0 (0.0%)	0	0 (0.0%)	0	0 (0.0%)	0	1 (9.1%)	2
Renal and urinary disorders										
Any event	2 (66.7%)	2	0 (0.0%)	0	0 (0.0%)	0	0 (0.0%)	0	2 (18.2%)	2
Haematuria	2 (66.7%)	2	0 (0.0%)	0	0 (0.0%)	0	0 (0.0%)	0	2 (18.2%)	2
Skin and subcutaneous tissue disorders										
Any event	0 (0.0%)	0	1 (33.3%)	1	0 (0.0%)	0	0 (0.0%)	0	1 (9.1%)	1
Rash	0 (0.0%)	0	1 (33.3%)	1	0 (0.0%)	0	0 (0.0%)	0	1 (9.1%)	1

AE, adverse event.

*Subjects may experience more than one preferred term within an organ class; therefore, percentages may total >100%.

Table S2. Eligibility criteria

No. and criteria type	Description
Inclusion criteria	
1	18 y of age or older.
2	Capable of providing informed consent.
3	History of radiation therapy for head and neck cancer, having received >45 Gy to the parotid glands because of primary or neck radiation.
4	Abnormal parotid gland function in the targeted parotid gland as judged by absence of unstimulated parotid salivary flow and a stimulated parotid salivary flow in the targeted parotid gland <0.2 mL/min per gland after 2% citrate stimulation.
5	Abnormal $^{99m}TcO_4$ scintiscan (reduced or absent uptake of $^{99m}TcO_4$) for the targeted parotid gland.
6	Abnormal sialogram (an altered ductal network with sialectasis) for the targeted parotid gland.
7	No current evidence of malignancy by otolaryngology assessment, including a clinical history, nasopharyngolaryngoscopy, and negative CT or PET scan.
8	Absence of shedding wild-type adenovirus in the saliva sample collected from the targeted gland at the predose visit 1. If stimulated saliva cannot be collected at the predose visit 1, this inclusion criterion is not applicable.
9	Must be disease-free for at least 5 y, with the disease-free interval calculated from date of last cancer treatment (i.e., date of last radiation, chemotherapy or surgery) to date of predose visit 1.
10	Willingness to practice the required birth control method ("barrier" contraception, i.e., condoms, diaphragm) until AdhAQP1 is no longer detectable in their serum or saliva. Women who cannot bear children (post menopausal or because of a surgical intervention) also will be required to practice barrier birth control methods until AdhAQP1 is no longer detectable in their serum or saliva.
11	Able to stay at the NIH hospital for the period necessary to complete each on-site phase of the protocol.
12	No history of allergies to any medications or agents to be used in this protocol.
13	On stable doses of medications (≥ 2 mo from the predose visit 1) for any underlying medical conditions.
Exclusion criteria	
1	Pregnant or lactating women. Women of childbearing potential are required to have a negative serum pregnancy test at predose visit 1 and a negative urine pregnancy test within 24 h of treatment.
2	Any experimental therapy within 3 mo of planned AdhAQP1 administration (day 1).
3	Any active respiratory tract infection in the 3 wk before planned AdhAQP1 administration (day 1).
4	Active infection that requires the use of intravenous antibiotics and does not resolve at least 1 wk before planned AdhAQP1 administration.
5	Evidence of active substance or alcohol abuse or history of substance or alcohol abuse within 2 y of predose visit 1.
6	Uncontrolled ischemic heart disease: unstable angina, evidence of active ischemic heart disease on ECG, congestive heart failure (left ventricular ejection fraction < 45% on MUGA or echo) or cardiomyopathy.
7	Asthma or chronic obstructive pulmonary disease requiring regular inhaled or systemic corticosteroids.
8	Individuals taking prescription medications (anticholinergics, antidepressants) likely to result in salivary hypofunction.
9	Individuals with a history of autoimmune diseases affecting salivary glands, including Sjögren's syndrome, lupus, scleroderma, type 1 diabetes, sarcoidosis, amyloidosis, and chronic graft-versus-host disease.
10	Use of systemic immunosuppressive medications (e.g., corticosteroids). Topical corticosteroids are allowed.
11	History of a second malignancy, within the past 3 y, with the exception of adequately treated basal cell or squamous cell carcinoma of the skin or in situ carcinoma of the cervix.
12	Active hepatitis B, hepatitis C or HIV infection tested using blood collected at predose visit 1.
13	WBC <3,000/μL or ANC <1,500/μL or Hgb <10.0 g/dL or platelets <100,000/μL or absolute lymphocyte count ≤ 500/μL using blood collected at predose visit 2.
14	ALT or AST > 1.5× upper limit of normal (ULN) or alkaline phosphatase >1.5× ULN using blood collected at predose visit 2.
15	Serum creatinine > 2 mg/dL using blood collected at predose visit 2.
16	Individuals who are active smokers.
17	Individuals who consume more than one alcoholic beverage per day.
18	Individuals who have an allergy to iodine or shellfish.
19	Individuals whose targeted parotid duct is not clinically accessible on screening sialography evaluations.
20	Individuals who on sialography have a distal stenosis in the targeted parotid gland that would impede vector delivery.
21	Individuals who likely would require use of a general anesthetic for ultrasound-guided core needle biopsy.
22	Significant concurrent or recently diagnosed (<2 mo from day 1) medical condition that, in the opinion of the Medically Responsible Investigator, could affect the participant's ability to tolerate or complete the study.
23	Live vaccines within 4 wk of first infusion.
24	Previous participation in a rAd5 vector gene transfer study.

Per protocol, this table contains a complete listing of all inclusion and exclusion criteria. A somewhat condensed version of this information was previously reported in chapter 5.9 of Sreebny and Vissink (1).

1. Sreebny LM, Vissink A eds. (2010) *Dry Mouth The Malevolent Symptom: A Clinical Guide* (Wiley-Blackwell, Ames, IA), pp 211–219.